S. HRG. 107–499

STEM CELLS, 2001

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS
UNITED STATES SENATE

ONE HUNDRED SEVENTH CONGRESS

FIRST SESSION

SPECIAL HEARINGS

JULY 18, 2001—WASHINGTON, DC
AUGUST 1, 2001—WASHINGTON, DC
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TUESDAY, JULY 18, 2001

WEDNESDAY, AUGUST 1, 2001

STEM CELLS

TUESDAY, JULY 18, 2001

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 9:41 a.m., in room SH–216, Hart Senate Office Building, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin, Murray, Landrieu, Specter, Cochran, Hutchison, and DeWine.

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. The Appropriations Subcommittee on Labor, Health and Human Services, and Education will come to order. This hearing of the Appropriations subcommittee will now proceed.

In November 1998 the country learned that Dr. James Thomson and John Gearhart had isolated pluripotent stem cells from early human embryos and grown them in a culture. It marked a significant achievement in science and a new hope for a cure to many of the most cruel and debilitating diseases. One month later this subcommittee promptly held its first hearing on stem cells research and learned of the enormous potential this research had for the treatment of diseases like Parkinson's and Alzheimer's, ALS, Lou Gehrig's Disease, heart disease, and other diseases.

Since then this committee has held six more hearings on this important subject, chaired by my good friend and then chairman Senator Arlen Specter. Today it is my turn, but the purpose will be the same. Senator Specter and I have been partners for a long time in our efforts to increase funding for medical research and in particular for stem cell research in particular.

I have co-sponsored with Senator Specter a bill that would allow federally funded scientists to derive human stem cells from embryos under four conditions: first, the embryos must be obtained from an in vitro fertilization clinic; second, the donors must have provided informed consent; third, the embryo must no longer be needed for infertility treatments; and fourth, there can be no payment to the donors.

The American Society of Cell Biology has estimated that about 100,000 human embryos are currently frozen in IVF clinics in excess of their clinical need.

Let me be clear about why we are here and why we have introduced our bill and why we fought so hard to make sure that the Federal Government supports this research. We introduced this

legislation because we want to save lives and we want to find cures for some of the most debilitating diseases that affect mankind. We have seen the human faces of these diseases. We have been moved by the testimony of doctors and patients, family members and advocates that have been touched by juvenile diabetes, Parkinson's, ALS, Alzheimer's. I particularly remember the poignant testimony of Mr. John Wagenaar from George, Iowa, who is suffering from Alzheimer's.

That is really why we are here. This is not an abstract issue. It is about saving the lives of millions of human beings. I believe it is imperative that the Federal Government support this research. The government has an important role to play in basic science and basic science will always be underfunded by the private sector because this type of research does not immediately get products onto the market. There is no immediate profit, but there are tremendous long-term benefits. That is why the Federal Government has been involved in supporting basic research.

Equally important are the strict ethical guidelines that will come with Federal funding. It is important to note that stem cell research in the private sector is not subject to Federal monitoring and these guidelines.

This morning Dr. Lana Skirboll with the National Institutes of Health will release the NIH report which reviews the current state of the science of stem cell research. We received a copy of that report yesterday and it is clear when you read the report that stem cell research holds promise in the treatment of diseases.

Some say that stem cell research is fine as long as you use just adult cells. I disagree. The NIH's report is clear on this important point. Embryonic and adult stem cells are different and both present immense research opportunities for potential therapies. I think it would be irresponsible to wait for years to determine the potential of adult stem cells before studying the benefits of embryonic stem cells.

There are still a lot of unanswered questions. For example, are there enough existing stem cells to do the research that needs to be done, and what are the differences between adult and embryonic stem cells? At this hearing we will try to get some of the answers to those questions.

We have a distinguished panel of experts before us today. I especially want to thank Dr. Mary Hendrix of the University of Iowa. Dr. Hendrix has been invaluable to my staff and me as she has patiently answered our questions about the science of stem cells.

At many points in our history religion and science have intersected, and at every point we have paused to measure our morality and the ancient lessons of religion against our science and the new frontiers we explore, as well we should do that. Science must be infused with morality and humanity. When it is not, it can be more about amusing ourselves with our own ingenuity than pursuing real scientific breakthroughs that improve our lives.

PREPARED STATEMENT

In the case of stem cell research, I strongly believe that we have measured the question carefully and that it is time to move forward. Where there cannot be new life, there can be new hope, new

hope for thousands of Americans suffering from horrible and debilitating disease that withers the mind and the body and robs us of our loved ones. In the case of stem cell research, we can be true and loyal to our loved ones and true and loyal to our values. In fact, it would be an affront to our values if we did not proceed with caution and under ethical guidelines and investigate how stem cell research can better our lives and the lives of all people.

[The statement follows:]

PREPARED STATEMENT OF SENATOR TOM HARKIN

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I have co-sponsored with Senator Specter a bill that would allow federally-funded scientists to derive human stem cells from embryos under three conditions: the embryos must be obtained from an IVF clinic; the donor must have provided informed consent; and the embryo must no longer be needed for infertility treatments. The American Society of Cell Biology has estimated that 100,000 human embryos are currently frozen in IVF clinics, in excess of their clinical need.

Let me be clear about why we are here, why we have introduced our bill, and why we have fought so hard to make sure that the Federal government supports this research.

We introduced this legislation because we want to save lives and to find cures for some of the most debilitating diseases that affect mankind. We have seen the faces of human face of these diseases. We have been moved by the testimony of doctors, patients, family members and advocates that have been touched by Juvenile Diabetes, Parkinson's, ALS and Alzheimer's. I particularly remember the poignant testimony of Mr. John Wagenaar, from George, Iowa who is suffering form Alzheimer's. That is why we are here. This is not an abstract issue. It is about saving the lives of millions of Americans.

It is imperative that the Federal government support this research. The government has an important role to play in supporting basic science. Basic science will always be underfunded by the private sector because this type of research does not immediately get products onto the market. There is no immediate profit—but there are tremendous longterm benefits.

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There are still a lot of unanswered questions. For example, are there enough existing stem cell lines to do the research that needs to be done and what are the differences between adult and embryonic stems cells. At this hearing we will try to get some of the answers to those questions. We have a distinguished panel of experts before us today; I want to especially welcome Dr. Mary Hendrix, of the University of Iowa. Dr. Hendrix has been invaluable to my staff and me as she has patiently answered our questions about the science of stem cells.

At many points in our history, religion and science have intersected. And at every point, we have paused to measure our morality and the ancient lessons of religion against our science and the new frontiers we explore. As well we should.

Science must be infused with our morality and humanity. When it is not, it can be more about amusing ourselves with our own ingenuity than pursuing real scientific breakthroughs that improve our lives.

In the case of stem cell research, I strongly believe that we have measured the question carefully, and that it is time to move forward. Where there cannot be new life, there can be new hope—new hope for the thousands of Americans suffering from horrible and debilitating disease that withers the mind and body and robs us of our loved ones. In the case of stem cell research, we can be true to our loved ones and true to our values. In fact, it would an affront to our values if we did not proceed, with caution, and investigate how stem cell research can better our lives and the lives of all Americans.

I look forward to hearing from a number of Senate colleagues on this important issue. I want to welcome Senator Hatch, Senator Frist, Senator Smith and Senator Brownback who are taking time out of their busy schedules to testify before us this morning. But before we turn to their testimony, I yield to my friend and colleague, Senator Specter, for his opening remarks.

Senator HARKIN. I look forward to hearing from a number of our Senate colleagues who are here today on this important issue. I want to welcome Senator Hatch, Senator Frist, Senator Smith, Senator Brownback, who are taking time out of their busy schedules to testify before us this morning.

Before I turn to them, I would yield to my friend and one of our great leaders on basic scientific research, Senator Specter.

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Thank you very much, Mr. Chairman. I thank you for your leadership and your work on this very important subject, as well as your work on increasing NIH funding. As you have outlined, when the stem cell issue became public in November 1998 this subcommittee immediately started a series of hearings. This is our eighth hearing, which is a very substantial number, and as these hearings have progressed and as the public has become better acquainted with the potential for stem cells for curing Parkinson's, delaying Alzheimer's, spinal cord injury, important on cancer, on heart ailments, and virtually all of the other maladies confronting the human race, there has been a groundswell of support for stem cell research. I think it is now an avalanche.

I have talked to many, many of our colleagues in the Senate, and I had said last week that I thought there were 70 votes in favor of stem cell research and now I believe it is in excess of 75. I thank our colleagues for coming here today. Senator Hatch, he is a very strong pro-life Senator who has gone into the lion's den in taking a stand in favor of stem cell research, and his testimony, which we will hear, is very, very important.

Senator Frist—and not all of us agree on all aspects of this matter—is our doctor in residence. Senator Brownback has been candid in his opposition and we have debated this subject and doubtless will continue to do so.

Senator Gordon Smith I think capsulated the matter. I quote him frequently. It may not be a good idea to quote him in his presence. He will speak for himself. But when he made the distinction between an embryo in the womb of a woman, where life eventuates, contrasted with an embryo in a laboratory dish, it is hard to top

that kind of a presentation or rationale for no funding stem cell research.

There is one matter that I feel constrained to comment upon, and that is the difficulty of this subcommittee in getting the unvarnished facts from the Department of Health and Human Services. In advance of our appropriation hearing with the National Institutes of Health, Senator Harkin and I wrote to the NIH Institute directors asking for their evaluation of stem cell research. There is no better time to get information than when a Federal agency is applying for an appropriation. That is a superb time to get information.

But I am very distressed to have to report—and I have taken this up personally with the Secretary of Health and Human Services—that of the 15 letters which were submitted there were 21 deletions in 10 of the letters. I am going to put all of the deletions into the record because they are too long to go into at this time. But a couple are illustrative.

[The information follows:]

A total of 21 deletions were made in 10 of the 15 letters submitted to the Subcommittee by the Department. The deletions relate mainly to four issues:

—How a ban on Federal funding for stem cell research would affect current and future research.

—The advantages of embryonic stem cells over adult stem cells, and the need to compare the two.

—Discussion of embryonic stem cell research in the private sector.

—Concluding statements regarding the potential of embryonic stem cells.

A summary of the deletions are as follows:

How would a ban on Federal funding for stem cell research affect current and future research?

"While many questions remain unanswered, the opportunities that would be lost, if there were a lack of NIH support, would be greater and devastating to this realm of research. This research offers tremendous opportunity to restore lost sensory function, including the regeneration of lost hair cells, as well as develop future therapeutic strategies important to every known human disease, including severe neurological disorders such as Alzheimer's and Parkinson's disease. It would be unfortunate if the ban on NIH support for human stem cell research results in a missed opportunity to restore hope and quality of life to affected individuals."——James Battey, Jr., M.D., Ph.D., National Institute on Deafness and Other Communication Diseases

"A ban on funding for stem cell research would affect the National Institute of Dental and Craniofacial Research's ability to progress toward developing innovative solutions to complex conditions and diseases. Although research with adult stem cells has contributed to significant research advances, it has yet to be established that adult stem cells are as versatile as those derived from embryonic tissue. Thus a ban on embryonic stem cell research will limit our ability to understand the full potential of this therapeutic modality to treat the many complex conditions and diseases of interest to NIDCR."——Lawrence Tabak, D.D.S., Ph.D., National Institute of Dental and Craniofacial Research

"The ban on Federal Stem cell research would likely limit the use of this important research tool to non-federally funded projects, including those within the private sector and other countries."——Jack McLaughlin, Ph.D., National Eye Institute

"A Federal ban on human stem cell research is likely to hurt current and future research in at least two ways. First, we believe that a ban on this research would produce a chilling effect that would result in a decreased number of research grant applications on embryonic stem cells of animals, such as mice, in which most of the embryonic stem cell work has been done. . . . Although, it is difficult to prove cause and effect, the ban on human embryo research is likely to be the reason that we currently receive a very small number of applications per year on embryo research in mice and other animals. . . . Second, a Federal ban on human embryonic stem cell research would mean that research on this topic in the United States will be conducted in private laboratories without scientific and ethical oversight. . . . It also would be subject to public monitoring for compliance with ethical guidelines.

In essence, Federal funding of this important research would open it to public scrutiny."——Duane Alexander, M.D., National Institute of Child Health & Human Development

The advantages of embryonic stem cells over adult stem cells, and the need to be able to compare the two.

"It is known that embryonic stem cells have vast potential to develop into tissues of any type, while only a small number of studies have indicated a possible limited potential for adult stem cells." . . . "It is not known how long adult stem cells will survive and function, while embryonic stem cells do not have this limitation." . . . "The use of adult stem cells for cell therapy at this time, without knowing how much better embryonic stem cells would perform, is considered by many researchers to be premature." . . . "If embryonic stem cells are not used, optimal therapies may not be developed."——Allen Spiegel, M.D., National Institute of Diabetes and Digestive and Kidney Diseases

"Not knowing whether adult or embryonic stem cells will ultimately prove to be of value makes it important that research proceed using both types of stem cells."——Claude Lenfant, M.D., National Heart, Lung, and Blood Institute

"In cancer patients, normal tissues can be damaged by both the disease and by the treatment (surgery, radiation, and chemotherapy). We already know that embryonic stem cells have all the characteristics that would be needed for regenerating healthy tissues but there is no way to establish the relative potential of embryonic stem cells to adult stem cells unless we can compare the two."——Richard Klausner, M.D., National Cancer Institute

Discussion of embryonic stem cell research in the private sector.

"Researchers funded by the private sector have also reported progress with respect to the application of stem cell research to liver disease. It has been reported that scientists at Geron in California have coaxed their embryonic stem cell lines to produce 'liver-like' cell. . . . It may well be that there are other such studies supported by private industry, which are not being reported in the published literature and of which we are therefore unaware."——Allen Spiegel, M.D., National Institute of Diabetes and Digestive and Kidney Diseases

Concluding statements regarding the potential of embryonic stem cells.

"I share with my colleagues in the other Institutes enthusiasm for the great promise that stem cells hold for the treatment of disease, and NIGMS intends to continue its support for research into the fundamental genetic and cellular mechanisms that underlie this promise."——Marvin Cassman, Ph.D., National Institute of General Medical Sciences

"Continuous stem cell research is critical to cancer research, based on the knowledge that cancer cells often have certain stem cell properties, in particular their arrest in development and the ability to renew themselves."——Richard Klausner, M.D., National Cancer Institute

"I would like to conclude by stating that embryonic stem cells are truly remarkable cells. We are on our way to understanding how they form and how they can be used for the treatment of human diseases and disorders. The evidence we have at present indicates that they have enormous potential in this regard."——Duane Alexander, M.D., National Institute of Child Health & Human Development

"Research on human stem cells offers the greatest potential in the eons of modern human history for mankind to experience a major breakthrough in the medical treatment or cure of a wide-range of devastating human diseases and disorders. . . A ban of Federal funding for stem cell research would deprive the American public of the benefits of 100 years of scientific research and 20 years of progressive stem cell research—the vast majority of which was paid for by Federal funds from the American public as an investment in health care research."——Kenneth Olden, Ph.D., National Institute of Environmental Health Sciences

LETTER FROM SENATORS TOM HARKIN AND ARLEN SPECTER

U.S. SENATE,
Washington, DC, June 29, 2001.

Hon. TOMMY THOMPSON,
Secretary, Department of Health and Human Services,
Washington, DC.

DEAR MR. SECRETARY: We were surprised to read in the June 26, 2001, New York Times, an article written by Robert Pear, detailing the recently completed Stem Cell Research Study conducted by the National Institutes of Health.

It is particularly troubling that several requests made by our respective staff to obtain a copy of the report, titled "Stem Cells: Scientific Progress and Future Research Directions," were denied.

Given our great interest in stem cell research, we request that the Department immediately provide us with a copy of the study for our review.

Thank you for your attention to this matter.

Sincerely,

TOM HARKIN,
Chairman.

ARLEN SPECTER,
Ranking Republican Member.

LETTER FROM SENATOR ARLEN SPECTER

U.S. SENATE,
Washington, DC, July 11, 2001.

Hon. TOMMY THOMPSON,
Secretary, Department of Health and Human Services,
Washington, DC.

DEAR SECRETARY THOMPSON: I want you to know that I am very displeased with your decision not to turn over a copy of the report, "Stem Cells: Scientific Progress and Future Research Directions".

It is my view that our Subcommittee, or, at a minimum, the Chairman and Ranking Member, have an absolute right to that stem cell report.

It is insufficient for me to be limited to having my staffer go to your office to read the report. I want to read it myself and I cannot reasonably come to your Department to read it.

I also want you to know that I am displeased with the censoring by your Department of the responses by the NIH Institute Directors in answer to my May 4, 2001 letter posing specific questions regarding stem cell research. Those full letters should have been transmitted to the Subcommittee promptly and we should not have had the delays or the necessity to push you for these letters.

Sincerely,

ARLEN SPECTER.

LETTER FROM SENATOR ARLEN SPECTER

U.S. SENATE,
Washington, DC, July 17, 2001.

Hon. TOMMY THOMPSON,
Secretary, Department of Health and Human Services,
Washington, DC.

DEAR SECRETARY THOMPSON: At 9:45 a.m. this morning, I finally received a copy of the 202 page report entitled "Stem Cells: Scientific Progress and Future Research Directions".

As you know, the Appropriations Subcommittee covering your Department has a stem cell hearing tomorrow morning at 9:30 a.m. I consider the response by you and your Department to my letter of July 11, 2001 and the late availability of this report to be absolutely insulting.

Since I am advised that you have declined the Subcommittee's request to testify tomorrow, I am writing to give you advance notice, in the event you wish to make

some response, that I intend to comment on your Department's conduct and to put this letter and my letter of July 11, 2001 in the record.

Sincerely,

ARLEN SPECTER.

LETTER FROM TOMMY G. THOMPSON

THE SECRETARY OF HEALTH AND HUMAN SERVICES,
Washington, DC, July 17, 2001.

Hon. ARLEN SPECTER,
U.S. Senate,
Washington, DC.

DEAR SENATOR SPECTER: I received your letter this afternoon and felt it was important to respond to you as quickly as possible. I take concerns about the responsiveness of the Department of Health and Human Services very seriously, which is why we are undertaking a variety of management reforms. I also can appreciate how passionately you feel about the issue of stem cell research. It is an important scientific, issue and the media frenzy surrounding it has only served to intensify an enormously emotional debate.

However, I feel it is important to clarify some matters regarding the hearing being held by the Labor-HHS Appropriations subcommittee tomorrow, and the report prepared by NIH: "Stem Cells: Scientific Progress and Future Research Directions."

When you originally approached us about both my participation in the hearing and obtaining copies of the report, we made what accommodations we could. As you may know, I have spent a several days each month working from the various operating divisions of this department. My intent is to learn as much as possible so that I can most effectively run this Department. Before receiving your invitation, I had committed to work from the Food and Drug Administration this week. My staff did work, however, to ensure you would have a representative of this Department to appear before the committee.

The report that we sent to your committee this morning was developed at my request. I asked NIH to provide me with a review of the available science so that I am as well versed and understand this issue as well as possible. The undertaking was enormous. The scientists at NIH reviewed more than 1,200 documents and spoke to more than 50 scientists.

The report was not finalized until a few hours before I sent it to you. In fact, they worked throughout the weekend to endure it would be available to you and your committee before the hearing tomorrow. In addition, we allowed members of your staff to review a draft version of this report—before the scientists were ready to consider it final.

As you know, I try to make myself available to personally address concerns about this Department. I sincerely hope that you and I can work together on this and other issues going forward.

Sincerely,

TOMMY G. THOMPSON.

Senator SPECTER. Dr. Richard Klausner, the head of the National Cancer Institute: "Continuous stem cell research is critical to cancer research." Not given to this subcommittee until we had to extract it like a bicuspid from the Department of Health and Human Services.

Dr. James Batty [commented]. "Opportunities would be lost if there were a lack of NIH support. It would be devastating in this realm of research."

Dr. Dwayne Alexander. "A ban on this research would produce a chilling effect that would result in a decreased number of research grant applications."

Now, we may not agree with the administration, but Congress has a right to the facts and we ought not to be getting censored information.

Then there is the issue of the report. I read about the report in the New York Times on June 27—I like to get my information from

the Secretary, not the New York Times—and immediately wrote to the Secretary thereafter requesting the report. I could not get a copy of the report. Finally our staff had to go to the offices of HHS on the afternoon of July 3 and read it over there, no copies, no copies available to the subcommittee. Two of our staffers, Senator Harkin's and mine, had to share one report, after a long wait.

So I wrote to the Secretary last week on July 11 and said, I would like a copy of the report, I would like to prepare for this hearing. Yesterday morning at 9:45 I got a copy of this 202-page report. I am not too slow at reading, but that is just not right.

Yesterday afternoon I got a copy—I wrote to the Secretary again and I am going to make copies for the record my letters of June 29, 2001, July 11, July 17, and Secretary Thompson's reply to me yesterday. But the Secretary does not deal with the censorship issue. He is going to have to deal with that yet. He said that we got a copy of the report just as soon as it was finalized.

But I am told that, except for a few editorial changes and printing, this report was available last week and really the week before. I intend to get to the bottom of it. The Secretary and the administration do not have to agree with us, but they cannot keep the facts from us. I am not unmindful of the consideration that there may be some in the administration who are in disagreement with Secretary Thompson's personal views and that he may be under substantial pressure. But we have a constitutional government in America and we have status in the Congress to find out the facts and to make our judgments.

I am hopeful we can work it out in a collegial way with the administration. But if we cannot, we are going to get to the bottom as to why we did not get this report in a timely way, why these facts were censored, and it is a matter for congressional consideration. The Congress still establishes public policy in the United States, subject to the President's concurrence or congressional override. We intend to pursue it.

Thank you, Mr. Chairman.

Senator HARKIN. Thank you, Senator Specter.

Senator Murray.

OPENING STATEMENT OF SENATOR PATTY MURRAY

Senator MURRAY. Thank you very much, Mr. Chairman, for holding this very important hearing. I think stem cell research offers a lot of hope for millions of patients and I really appreciate you and Senator Specter for your work to implement the NIH guidelines that support embryonic stem cell research, and I am proud to be a co-sponsor of the legislation that you have introduced to codify those guidelines.

Mr. Chairman, delaying NIH support for stem cell research is going to delay hope for millions of patients struggling with diseases like MS, Parkinson's, diabetes, cancer, ALS, and spinal cord injuries. My father was diagnosed with multiple sclerosis when I was 15 years old. I lived with a family member with MS until he died a few years ago. I know the devastating impacts, the pain, the suffering, the agony, for the patient and the family, and the thought that there is going to be progress out there that could be stymied by action here in Washington, DC, to me is really frightening.

I know how important this research is and how important it is that we can say to families in the future that they will not have to live with what my father lived with, to say to patients like my father that they would not have to live with this because we have research that can improve their lives, I think is extremely important.

This is not about abortion. Stem cells are not a result of abortions. It is not about destroying life. It is about improving life and in many cases saving lives. Federal support of stem cell research does not legitimize abortion. It does not reduce the value of all human life. But it does give us a promising new avenue for research that I believe could save many lives.

I do think we need to set some standards to guide this research and I believe the standards that have been developed by NIH are appropriate. I know that the former Administrator of NIH, Dr. Varmas, conducted an exhaustive process to develop the guidelines for support of stem cell research. Bioethical standards were high and every effort was made to separate the issue of abortion from the debate. NIH-supported research will ensure that these bioethical standards are followed.

Mr. Chairman, without Federal guidelines the private sector will determine the direction of research and the ethical standards that are employed. I think this is an opportunity for us to help advance the science that millions of patients are waiting on. We should be taking a strong leadership role in this new exciting technology.

My own State of Washington is where there are a lot of promising research institutes that are working on this: Fred Hutchinson Cancer Research, University of Washington. I have listened to the researchers, I have listened to the patients and families from across my State, and hundreds of them have contacted me to urge me to support embryonic stem cell research.

So I want to thank all of the witnesses who have come here today to share their views and their concerns and to let you know that your testimony will help us implement sound research guidelines for NIH.

So Mr. Chairman, again I thank you for your strong work on this, for your continued work on this, and I look forward to working with you.

Senator HARKIN. Thank you very much, Senator Murray.

Senator DeWine.

Senator DEWINE. I have no comment, no opening statement.

Senator HARKIN. Thank you very much.

Senator DEWINE. I thank you for holding the hearing.

Senator HARKIN. Thank you, Senator DeWine.

Now we turn to our distinguished group of Senators who are here today. We will go in order of seniority. Thus I would like to first recognize my good friend Senator Orrin Hatch of Utah, first elected to the Senator in 1976, ranking member on the Senate Judiciary Committee and member of the Finance, Intelligence, Indian Affairs, and Joint Economic Committees. Senator Hatch received his B.S. from Brigham Young University and his law degree from the University of Pittsburgh.

Then I will go in order of Senator Hatch and then Senator Frist and Senator Brownback and Senator Smith. Senator Hatch, welcome to the committee. The floor is yours. Proceed as you so desire.

STATEMENT OF HON. ORRIN G. HATCH, U.S. SENATOR FROM UTAH

Senator HATCH. Well, thank you, Mr. Chairman. I thank you and Senator Specter for inviting me to testify today.

As a long-time supporter of biomedical research, I applaud the bipartisan leadership this committee has demonstrated in working toward the goal of doubling the NIH research budget by 2003. This investment in biomedical research is helping to usher in a new age of science in which the mysteries of human health and disease are unraveled.

Today's hearing centers on a major opportunity presented to the biomedical research community, stem cell research. Nobel laureate and former NIH Director Harold Varmas has characterized the situation by saying that "It is not unrealistic to say that stem cell research has the potential to revolutionize the practice of medicine."

I would like to take this opportunity to share with you how I came to my decision to support Federal funding for embryonic stem cell research. Over many months I devoted hours of study to this important issue, reflecting on my spiritual teachings, the law, the science, and the ethical issues presented by embryonic stem cell research. Let me be absolutely clear. I hold strong pro-life, pro-family values and strongly oppose abortion.

I conclude that support of embryonic stem cell research is consistent with and advances pro-life and pro-family values.

Let me emphasize four points for you this morning. First, I think that the support of this vital research is a pro-life, pro-family position. This research holds out promise for more than 100 million Americans suffering from a variety of diseases, including heart disease, multiple sclerosis, Parkinson's, Alzheimer's, ALS, cancer, and diabetes.

Second, in the in vitro fertilization process it is inevitable that extra embryos are created, embryos that simply will not be implanted in a mother's womb. As these embryos sit frozen in a test tube outside the womb, under today's technology there is no chance for any of them to develop into a person. While I have no objection to considering ways to foster adoption of embryos, there are a host of issues associated with this which must be worked out.

While these issues are being considered, the reality today is that each year thousands, and I am told the number may be tens of thousands, of embryos are routinely destroyed. Why should not these embryos slated for destruction be used for the good of mankind?

Third, while I understand that many in the pro-life community will disagree with me, I believe that a human life, a human's life, begins in the womb, not in a petri dish or a refrigerator. It is inevitable that in the IVF process extra embryos are created that will simply not be implanted in a mother's womb. To me the morality of the situation dictates that these embryos, which are routinely discarded, be used to improve and extend and facilitate life. The tragedy would be in not using these embryos to save lives when the alternative is that they would be destroyed.

Fourth, there is no guarantee that any stem cell research will reap the benefits we hope, but it is clear that embryonic stem cell research holds tremendous promise. Some hold out adult stem cell research as a good alternative. By all means we should continue adult stem cell research, but I do not believe it would be wise to cut off support for embryonic stem cell since many eminent scientists believe it is the more promising avenue of research.

The committee will hear from scientific experts this morning. You will hear from NIH about the report, this very comprehensive report on stem cell research that the agency will formally issue today. While I am not a scientist, my preliminary reading of the report strongly suggests that embryonic stem cell research may have some substantial advantages over adult stem cells, at least at this stage of the research.

Consider the following excerpts from the summary of the new NIH stem cell report: "Stem cells in adult tissues do not appear to have the same capacity to differentiate as do embryonic stem cells or embryonic germ cells." Consider this next statement: "Human embryonic stem cells can be generated in abundant quantities in the laboratory and can be grown, that is allowed to proliferate, in the undifferentiated or unspecialized state for many, many generations."

Then this last one: "Researchers have had difficulty finding laboratory conditions under which some adult stem cells can proliferate without becoming specialized." Finally: "Current evidence indicates that the capability of adult stem cells to give rise to many different specialized cell types is more limited than that of embryonic stem cells."

However, it is also important to note what the NIH report does not say. It does not say that the promise of embryonic stem cell research obviates the need to pursue adult stem cell research. The report indicates that both embryonic and adult stem cell research holds great promise, and I believe that both avenues should be zealously pursued.

In the end, it is my hope that we are able to conduct research that will improve and prolong human life. I truly believe that the cures for diseases like diabetes, Parkinson's, Alzheimer's, ALS, cancer, multiple sclerosis, heart disease, et cetera, can be found if we continue this promising research. That is why we must take advantage of all ethical and promising types of research.

Before I close, I would like to comment on the work of the Jones Institute for Reproductive Medicine in Norfolk, Virginia, which is creating embryos in order to conduct stem cell research. I find the work of this clinic extremely troubling. To me this type of research is indicative of the problems we will continue to encounter if we do not allow Federal funding with strict research guidelines for embryonic stem cell research.

As this case illustrates, without stringent NIH ethical requirements, we are opening the door to an array of different research standards, which I believe could create some very serious consequences.

Mr. Chairman, today we stand on the threshold of a great opportunity. Embryonic stem cell research may be the single most important scientific discovery in all of our lifetimes. The most renowned

scientists in the country have told us that this research holds forth the promise of treatments and perhaps cures for some of the most debilitating diseases affecting our entire Nation and the world.

PREPARED STATEMENT

I think it would be a mistake to cut off Federal support for this research.

I appreciate the opportunity to testify before your subcommittee and would be happy to answer any questions from members of the subcommittee, and I am sorry I went over just a little bit.

[The statement follows:]

PREPARED STATEMENT OF SENATOR ORRIN G. HATCH

Mr. Chairman, thank you and Senator Specter for inviting me to testify today.

As a long time supporter of biomedical research, I applaud the bipartisan leadership this Subcommittee has demonstrated in working toward the goal of doubling the NIH research budget by 2003. This investment in biomedical research is helping to usher in a new age of science in which the mysteries of human health and disease are unraveled.

Today's hearing centers on a major opportunity presented to the biomedical research community: stem cell research. As Nobel laureate and former NIH Director, Harold Varmus, has characterized the situation by saying that, it is not unrealistic to say that [stem cell research] has the potential to revolutionize the practice of medicine.

I would like to take this opportunity to share with you how I came to my decision to support federal funding for embryonic stem cell research.

Over many months, I devoted hours of study to this important issue, reflecting on my spiritual teachings, the law, the science, and the ethical issues presented by embryonic stem cell research.

And let me be absolutely clear: I hold strong pro-life, pro-family values and strongly oppose abortion. I conclude that support of embryonic stem cell research is consistent with and advances pro-life and pro-family values.

I would like to submit for the record copies of my letters to President Bush and Secretary Thompson in which I give my views on this issue.

And I would also like to submit for the record a statement by former Secretary of Health and Human Services, Dr. Louis Sullivan in which he gives his support for embryonic stem cell research.

Let me emphasize four points for you this morning.

First, I think that support of this vital research is a pro-life, pro-family position. This research holds out promise for more than 100 million Americans suffering from a variety of diseases including heart disease, multiple sclerosis, Parkinson's, Alzheimer's, ALS, cancer, and diabetes.

Second, in the *in vitro* fertilization process, it is inevitable that extra embryos are created, embryos that simply will not be implanted in a mother's womb. As these embryos sit frozen in a test tube, outside the womb, under today's technology, there is no chance for them to develop into a person.

While I have no objection to considering ways to foster adoption of embryos, there are a host of issues associated with this which must be worked out. And while those issues are being considered, the reality today is that each year thousands and I am told the number may be tens of thousands—of embryos are routinely destroyed. Why shouldn't these embryos slated for destruction be used for the good of mankind?

Third, while I understand that many in the pro-life community will disagree with me, I believe that a human's life begins in the womb, not in a petri dish or refrigerator.

It is inevitable that in the IVF process, extra embryos are created that will simply not be implanted in a mother's womb. To me, the morality of the situation dictates that these embryos, which are routinely discarded, be used to improve and extend life. The tragedy would be in not using these embryos to save lives when the alternative is that they will be destroyed.

Fourth, there is no guarantee that any stem cell research will reap the benefits we hope, but it is clear that embryonic stem cell research holds tremendous promise. Some hold out adult stem cell research as a good alternative. By all means, we should continue adult stem cell research. But, I do not believe it would be wise to

cut off support for embryonic stem cell research, since many eminent scientists believe it is the more promising avenue of research.

The Committee will hear from scientific experts this morning. You will hear from NIH about the report on stem cell research that the agency will formally issue today.

While I am not a scientist, my preliminary reading of the report strongly suggests that embryonic stem cell research may have some substantial advantages over adult stem cells at least at this stage of the research.

Consider the following excerpts from the summary of the new NIH Stem Cell Report:

"Stem cells in adult tissues do not appear to have the same capacity to differentiate as do embryonic stem cells or embryonic germ cells."

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"Human embryonic stem cells can be generated in abundant quantities in the laboratory and can be grown (allowed to proliferate) in their undifferentiated (or unspecified state for many generations."

* * * * * * *

". . . researchers have had difficulty finding laboratory conditions under which some adult stem cells can proliferate without becoming specialized."

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"Current evidence indicates that the capability of adult stem cells to give rise to many different specialized cell types is more limited than that of embryonic stem cells."

However, it is also important to note what the NIH report does not say. It does not say that the promise of embryonic stem cell research obviates the need to pursue adult stem cell research. The report indicates that both embryonic and adult stem cell research hold great promise. I believe that both avenues should be zealously pursued.

In the end, it is my hope that we are able to conduct research that will improve and prolong human life. I truly believe that cures for diseases like diabetes, Parkinson's, Alzheimer's, ALS, diabetes, multiple sclerosis, heart disease and cancer can be found if we continue with this research. That's why we must take advantage of all ethical and promising types of research.

Before I close, I'd like to comment on the work of the Jones Institute for Reproductive Medicine in Norfolk, Virginia, which is creating embryos in order to conduct stem cell research. I find the work of the clinic extremely troubling.

To me, this type of research is indicative of the problems we will continue to encounter if we don't allow federal funding with strict research guidelines for embryonic stem cell research. As this case illustrates, without stringent, NIH ethical requirements, we are opening the door to an array of different research standards, which I believe could create some serious consequences.

Mr. Chairman, today we stand on the threshold of a great opportunity. Embryonic stem cell research may be the single, most important scientific discovery in our lifetimes. The most renowned scientists in the country have told us that this research holds forth the promise of treatments and perhaps cures for some of the most debilitating diseases affecting our nation, and the world. I think it would be a mistake to cut off federal support for this research.

I appreciate the opportunity to testify before your Subcommittee and would be happy to answer any questions from members of the Subcommittee.

Senator HARKIN. Shut those lights off anyway. Do not pay any attention to those lights.

Thank you very much, Senator Hatch. I do not know what your time frame is, but I would like to have all the Senators testify.

Senator HATCH. I do need to go to Judiciary, but I will be glad to wait.

Senator HARKIN. I would appreciate that.

Next we turn to Senator Bill Frist of Tennessee, elected to the Senate in 1994, who is the only physician serving in the U.S. Senate. He serves on Budget, Foreign Relations, and Health, Education, Labor, and Pensions Committees, received his under-

graduate degree from Princeton University and his M.D. from Harvard Medical School.

Senator Frist, please proceed as you so desire.

STATEMENT OF HON. BILL FRIST, U.S. SENATOR FROM TENNESSEE

Senator FRIST. Thank you, Mr. Chairman. I want to thank both you and Senator Specter for the opportunity to share my views on what is a very challenging moral, ethical, and policy issue that is before us today and over the coming weeks.

Mr. Chairman, it is easiest for me to make four points, but all four of these points stem from my personal experience of spending about 20 years in the field of training and practicing medicine, and before coming to the U.S. Senate the most significant aspect of my professional practice was the transplantation or transfer of living tissue from one individual to another on a daily basis, and on a nightly basis I dealt with issues surrounding life and death and health, obtaining informed consent in order to transfer tissues from an individual in many ways otherwise healthy to another, to the benefit of other people.

Four points I would like to make:

No. 1, I too am pro-life, oppose abortion, and in terms of my voting and policy record here in the U.S. Senate it is very consistent or 100 percent consistent with that position. I mention that philosophy because in every one of our cases we are going to come back and what we ultimately decide is going to be colored on our own spiritual beliefs, on our own moral beliefs, on the experience we have had. Mine happens to have been in the field of medicine and of science, where I spent these 20 years.

Again just so people will understand, because it does color my views, there is no question about it, I believe that we have a normal progression of life that begins with fertilization, continues through the blastocyst phase, continues through the embryo phase, continues through the fetal stage, continues through what we know as birth to the child, to the adolescent and to the adult. It is a continuum to me.

I do give moral significance to the embryo and I indeed give moral significance to the blastocyst, unlike some of the other comments that have been made earlier today.

No. 2, I am a transplant surgeon. I have served on ethics committees of individual hospitals. I have served the United Network for Organ Sharing, which is the coordinating body, the registry for the transplantation of all human tissue or all human organs in the United States of America, a body that was set up by our U.S. Congress to coordinate, to ensure that there is full public accountability and transparency for the transplantation of tissues and organs.

I have been author of scores of peer-reviewed papers in the medical literature on transplantation, the ethics surrounding transplantation as well. I, as an individual, wrestle with the decisions of life and death and health and healing. I have had the opportunity to routinely deal with transplanting tissue into six day old babies who would otherwise die without that transplant of a heart and transplanting people well into their fifties years of age.

I have had the blessing to see the miracle, the miracle, that results from the transplantation of tissue, of taking a beating heart out of an individual who has healthy lungs and a healthy kidney and a healthy liver and taking that heart and placing it into another for the benefit of others.

I have had the opportunity to see a very rigorous consent process which we developed in 1968 through the seventies, a rigorous consent process that is well established, which makes sure that we avoid the potential abuse that is inevitably associated with the use of a scarce tissue that literally gives life as well as hope to other individuals.

Based on this experience, I am absolutely convinced, based on the knowledge and the experience, but also what we as policy makers that we can do, that we can address the use of living tissue, of living cells that otherwise would not be used, that otherwise would not be used—the words are tough, but discarded, disposed of. That particular subset of tissues I believe, with an appropriate ethical construct, we can use that tissue to the benefit of hundreds of others, thousands of others, maybe millions of others.

It was not easy in transplantation. We addressed many of these issues in the 1960's and 1970's. We defined brain death in the year 1968. It was debated in Congress. It was debated in the scientific literature. That sort of public discourse we have to have today, I believe. That addressed issues of human beings at 15 years of age and 30 years of age and 50 years of age.

But now we are much earlier in this life cycle, but we are addressing the same issues of informed consent, of using living tissue.

The consent process itself is inadequate today. We absolutely must have a comprehensive consent process to avoid abuse, avoid the potential for commercialization, avoid the potential for incentives, of traveling down the so-called slippery slope.

No. 3, is research. You know, we have to be very careful. Everybody will put this long list of diseases: Alzheimer's, Parkinson's, diabetes, diseases that we are all exposed to. We need to make it very clear to our colleagues and to people broadly, this is untried, untested research. Huge potential, huge potential, yes, but it is just that, it is potential. It is untried. It is untested. Yes, we need the research itself, but let us not put every hope for every disease to be cured by this one aspect of research. But huge potential.

It has become to mean hope to most people and that is good, and I love it when people come up and say, that is the only hope that we have for the cure of my child. That is really not true. There are lots of other areas that we can explore as well. But it is important. It is evolving science. Whatever structure we set up, I believe we have to set it up in a way that will continue to address new ethical issues that are introduced.

We have seen it in the newspapers over the last 2 weeks. We do not know what is being done today. We certainly do not know 6 months from now, and whatever ethical construct we set up, we must have it ongoing and responsive as we go forward.

There is the potential for abuse of this research. How far should we go? Scientists will say, let us just open it broadly. I again as a scientist want to say that we do have to recognize that this re-

search can be abused. There is a lack of predictability. We must build in the safeguards.

No. 4, and last point is Federal funding. I will say that we should fund adult stem cell research, we should increase adult stem cell research, but I also conclude that both embryonic stem cell research as well as the adult stem cell research should be Federally funded within a very carefully regulated, fully transparent framework that ensures the highest respect for the moral significance of the human embryo.

I will just read very quickly ten components of a comprehensive framework that I think is very important. Again, this comprehensive framework in my mind is the only way that we should allow embryonic stem cell research to progress, because I believe, based on my experience with the transplantation of tissues, that only by having a comprehensive framework such as I outline will we be able to progress in a manner that is respectful of the moral significance of the human embryo and the potential of stem cell research to improve health.

Those 10 components, and I will just read them:

No. 1, I would recommend that we ban embryo creation for research. I believe that the creation of human embryos solely for research purposes should be strictly prohibited.

No. 2, I would continue the funding ban on the derivation. I think we need to strengthen and codify the current ban on Federal funding for the derivation of embryonic stem cell.

No. 3, I would ban human cloning. I would prohibit all human cloning to prevent the creation and exploitation of life for research purposes.

No. 4, I would increase adult stem cell research funding.

No. 5, I would provide funding for embryonic stem cell only from blastocysts that would otherwise be discarded. I would allow Federal funding for research using only those embryonic stem cells derived from blastocysts that are left over after in vitro fertilization and would otherwise be discarded.

No. 6, require a rigorous informed consent process. I will not elaborate now on that, but I can tell you, based on the well-established consent process with transplantation, it is critical, it is critical that we address this in a thorough manner. It has not been addressed to date.

No. 7, I would limit the number of stem cell lines. I would restrict the Federally funded research using embryonic stem cells derived from blastocysts to a limited number of cell lines.

No. 8, I would establish a strong public research oversight system. This oversight mechanism is critical. We did it in transplantation in a very successful way. I believe we need a national research registry to ensure the transparent in-depth monitoring of Federally funded and Federally regulated stem cell research and to promote the ethical high quality research standards.

No. 9, require ongoing independent scientific and ethical review. I do believe we need ongoing scientific review by the Institute of Medicine. I do recommend that we create an independent presidential advisory panel to monitor the evolving bioethical issues surrounding stem cell research and I believe that we should have annual reports to Congress.

No. 10, I believe we need to strengthen and harmonize the fetal tissue research restrictions. Transplantation was a little bit later in life. We addressed that 20 to 30 years ago. Fetal tissue research we moved into about 6 or 7 years ago. Now we are moving earlier in that time line to embryonic stem cells, which I believe we should address in the manner that I have outlined. As we address the embryonic stem cells, which are the early precursor cells, I believe we need to go back and harmonize the process for fetal tissue research as well.

Mr. Chairman, I thank you for the opportunity to outline what I view is an appropriate public policy response to one of the more challenging moral and ethical issues of our time.

Senator HARKIN. Senator Frist, thank you, as well as Senator Hatch, for two thoughtful statements and for your involvement in this issue.

I now will turn to Senator Sam Brownback from Kansas, elected to the Senate in 1996. Senator Brownback serves on the Commerce, Science and Transportation Committee, as well as Judiciary and Foreign Relations. Law degree from the University of Kansas, B.A. from Kansas State University.

Senator Brownback testified last year on this issue before this subcommittee. We welcome you back, Senator Brownback.

STATEMENT OF HON. SAM BROWNBACK, U.S. SENATOR FROM KANSAS

Senator BROWNBACK. Thank you very much, Mr. Chairman, and it is a pleasure to be back. Thank you for inviting me to give another perspective on this particular issue.

I want to start off with my thanks and appreciation to you and to Senator Specter for holding these hearings, for looking at this in depth, and also for your push for doubling the NIH funding, which I have strongly supported. I believe it is one of the great things that we have done during my tenure of being in Congress.

We are on the edge of a frontier of great discovery, of great hope and opportunity for a number of people. That is one of the great things that we can do. Similar to the space program in the sixties that gave us vision, this one gives us great opportunity, and you have led that charge, and I appreciate your efforts.

This is a fast-developing field that we are talking about now. The study that was just released, to which Senator Hatch pointed, I have not received an advance copy of that either to be able to look through. I have looked at the news report articles of it. I am hopeful of getting the information. They do point out in the report that they do not deal with the one issue that I raised to you last time that I testified in front of this committee, which I will raise again today.

That is simply the issue that we all on this panel, I believe, all in this room, agree that this embryo is alive. The central question remains is it a life, or is it a mere piece of property to be disposed of as its master chooses? That is the central legal and ethical question that we have in front of us. It was there a year ago, it remains here today for us to examine: It is alive; is it a life?

We really have to determine the answer to that question before we can proceed forward with any of the hope or the promise of what one might want to try to consider with this.

The field is fast developing. Last week a group in Virginia announces that they were creating embryos for research purposes. They were creating the most hardy ones of the eggs and the sperm joined together to get the most robust stem cell line.

I come from an agricultural background. Those are livestock terms, when you create a robust and hardy line, which is what they were talking about. I think that is a terrible thing that they are moving towards in the Virginia group.

Last week we also had an announcement from Massachusetts that for a year now a group there has been working on human cloning. I want to talk about human cloning a little bit more in my discussion, because I think inevitably the direction that we are moving leads towards human cloning. I want to develop that point with you if I could in a moment.

Second, we now have the other side of the face of this, and I would like to share, if I could, a face of the human embryo. We had testimony yesterday in the House side and a front page lead picture in the New York Times. There is a picture of two children adopted from an in vitro fertilization clinic and they are human and they are bouncing children today and they are beautiful children.

Here is another one, if I could point to a picture of Hannah when she is conceived, when she is frozen, when she is adopted, implanted, the development takes place, and where she is in April at age 28 months. Hannah was frozen in an in vitro fertilization clinic and is another face I think that we should also be considering as we really discuss this issue. Clearly they are alive, are they a life.

I applaud President Bush for his principled stand that he has taken to date on this issue. I think it is bold and quite principled in the stand for human life. I would like to submit to the record his letter that he sent to the Culture of Life Foundation May 18, 2001 of this year.

Senator HARKIN. Without objection, that will be included.

[The information follows:]

LETTER FROM PRESIDENT GEORGE W. BUSH

THE WHITE HOUSE,
Washington, DC, May 18, 2001.

Mr. ROBERT A. BEST,
President, Culture of Life Foundation, Inc.,
Washington, DC.

DEAR MR. BEST: Thank you for your letter about the important issue of stem cell research.

I share your concern and believe that we can and must do more to find the causes and cures of diseases that affect the lives of too many Americans.

That's why I have proposed to double funding for National Institutes of Health medical research on important diseases that affect so many American families, such as breast cancer. My proposal represents the largest funding increase in the Institutes' history. I also have called for an extension of the Research and Development tax credit to help encourage companies to continue research into life-saving treatments.

I oppose Federal funding for stem-cell research that involves destroying living human embryos. I support innovative medical research on life-threatening and debilitating diseases, including promising research on stem cells from adult tissue.

We have the technology to find these cures, and I want to make sure that the resources are available, as well. Only through a greater understanding through re-

search will we be able to find cures that will bring new hope and health to millions of Americans.

Sincerely,

GEORGE W. BUSH,
President.

Senator BROWNBACK. Thank you.

Mr. President, let me also say that I testify with a number of my colleagues today, and all of us share a deep and abiding desire to cure the diseases which plague humanity—as do the people on this committee. Can we? Are we on the brink of being able to solve such terrible diseases as Parkinson's, ALS, diabetes, juvenile diabetes, and cancer? I think we are, and I think there is a right route that we can go with this, and I think it is the adult stem cell route that does not have the ethical and moral questions that we have surrounding the embryonic, stem cells. Adult stem cell research is also showing a great deal of promise by the NIH reports and studies, and it, is also showing fewer of the problems that we are seeing with embryonic, stem cell research.

Two weeks ago we had a report out in Science magazine saying the embryonic stem cells are not stable. I know my colleague Dr. Frist has pointed out that we should not hang all of our hopes on this research. It looks promising, but there are a lot of questions.

We know from this report, the NIH report, the earlier studies, earlier reports released from it, that some of the embryonic stem cells are creating tumors. These are fast-growing cells. In many respects they may be placing the new wine in old skins parable that we see in front of us. We are not certain, but we do see that in some of the early and preliminary results.

Far from lagging behind the embryonic stem cell, the adult stem cell lines are already being used in human patients to assist in recoveries, from cancer and leukemia, restoring sight to the blind, curing severe combined immune deficiency, repair damaged bone and cartilage.

On the contrary, recent animal trials using embryonic stem cells have shown a disturbing tendency for these cells to form, as I stated, uncontrollable tumors when transplanted. To my knowledge, and my contact with the scientific literature confirms this—I am not a scientist, but I do read—there is no embryonic stem cell work even close to treating humans today.

I would also like to point out that many of the proponents of destructive embryo research are now advocating the so-called use of therapeutic cloning. I want to put this term on the table and I want to put this term into the debate because that is where this issue is headed. At a recent hearing that I held on the issue of human cloning, both the president of Biotechnology Industry Association and a representative of the American Society for Cell Biology emphasized their strong support for so-called therapeutic cloning as the ultimate source of embryonic stem cell that will not face rejection.

Therapeutic cloning is where you take the young embryo, or in some cases you can take an egg, de-nuclei it, take DNA from my skin cell, yours, somebody here, insert it into the egg or the embryo, start it growing again for a period of several days, and then harvest—and I use that term again because we are talking almost in livestock terms here—harvest the stem cells that will genetically

match the person for whom we seek to be able to fix, repair or replacement an organ.

Both of these gentlemen testified that they are going to need and that they strongly support therapeutic cloning. This is the route they prefer to go to get stem cells that genetically match up.

Dr. Rudolph Jaenisch testified that with therapeutic cloning no rejection will occur because these cells, which come from the cloned embryonic stem cell, are the same immunological makeup as the patient's cells. The testimony of both Dr. Jaenisch and Mr. Feldbaum recognizes that for the purposes of possible clinical applications, particularly to avoid possible tissue rejection, human cloning is the logical next step or so-called therapeutic cloning. This means that live embryos created by researchers can be experimented on and then disemboweled at the leisure of the researchers for purported benefits of patients.

This is truly a slippery slope. Cloning of humans should be and I believe it must be stopped. I say "slippery slope" because the current proposals seek to undo any principled limitation by rejecting true principle on this. The principle being denied in this case is the dignity of the young human, effectively making the human embryo equal to mere plant or animal life or property, or even livestock, to be disposed of according to human choice, governed by mere legal and pragmatic considerations.

Is that really the direction we want to go? I want to cure these diseases, and I think we have an ethical route to go as well with the adult stem cells.

How many of us were repulsed when we heard of cases in other countries, in China where people were executed and then their organs harvested? Now, you could say, well, they are being destroyed and somebody is going to be saved. Somebody is going to get a heart that needs a heart out of this. Yet do you not just repulse when you hear that? This is not the right way to go.

The embryo is alive. Is it a life, or is it mere property? We really must address this question first and foremost.

Finally, Mr. Chairman, I want to make the point of this. I have two letters from people who suffer from terrible diseases who do not want to see embryonic stem cell work move forward. I would ask for that submission into the record.

[The information follows:]

LETTER FROM CHRISTOPHER CURRIE

JULY 17, 2001.

Hon. SAM BROWNBACK,
U.S. Senate,
Washington, DC.

DEAR SENATOR BROWNBACK: People who suffer from diseases shouldn't have to destroy their souls to save their bodies.

Yet that's exactly what some medical-research advocates would have us do by persuading Congress to fund therapies that would involve killing living human embryos in order to treat victims of certain diseases.

I am one of those disease victims. Diagnosed as a Type I diabetic at age 11, I've been insulin-dependent for the past 27 years. My treatment regimen consists of continuous insulin infusion through a wearable pump, at least four daily blood tests to measure plasma glucose levels, and careful control of diet, exercise and other daily activities.

In addition to the threat of sudden death from insulin shock or ketoacidosis, I must contend with the advance of several complications of the disease that may lead

to blindness, kidney failure, loss of limbs, chronic pain, stroke, heart disease, and, ultimately, death. Knowing that I can expect to lose a third or more of a normal lifespan, I worry about my wife and two young children, for whom I am the sole source of support.

Stem-cell research may hold promise for diabetics like me who desperately hope for a cure. But treatments that depend on the destruction of human embryos will not help me or many thousands of patients like me. To do so would make us accomplices in the deliberate destruction of life for research purposes.

It's easy enough for many to dismiss the claims upon our consciences from unseen and unheard human embryos, especially when they're focused on the conquest of a disease or perhaps the sufferings of a loved one. But when you enter into a relationship with that tiny human being, the relationship between donor and recipient, the moral weight of that little one is much harder to ignore.

Would that person have had the chance to live, to love, to experience all the joys of life that I have, if she hadn't been killed to help me? These are the kinds of questions that torment the disease victim who contemplates a treatment purchased at the cost of another human life, and they are not so easily dismissed.

In my view, Congress should spend our tax dollars on treatments that all taxpayers can support, and that all patients can accept without violating their consciences. Fortunately, there are alternatives, including research that involves stem cells taken from adult donors and umbilical cord blood.

Congress need never sanction the destruction of some human lives in order to help others. Please honor your own consciences as you honor those of millions of others like me.

Very truly yours,

CHRISTOPHER CURRIE.

LETTER FROM JULIE DURLER

JUNE 30, 2001.

Hon. SAM BROWNBACK,
U.S. Senate,
Washington, DC.

RE: Funding for Diabetes Research

DEAR SENATOR BROWNBACK: I was recently made aware of a hearing last week before the Senate Permanent Subcommittee on Investigations (Senate Government Affairs Committee) wherein actress Mary Tyler Moore and others requested increased funding for diabetes research and support for embryonic stem cell research which she called "truly life affirming".

As an insulin-dependent diabetic myself for the past 16 years, I would like to see a cure for diabetes. I know that through research a cure can be found (or at the very least improvements in the treatment for diabetes). However, I do NOT support embryonic stem cell research to accomplish this goal. I believe it is wrong to use stem cells taken from aborted babies (or any embryo/fetus if it means the death of such child) for research. Stem cells taken from consenting adults for research is another matter, and one which I would support.

What is your position on using embryonic stem cells for research for diabetes or other medical ailments? Will you support a "truly" life affirming stand and support increased funding for diabetes research ONLY if it DOES NOT provide for the use of embryonic stem cells in the research?

Thank you for your time. I look forward to your response.

Sincerely,

JULIE M. DURLER.

Senator BROWNBACK. I would point out as well that this is an issue of enormous magnitude. It should not be done in an appropriations bill. This should be done free-standing on the floor, with a lengthy debate. We are going into a new bold, some would refer to brave, new world. I think this is an area that we should have set on a free-standing bill with thorough discussion and debate, and not something that we would do as part of an appropriations process.

If that were to occur, there would be a lot of vigorous debate on the floor about doing something of this magnitude and this nature in an appropriations bill.

Thank you very much for your heart and for your patience.

Senator HARKIN. Thank you very much, Senator Brownback, again for a very thoughtful statement now and the one last year also.

We now turn to Senator Gordon Smith, elected to the Senate in 1996, a member of the Energy and Natural Resources, Foreign Relations, Budget, Commerce, Science, and Transportation Committees. Senator Smith graduated from Brigham Young University, the same as Senator Hatch, and received his law degree from Southwestern University.

Senator Smith, welcome. Please proceed.

STATEMENT OF HON. GORDON SMITH, U.S. SENATOR FROM OREGON

Senator SMITH. Thank you, Mr. Chairman and colleagues of this committee.

Each of us as U.S. Senators come to this place, this public place, as the sum of our beliefs, our experiences, and our values. None of us checked them at the door when we came here. I thought in the spirit of trying to be helpful to your deliberations I would share with you what I have experienced and what I believe.

As a young boy I watched my Grandmother Udall die of Parkinson's disease. Growing up, I watched my cousin Congressman Morris Udall literally die in public of Parkinson's disease. Last April I buried my uncle Addison Udall of Parkinson's disease. Last weekend my brother-in-law Dan Daniels informed me that he now suffers from Parkinson's disease.

In the experience of my life I have not been a stranger to hospitals and trying to provide care and comfort to those who suffer and seek to be well. So for me, this debate presents me with the ultimate question, one for which I believe I will be held accountable in this life and hereafter. That question is, when does life begin? Senator Brownback has stated it well.

Some say it is at conception. Others say that it is at birth. For me in my quest to be responsible and to be as right as I know how to be, I turn to what I regard as sources of truth. I find this: "And the lord God formed man of the dust of the ground and breathed into his nostrils the breath of life, and man became a living soul." This allegory of creation describes a two-step process to life, one of the flesh, the other of the spirit.

Cells, stem cells, adult cells, are I believe the dust of the earth. They are essential to life, but standing alone will never constitute life. A stem cell in a petri dish or frozen in a refrigerator will never, even in 100 years, become more than stem cells. They lack the breath of life. As an ancient apostle once said: "For the body without the spirit is dead."

I believe that life begins in the mother's womb, not in a scientist's laboratory. Indeed, scientists tell me that nearly one-half of fertilized eggs never attach to a mother's womb, but naturally sluff off. Surely life is not being taken here by God or by anyone else.

For me, being pro-life means helping the living as well. So if I err at all on this issue, I choose to err on the side of hope, healing,

and health. I believe the Federal Government should play a role in research to assure transparency, to assure morality, to assure humanity, and to provide the ethical limits and moral boundaries which are important to this issue. Those boundaries and limits must stop at a mother's womb, for again that is where life begins. The puritans called it a quickening, and the scriptures, I think speak to that effect as well.

In conclusion, I say with deepest respect for those who have views different from my own, both theologically or scientifically, that I respect those views, but share with you my own views and my own experience in seeking cures for the most dreaded diseases on this planet. We are at a confluence between science and theology. I believe we must err on the broadest interpretations to do the greatest amount of good. It is in that spirit, Mr. Chairman, that I am here, and I thank you for this time.

Senator HARKIN. I am going to yield to Senator Specter for questions, but before I do I just want to say, I think in my 27 years that I have been privileged to serve in both the House and the Senate, I do not believe I have ever heard testimony as powerful and as deeply thought out and as moving as what I have just heard from the four of you. Regardless of whether I may agree or disagree, I think you have touched me very deeply.

I just want all who are in this room, I hope all who have heard your testimony and those who may be watching—I believe you really have raised the stature of the U.S. Senate. I think people who are listening and watching, I hope they have a renewed faith in and confidence that those of you and those of us who serve here do not take these issues lightly. These are things that we wrestle with on a daily basis, and we try to come up with what we hope are the best results and solutions that will enable us to adhere to our basic values and our religious beliefs and yet try to meet the needs of people who are suffering.

So I just want you all to know that I really appreciate your testimonies and the thought and concern and the compassion which each of you have brought to this issue. You do us proud.

With that, I will turn to Senator Specter.

Senator SPECTER. Thank you, Mr. Chairman.

Supplementing what Senator Harkin said, the U.S. Senate is frequently quoted as the world's greatest deliberative body. Occasionally people watch on C-SPAN2 have some reason to doubt that. But anybody who has heard this testimony I think would concur that the quality of deliberation is extraordinary in thoughtfulness.

While Senator Brownback and I have some disagreements on this issue, I agree with him that this matter ought to be taken up with full debate. An appropriation bill may turn out to be the appropriate line because right now the prohibition comes from an appropriation bill out of this subcommittee from 1995. But on the substantive matters about having thorough consideration, I believe you are correct, Senator Brownback.

I thank you, Senator Hatch, for your very, very thoughtful testimony, coming at the issue in so many directions with your experience and your stature in the Senate, and a strong pro-life, pro-family advocate for so many years, having been elected here in 1976.

Senator Gordon Smith, very profound as you articulate those views. Senator Frist, we are very appreciative for your appearance here today. You and I have discussed this matter on many, many, many, many occasions and I am glad to see your position coming forward today, and as you articulate 10 standards, I agree with you about eight, but I want to discuss with you the two remaining.

We will later here today testimony from Dr. Diane Krause, and let me lay out a couple of lines of concerns. Dr. Krause would take issue with the standards which you have articulated on number two and number seven, which are really overlapping: number two, the continue the funding ban on derivation, that is the Federal funding ban; and number seven, to limit the number of stem cell lines.

Dr. Krause in her written testimony has raised this issue, that the proposals to limit funding research to only existing cell lines is far too limiting. Scientists need to compare multiple cell lines in order to better understand the common factors that give embryonic stem cells their incredible plasticity, as she put it.

Dr. Lawrence Goldstein, professor of pharmacology at the Division of Cellular and Molecular Medicine at the University of California at San Diego, has raised a concern about the current number of stem cell lines being insufficient because you need more genetic variety. The current stem cell line established by NIH is only 30 and there are suggestions by other scientists in the field that you need a minimum of 200.

Then let me put the second consideration before you all at the same time. When we talk about the NIH guidelines, they would not be met by the existing cell lines because embryos must have been frozen, there is not sufficient documentation of informed consent, which I think you are exactly right about, and the prohibition against creating for medical research purposes the cell lines is part of the NIH guideline. There again, I agree with you that if we do not legislate on this field in a comprehensive way we have the problems of cloning, which trouble everyone, and the problems of creating these embryos for medical research, which again are extraordinarily cloning.

But in this area, Senator Frist, Dr. Frist, I think we join a critical issue which our colleagues will be looking at when we examine the scope of legislation on this important subject.

Senator FRIST. Thank you, Senator Specter. I do—let me comment on several of the points, and then I know that you have a lot of people to talk specifically about these.

First of all, there are major differences with what I proposed and what you have in an underlying bill, and I think we pointed to that's where the differences are. I do not believe we should be funding derivation, which you mentioned. The consent process, the informed consent process, we absolutely must address, which I believe again it is something that we have not focused enough attention on.

I believe we should ban human cloning, which is another of the issues which in your legislation you do not. And I do not believe that you ban the creation of embryos for research only. I really feel strongly on this publicly accountable oversight system.

Those are sort of the big differences, I think. I summarize those right now so that the American people understand the differences. Cell lines, number one, it is worth talking to the scientists about that. What are cell lines? First of all, transplantation. When I transplant a human heart, I take it from one individual who otherwise has normal kidneys, lungs, blood is flowing, warm, the like, take that heart and put it into another person, and that helps that one individual.

The really exciting thing about embryonic stem cells, it is not sort of a one for one. It is not like that you have to take a blastocyst, which is really 20 to 30 inner cells coupled with an outer supportive framework. You do not have to take one of those to do one—help one research project and then take another one to help another research project or another. The great power and potential—again, it is unpredictable—of these is the fact that these will perpetuate themselves forever and that once you take a cell line, that cell line you can grow and you can grow it in an identical fashion and share with researchers all over the world, as long as that informed consent. That is the real power.

Therefore, how many cell lines do we have today? We can talk more about that with the scientists, but we maybe have 7, 10, 12 cell lines today. That is a pretty good amount. Some will say you can limit it just to that. I would propose that we have a discussion with the scientists to say, how many do you really need. The point is you do not need thousands and therefore you do not need thousands of blastocysts to do this. It might be 20, it might be 30, it might be 100, or you mentioned 200 cell lines. What is a cell line? A cell line is in essence the genetic—or the makeup of a single blastocyst or embryo.

I think that is an important concept because people have in their image that all these embryos are going to be created and they are living and there is going to be destruction of these embryos that is going to go on millions and millions and thousands of times. It is just important for people to understand you do not need unlimited cell lines. Exactly how many, I think it is worth talking to the scientists about.

The informed consent process we mentioned. I will stop. I should probably stop there, but I think this larger moral, ethical construct which is inadequate in NIH guidelines today, using informed consent as one example, absolutely must be addressed. Therefore, I would urge also that we do not rush with a very narrow bill on an appropriations bill that does not take that into consideration.

Senator SPECTER. Senator Frist, the question as to how many cell lines let us leave open. Let us get the scientific interpretation. The information I have heard is that we need a lot more than 7 to 12. Two hundered may be a line. Let us rely on the scientists on that.

The one point where I do think we have a fundamental disagreement is on the Federal funding. The current status of the appropriations law is no Federal funds may be used on stem cell derivation from embryos, and that has been interpreted by an opinion from general counsel in HHS a couple of years ago to prohibit Federal funding to extract stem cells from embryos, but not to prohibit

Federal funding to research on the stem cells once they have been extracted.

Senator FRIST. Yes, sir.

Senator SPECTER. As I understand your testimony, you want to maintain the ban, which would limit Federal funding to extract stem cells from embryos.

Senator FRIST. That is correct.

Senator SPECTER. We are prepared on the Specter-Harkin bill to yield to you on 8 of your 10 points, making it the Frist-Specter-Harkin bill. But I think we are not prepared—I will let Senator Harkin speak for himself—on the issue of funding for extracting stem cells from embryos, because of our concerns.

Everybody has applauded what we have done, the leadership from this subcommittee on increasing NIH funding from $12 billion to more than $20 billion. If this year's idea goes through, we will have doubled it. But when you use the private sources, first of all, in a marketplace society they will do for profit. When NIH is doing the research on extracting stem cells from embryos, they are subject to the ethical considerations and also to the brilliance within the NIH family and the grants which they may allow.

So, moving right to the core of the issue, how can you adequately deal with this vital, vital subject if you do not have these NIH funds, which we have increased so dramatically, available for the critical aspect of extracting stem cells from embryos?

Senator SPECTER. Yes, sir. Very quickly, the overall ethical-moral construct, including the bioethics advisory committees, oversight, registry, would apply quite broadly. I think it is absolutely critical that you link the last question to this question. We do not need an unlimited number of stem cell lines. Therefore, for each experiment, for each investigation, you do not have to go out and take another blastocyst, take out those 20 or 30 cells, grow them, and start from scratch. That is why this is so different in terms of the power and the potential.

You just said I am not sure whether we need 7 cell lines or 25 cell lines or 50. You could also argue you should be doing it in animals instead of humans as you determine just that and make these comparisons, but that is a separate issue. But let us just say you need 100 cell lines. I think if you talk to enough scientists they will say, for right now, given where we are in terms of the evolution of science, the potential for abuse, the lack of an ethical construct in which to both debate and carry on public discourse, that you do not need 200 cell lines.

But even if, let us say you needed 100 cell lines. The derivation of the cells, the taking of 20 cells out, would have to occur 20 times or 40 times or 60 times or 80 times. It is not an ongoing process because once those cells are taken out you can do thousands of experiments with thousands of investigators all over the world.

That is why it is important. So the derivation to me, I think you are exactly right, we have heard of the great moral challenges we have today in terms of are you destroying. Senator Brownback, that is a human being to Senator Brownback. You are destroying that, and you are. It is going to be discarded otherwise, but in his mind.

Therefore, to take Senator Brownback's taxpayer dollars or the dollars of his constituent to do something, even on a very limited basis, that is against his moral conscience, we are not ready to do as a society.

Senator SPECTER. Well, Dr. Frist, I understand what you are saying and I am prepared to, as you seem to be, rely upon the scientists to tell us how many cell lines we need. But I am not prepared to leave it to the private sector to extract the stem cells from the embryos. I think that is where we have our disagreement.

I think that with the NIH expertise and their ethical standards and the funding which the Congress has provided, all of those resources ought to be brought to bear on the removal of the stem cells from the embryos on this very important subject.

I thank you very much, Dr. Frist. There are a lot of questions which could be asked of Senator Hatch and Senator Brownback and Senator Smith, but I will yield that chore to others.

Senator HARKIN. Thank you very much, Senator Specter.

Senator Murray.

Senator MURRAY. Thank you, Mr. Chairman. I do not have any questions at this time. I just want to thank all of our colleagues for obviously a very courageous and thoughtful discussion on a very difficult issue. I think you have helped us move the debate forward and I appreciate it.

Senator HARKIN. Senator DeWine.

Senator DEWINE. No questions, Mr. Chairman. Thank you very much.

Senator HARKIN. Senator Cochran.

OPENING STATEMENT OF SENATOR THAD COCHRAN

Senator COCHRAN. Mr. Chairman, I just want to thank the Senators who are here today. I think this is a defining moment for the Senate. We are blessed to have these four Senators available to us for counsel and advice and information. I am pleased we also have technical and scientific guidance from others in this process.

It is truly a matter of life or death. This issue deserves our best efforts to learn the facts and act no them, to serve the public interest. This is not an issue where we try to be just politically correct. Our obligation is more than that. We just use our best judgment, enlightened by the best evidence.

This hearing is a very important step in that process, and I appreciate the seriousness with which the committee leadership has undertaken to outline an agenda and select witnesses to come before us to see that we do the best we possibly can on this issue.

Thank you.

Senator HARKIN. Thank you, Senator Cochran.

I just would just follow up with what Senator Specter was saying. I am glad you clarified, Senator Frist, on limiting the cell lines. Now I have a better understanding of what you mean by that. But I still have a problem with number two, as Senator Specter does. While I agree we do not need an unlimited number of cell lines, I wonder about the logic that would allow our Federal researchers to work on stem cells, but not to derive them. It is sort of, you go ahead and do it, then you give them to me, but I do not want to have my hands in it. I do not understand that logic. I do not want

to be flip about it, but it is like, do not tell me what bank you robbed, just give me the money.

I do not want to be flip about it, but I do not understand the logic of saying you can work on the cell lines, but you cannot derive them.

Senator FRIST. Right. I think the question is very legitimate, and for me it is a matter of Federal funding. That is the issue that we are talking about. Right now, given where we are today in terms of the derivation, when there are a significant number of people—and I believe life does begin with fertilization. I give moral significance throughout, and that is based on the spiritual values and moral values and religious values and the medical view that I have.

Therefore, I think, in terms of taking taxpayer dollars of probably 40 percent of the people that are listening to us right now and saying that we are going to use that very specifically, a part of the process which in truth is very small when you look at the research that is going to be done, very small—and that is very clear for us to understand. The derivation part of it, it does not take that many. We talk about maybe 10, 15, 20, maybe 200 cell lines. It is a very small part.

So I think from a moral standpoint it is not right to take taxpayer dollars and use that when there are—and I do not know what the percentage is, but 40 percent of most people's constituents would say it is not the right thing to do, when it is not going to slow down the research. I do not believe it will slow down the research if you do not, if you do not pay for it.

Senator HARKIN. Does anybody have any other thoughts?

Senator HATCH. Could I just add one thing?

Senator HARKIN. Yes, yes.

Senator HATCH. It is my understanding that the in vitro fertilization process is basically completely private sector, although there has been some research done in the Federal Government. Maybe I am wrong on that, but I believe I am correct. If that is the case, that is where these cells are coming from.

Now, look. I think Senator Frist was very cogent in his whole discussion of this. But what it comes down to probably is a political process problem, that should the Federal Government be paying to extract these cells from a blastocyst, which then of course is discarded, and which would have been discarded anyway if we had not taken the pluripotent cells from it.

The House has, I think, has been unwilling to have Federal funding of any type of abortion approach, and to some in the House they feel this is a similar situation. So I think Senator Frist has really described the political situation quite well. But as far as stem cell lines, what I have been told is that 12 to 20 would not be enough, but approximately around 100 would probably be sufficient. Senator Specter, you said 200 and I am sure there are some scientists who do say that. But the ones that I have chatted with have indicated about 100 stem cell lines would be adequate.

But I think that basically, if the Federal Government is not doing the in vitro fertilization process itself, they are going to get these cells primarily from the private sector. But what Senator Frist is saying—and I do not mean to speak for him; it is just that

I agree with him on all 10 of his points. What he is bringing out is that this work has to be done under the strictest guidelines and rules and regulations, and NIH has those, although they may be enhanced through these hearings and other considerations by Congress.

If that is done, that will go a long way to alleviate some of the concerns of some people in our society. But I am concerned about the fact of getting the Federal Government into the whole process.

Senator HARKIN. Just on that one point, the bioethics committee that was set up that was headed by Dr. Shapiro of Princeton University—if you look at the list of all of the people that are on there, I mean, these are some of our best ethicists, philosophers, religious leaders in this country, and they came up with these guidelines. Maybe they can be enhanced. I do not know. But I thought they were pretty well thought out guidelines that NIH had come up with by this distinguished group of citizens.

Senator HATCH. I have no problems with those. I have no problems with those guidelines.

Senator SMITH. Mr. Chairman, on your point——

Senator HARKIN. Yes, Senator.

Senator SMITH. I think you are exactly right, that if we are going to incentivize this, if we are going to pay for the product, but we do not want our hands in the process, we are doing the same thing with two steps that we are in one. I recognize my colleagues look at this somewhat differently, but it is a just give me the money, do not tell me where it came from, type of process. That is why I think you cannot go that route if you are deeming that this is an inappropriate thing to do in the first place. You cannot incentivize the product and then say, I do not want to look at the process.

Senator HARKIN. The other question I have is, again for any of you, Senator Frist, is if you say, well, we cannot have NIH fund the derivation, but we can do the research, if the derivation is done in the private sector, that does cost money. What incentive will the private sector have to derive the stem cells if all they are going to do is give them free to NIH? Or is NIH going to have to purchase these? Would that be acceptable?

Senator FRIST. Mr. Chairman, I think that would be acceptable, but I think the larger issue—in terms of purchase, I do not think—that sort of thing in terms of science is not uncommon. In transplantation, for example, which is the transfer of human tissue from a live entity to another live entity, but actually similar in many ways—again, you will see I call upon this, but about 30 years ago we had to decide, after 2,000, 3,000, or 4,000 years of thinking death is the heart and the lung when they stop, we had to redefine it as brain death with everything else normal.

I think we are going through a little bit similar process as we work through the definitions. There are two parallels. One is that the tissue from transplantation before I take out the human heart of a body that is otherwise normal except there is one organ gone, but everything else is normal, before I take that heart out you go through this consent process, which is inadequate in the statute now. The National Bioethics Advisory Committee looked at it, so it is inadequate, so it does need to be strengthened.

That body is going to be going into a grave or discarded or disposed of, but that is living tissue itself. A lot were thinking—or I think we should think of it in a parallel way, in that the limitation that I place is in vitro fertilization. If a woman gives 20 blastocysts, has 5 implanted, 4 or 5 implanted, and there are 15 that she freezes, and that after an adequate consent process is set up she makes a decision whether to offer those, say 20 years later or 10 years later, for adoption—perpetual freezing, not many people are going to want to do that because they usually charge $1,000 or $500 or something a year to freeze them. A lot of people probably are not going to do that.

Those embryos today are discarded. You turn the freezer off and that is it. I think we do—I think we should today, because there is so much uncertainty, limit the research to the use of those cells, similar to transplantation, that otherwise absolutely, with full public disclosure, full transparency, full oversight by the Federal Government, is going to be discarded and not used.

Senator HARKIN. You are not opposed to in vitro fertilization?

Senator FRIST. No, sir.

Senator HARKIN. Senator Smith?

Senator SMITH. No, sir.

Senator HARKIN. Senator Hatch?

Senator HATCH. No, sir.

Senator HARKIN. Senator Brownback?

Senator BROWNBACK. No.

Senator HARKIN. No. I guess my question is that obviously in vitro fertilization is going on right now.

Senator FRIST. Yes, sir.

Senator HARKIN. So there will be, as you point out, left-over embryos, in essence.

Senator FRIST. Thousands and thousands and thousands.

Senator HARKIN. So if you are just saying—and this is a question I do not know, I am going to ask the scientists who are coming up here later on, that I understand that somehow the ones that are frozen, that there is a problem in the derivation of the stem cells.

Senator FRIST. We do not know what the freezing process does long-term with those cells. We do not know—also, we implant those cells in women, or women have them implanted. But in most of the consent forms that are given to women, you do not know what the freezing process long-term will do, and therefore scientists will come forward and say just freezing may drop back some of the totipotential or pluripotential components of the cell.

Senator HARKIN. Thank you. You are way ahead of me on that.

So if in vitro fertilization continues on and a woman and a man, the donor, if they have left over embryos at that point that are not frozen, could those be used to extract cell lines, again going through the ethical guidelines that are set up? We were focused so much just on the ones that are frozen. How about the ones that are all obviously being generated, I do not know how often, in an in vitro fertilization.

Senator FRIST. We are getting pretty technical there. In my own mind, IVF involves the creation of surplus—and these words are hard for people, discarding, disposing, and surplus. But that is the nature of in vitro fertilization today. You have to, and so you are

going to have 10 or 15. People elect either to freeze them or to discard them immediately.

So from my standpoint, from an ethical standpoint, they do not have to be frozen before you use them, as long as you have an appropriate consent. I think in transplantation at least, and I think it is important here, the consent process, you cannot have consent made under duress or when other decisions are being made. So I am not sure at the time you are deciding whether or not you are going to have children and when you are concerned about it and focused on it, that is the best time to be making this decision.

I almost think it should be a two-step consent process. You should say, I am going to do IVF, I am going to freeze the cells, and at some later point in time go through a consent process of saying adoption, discarding, turning the freezer off.

Senator SPECTER. A final comment, Mr. Chairman. I agree with Senator Brownback's reasoning, but come to a different conclusion, Senator Frist. When you say that you are prepared to have the Federal Government buy the extracted stem cells from the embryos, if the Federal Government is going to pay private concerns which have extracted embryos from stem cells and the taxpayers' money is being used, it is really not even indirect. It is very direct. Where is the money coming from?

But I come to the different conclusion, that if you are prepared to do that, Senator Frist, it makes more sense for NIH to be involved in the extraction of the stem cells from the embryos. A big issue which has arisen here which this subcommittee has looked at otherwise is the issue of the patents. There are a lot of people out there who want to make a lot of money, and if they are extracting the stem cells from the embryos and they are going to sell them to the Federal Government, it is going to be a lot more costly.

But if we are going to have the Federal Government pay the private concerns, it seems to me much wiser to have NIH do it directly.

Thank you very much.

Senator FRIST. One more statement about transplants. On the transplant field, the Federal Government does not pay for all transplantation of tissue, nor did it in the research component of it. We do have an oversight mechanism where every heart that I transplant or any transplant surgeon transplants or lung or kidney goes through a registry, where there is appropriate ethical oversight.

I think that that is a similar sort of approach. But I do not think we need to pay for everything. In terms of research—I know you are going to keep arguing for it, I am going to keep arguing against it. But I do not think you need to pay for every aspect of research, just like the Federal Government does not pay for all of transplantation. Through Medicare we pay for transplantation and Medicaid, most places do. But there is a huge private sector out there today in terms of the transfer of tissue. So I do not think you have to pay for all of it.

Senator HARKIN. Well, again I thank you all very much. You have just been great and I want to thank you. I especially want to thank Senator Smith. I went back and read Genesis after you talked to me yesterday and you are right. It gave me a whole new way of looking at this. I had not thought about that before, and I

would commend others to think about what you said today in your statement. I appreciate it very much.

Senator SPECTER. Senator Harkin, Senator Hutchison has joined us.

Senator HARKIN. Did you want to ask questions? I was going to let the Senators leave.

Senator HUTCHISON. I did want to ask a question.

Senator HARKIN. I would recognize Senator Hutchison.

OPENING STATEMENT OF SENATOR KAY BAILEY HUTCHISON

Senator HUTCHISON. Thank you, Senator Harkin, and I apologize for being late. I was on the floor.

But I wanted to make a brief comment and then I did want to ask Senator Frist a question. One of the things that I have found through my personal experiences with a family member with cancer is that much of the research on cancer by private companies is done on diseases where there would be enough patients for the return to the private company that is making the investment, that many of the diseases that do not have a large patient number have been not focused on.

That is where you think the NIH can make such a huge contribution, and our commitment in Congress to double the funding of NIH I think makes it important for us to look at all of the ways that we can assure that NIH will have the tools it needs to do the proper research. So I think that is why this is a very important issue.

I wanted to ask one question of Senator Frist, because it is my understanding that the longer an embryo from in vitro fertilization is frozen the less likely it is to be as viable. Maybe there is a 5-year window or so. My question is, if it is not viable as a potential life, is it still viable to be a stem cell donor?

Senator FRIST. Thank you, Senator Hutchison. We talked a little bit about that, and the scientists can comment more on that later. The standard consent forms today, because the science is just evolving in terms of IVF—we know the great miracles that can take place because of it. We know that surplus embryos are created and the option is there to freeze these embryos in case the first therapeutic trial does not work and you can use them later.

What we need to start thinking about socially as a society and as policymakers is what the ultimate destiny of those embryos are. We have inadequate oversight today and that is why I keep arguing, let us be very careful, let us make sure we look at the large ethical picture. We do not know what freezing actually does long-term and that is why in the consent form usually, the consent forms for an IVF, in vitro fertility clinic, will basically say something to that effect.

Therefore, we do not really know because we have not done the research in terms of whether or not the long-term viability will in some way slow down what is called the pluripotential nature of these cells or their ability to copy themselves over time. We just do not know at this juncture.

I should also say, we do not have to do all this research in human blastocyst cells. Before I figured out an operation, before I did my first heart-lung operations, I did not do it in human beings.

I did heart-lung surgery in animal models. Let us just not forget, we are talking about research that is hugely promising, that every one of us have heard from constituents that the answer is going to be and the hope and the tremendous cure is going to be of these cells. That is overselling it today, maybe for every disease. It is just unrealistic.

The hope is there, but it is unpredictable. It is like any new science, it is evolving, and therefore we have to be very careful. I would encourage us not to forget that there are other models besides human models to be doing this research.

Senator HUTCHISON. Thank you, Mr. Chairman.

Senator HARKIN. Thank you very much, Senator.

Again, I thank all of you for being here, for your time, and for your thoughtfulness and your suggestions to us on how we should proceed.

STATEMENT OF LANA SKIRBOLL, Ph.D., DIRECTOR, OFFICE OF SCIENCE POLICY, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Senator HARKIN. Let me now call up Dr. Lana Skirboll, Associate Director for Science Policy and the Director of the Office of Science Policy in the NIH. Dr. Skirboll is responsible for the development of NIH's guidelines for research using human pluripotent stem cells and led the team that wrote the report that we have in front of us here today.

Dr. Skirboll received her Ph.D. from Georgetown University Medical School and conducted her post-doctoral work at the Yale University School of Medicine. Dr. Skirboll, as you probably know, we are running way behind time and I am going to ask if you could hopefully summarize in 5 minutes, I would sure appreciate it. Then we will call on the next panel.

Dr. SKIRBOLL. Yes, I would be happy to do that. Good morning, Mr. Chairman, Senator Specter, and members of the subcommittee. I am Dr. Lana Skirboll, Director of Science Policy at the National Institutes of Health. Thank you for giving me the opportunity today to testify on our report entitled "Stem Cell Scientific Progress and Future Research Directions."

The report is based on a review of more than 1,200 scientific articles and interviews with over 50 leading private and public sector scientists conducting stem cell research. The report addresses both animal and human stem cell biology. It reviews research on adult stem cells as well as stem cells derived from embryos and fetal tissue.

A stem cell, as you heard this morning, is unique. Unlike most cells, it has the capacity to both renew itself and to give rise to specialized cell types, like heart muscle and blood. Research on stem cells is not new. Scientists with the support of NIH have been studying stem cells for many years. In fact, animal research revealed more than two decades ago that there is a class of stem cell called the embryonic stem cell which has exceptional capabilities. It can make copies of itself indefinitely in culture and it can develop into almost all of the bodies many cell types.

But until recently a human cell with these qualities has been elusive. In 1998, for the first time researchers were able to isolate this type of human stem cell from the very early human embryo.

About the same time that human embryonic stem cells were first isolated, research was also revealing exciting information about previously unsuspected qualities of the adult stem cell. Adult stem cells are also unspecialized. They are present in many tissues and organs in the body, but they are rare in those tissues. The job of the adult stem cell is to develop into specialized cells of the tissue in which it resides, usually for the purpose of replacing damaged or lost cells.

For example, the hematopoietic stem cell, which I think most of you have heard of, does the important work of ensuring a continual supply of new blood cells. Recently, scientists have found adult stem cells in more tissues than previously thought, like brain. They have also reported that adult stem cells from one tissue can develop into cell types that are characteristic of other tissue. This new characterization is called plasticity.

Taken together, these new findings have generated much excitement. You have had many hearings about that, about the potential of both embryonic and adult stem cells in the development of cell-based therapies. But in order to develop such cell therapies, what do we really need to do? What do scientists need to accomplish?

First, we need cultured cell lines that are pure, cell lines that in fact are well characterized and identical for safety reasons. We need cell lines that are diverse, that have the capacity to develop into as many kinds of cells that are possible to replace tissues that are destroyed or damaged from disease. And we need cells that proliferate, can make sufficient quantities in culture, so that many patients will have access to them.

With these goals in mind, what does the report show about whether human adult or human embryonic stem cells are equivalent in their potential for generating replacement cells in tissues? First, with regard to purity, using embryonic stem cells researchers can generate pure cell lines in culture, while, with very few exceptions, adult stem cells in culture are a mixed cell population.

Second, with regard to the ability to develop into many kinds of cells for treatment, embryonic stem cells in culture are pluripotent. Although certain kinds of adult stem cells have recently been shown to be plastic, no adult stem cell has been shown to be pluripotent in culture.

Finally, what about that important ability of these cells to make many copies of themselves? Human embryonic stem cells have been shown to remain unspecialized and proliferate indefinitely in culture, potentially yielding quantities needed for transplantation, while the capacity of adult stem cells to proliferate in culture and remain unspecialized is limited.

The report also addresses what we know and do not know, and there is much, about the ability of these cells to differentiate into specialized cells and ultimately to function. Three things we can say for sure: Both stem cell types may be useful in developing cell-based therapies; two, these kinds of stem cells are different; and three, right now there are more unanswered questions than there are answers.

Scientists all agree that stem cell research holds enormous promise to lengthen and improve the quality of life for many patients suffering from perhaps a broad spectrum of diseases: spinal cord

injuries, Parkinson's disease, heart disease, kidney disease, liver failure, multiple sclerosis, Alzheimer's disease, and diabetes, to name a few.

In sum, because we do not know from which stem cell type the best therapies will come for these diseases, scientists believe the door should be left open to conduct research on both embryonic and adult stem cells.

I would be pleased to answer any questions you may have. Thank you.

[The information follows:]

[CLERK'S NOTE.—The report "Stem Cells: Scientific Progress and Future Research Directions" can be found on line at http://www.nih.gov/news/stemcell/scireport.htm]

Senator HARKIN. Dr. Skirboll, thank you. In the interest of time, I think if I could ask you to stay at the table and let me bring up the next panel.

Would you please put up the name plates here. Mr. Richard Doerflinger, associate director for policy development at the Secretariat for Pro-Life Activities, the National Catholic Conference—the National Conference of Catholic Bishops, I am sorry. Anton-Lewis Usala, M.D., founder, chairman, and chief scientific officer for Encelle, Incorporated; Diane Krause, M.D., Ph.D., associate professor of pathology and medicine, the Yale University School of Medicine; Mary Hendrix, Ph.D., professor and head of the department of anatomy and cell biology at University of Iowa; William Gibbons, M.D., chairman of the Jones Institute for Reproductive Medicine; Susan Lanzendorf, Ph.D., associate professor at the Jones Institute for Reproductive Medicine at the Eastern Virginia Medical School; Michael West, Ph.D., president and CEO of Advanced Cell Technology.

Let me see where we are here. Where is Dr. West?

He was here. He maybe just stepped out and he will be back.

Let me start. Then I will start as I called them off. In fact, I may not go in the same order. I will just go from left to right. I will start with Mr. Doerflinger.

Again, I would like to ask—I hate to do this because this is something I could spend all day on. But if you could limit it to 3 or 4 minutes, I would sure appreciate it. Just give us the basic impetus of what you want us to know, and then we will open it up for questions.

Mr. Doerflinger.

STATEMENT OF RICHARD M. DOERFLINGER, ASSOCIATE DIRECTOR FOR POLICY DEVELOPMENT, SECRETARIAT FOR PRO-LIFE ACTIVITIES, UNITED STATES CONFERENCE OF CATHOLIC BISHOPS

Mr. DOERFLINGER. Thank you, Mr. Chairman.

Our title, by the way, now is the United States Conference of Catholic Bishops. We changed the name the beginning of July.

Senator HARKIN. It is not "National Conference"?

Mr. DOERFLINGER. Right. We decided to recognize other nations as sovereign nations as well.

In our view, forcing U.S. taxpayers to subsidize research the relies on deliberate destruction of human embryos for their stem cells is illegal, immoral, and unnecessary. Obviously, we agree with Sen-

ator Specter's comment that the current NIH guidelines, which have the NIH arrange for the destruction of embryos and then pretend to know not where—not to know where they came from, is hypocrisy and an evasion of the law, not a way of implementing the current appropriations rider, and therefore we certainly think that, out of respect for the law, the administration should find the NIH guidelines to be contrary to the statute, whatever else Congress may try to pass as legislation.

We think the represent is immoral. It violates the central tenet of all civilized codes of human experimentation beginning with the Nuremberg Code, approving doing deadly harm to a member of the human species solely for benefit to others. Aside from the fuller respect for human life across the board that the Catholic Church and others have promoted, even President Clinton's National Bioethics Advisory Commission, which has been given high accolades in the panel already, even to the point of fabricating religious leaders on the commission, which there were none of, the National Bioethics Advisory Commission conceded that the early human embryo is a form of developing human life that deserves our respect.

Where we disagree is whether the idea of scooping out the cells of a living embryo and throwing away the shell is a way of showing respect.

Finally, this proposal is unnecessary because adult stem cells and other alternatives are already achieving some of the goals for which embryonic stem cells have been proposed and new clinical uses are constantly being discovered. In that light, I think the National Bioethics Advisory Commission made a very interesting statement, that because of the claims of human life and the respect it deserves, that using these embryos for research is completely unjustified if there are morally less problematic alternatives available.

We know even from the NIH report, which was written by people with a particular ideological drive on this issue—it is, after all, the NIH that first recommended, its institutes unanimously recommended in 1994, a full range of Federal funding for destructive embryo research, including research that involves the special creation of embryos solely for research, which has been condemned by many others.

Even the NIH has conceded that adult stem cells are extremely useful and it is now unpredictable which will be most useful for various purposes. If that is the case, in this period of uncertainty it would be morally irresponsible to cross this moral Rubicon and begin acting as though there is no moral difference. Obviously, if embryo research is the last resort, if even President Clinton's advisors said that other avenues need to be exhausted first, then pursuing both at the same time and forcing millions of morally opposed taxpayers to fund it would be to force all the taxpayers to act as though they agree the that embryo is absolutely nothing in terms of moral status.

In fact, it would force us to pretend to agree with the chairman of the Juvenile Diabetes Foundation, who testified last year that the human embryo is more like a goldfish than a human being.

A subtly different argument from the argument that the embryo is not a life has been offered by those who simply say these would

be discarded anyway. The problem with that argument is that if it is an argument that is supposed to presuppose that other embryos really are human lives that deserve respect, it articulates a moral principle that is horrific for every patient subjected to human research.

Currently we do not kill terminally ill patients for their organs, though they will die soon anyway, and Federal law prohibits federally funded researchers from doing any harm to an unborn child slated for abortion, though that child will soon be discarded anyway.

In any case, the claim that the embryos to be destroyed under the NIH guidelines will necessarily be destroyed anyway is actually a canard. That is not in the guidelines. It covers embryos found to be in excess of clinical need and the option of destroying them for their stem cells clearly stated should be offered as an option along side all the other options, including the option of adopting from another couple or saving for one's own later use.

Finally, I think that the argument that somehow by funding this we prevent more of it is a bizarre argument to me, because already the NIH guidelines in its limited proposal for this has quickly led to a slippery slope in which we are discussing legislation to fund not only the destruction of these embryos for their cells, but the use of specially created embryos for research as well, as in the Specter-Harkin bill.

PREPARED STATEMENT

Obviously, once you fund a little of this you get a lot more of it. The only thing we can be sure of if we fund it is that there is going to be a lot of destruction going on to benefits that are at best speculative and we think can be better met by other research that destroys no one.

We think that the President and the Congress should unite to support promising medical research that everybody can live with.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF RICHARD M. DOERFLINGER

I am Richard M. Doerflinger, Associate Director for Policy Development at the Secretariat for Pro-Life Activities, United States Conference of Catholic Bishops. I am grateful for this opportunity to present the Catholic bishops' grave concerns on this critically important issue.

In our view, forcing U.S. taxpayers to subsidize research that relies on deliberate destruction of human embryos for their stem cells is illegal, immoral and unnecessary.

It is illegal because it violates an appropriations rider (the Dickey amendment) passed every year since 1995 by Congress. That provision forbids funding "research in which" human embryos (whether initially created for research purposes or not) are harmed or destroyed outside the womb.[1] National Institutes of Health guidelines approved by the Clinton Administration nonetheless give researchers detailed instructions on how to obtain human embryos for destructive cell harvesting, if they wish to qualify for federal grants in "human pluripotent stem cell research."[2] Clearly, obtaining and destroying embryos is an integral part of this project, even if the

[1] Section 510 of the Labor/HHS appropriations bill for fiscal year 2001, H.R. 5656 (enacted through Section 1(a)(1) of H.R. 4577, the fiscal year 2001 Consolidated Appropriations Act, Public Law 106–554).

[2] National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells, 65 Fed. Reg. 51976–81 (August 25, 2000).

specific act of destroying embryos does not directly receive federal funds. By implementing these guidelines, the federal government would encourage researchers to conduct destructive embryo experiments that are punishable as felonies in some states.[3]

This proposal is immoral because it violates a central tenet of all civilized codes on human experimentation beginning with the Nuremberg Code: It approves doing deadly harm to a member of the human species solely for the sake of potential benefit to others. The embryos to be destroyed by researchers in this campaign are at the same stage of development as embryos in the womb who have been protected as human subjects in federally funded research since 1975.[4] President Clinton's National Bioethics Advisory Commission (NBAC) and its 1994 predecessor, the NIH Human Embryo Research Panel, conceded that the early human embryo is a form of developing human life that deserves our respect.[5] Treating human life as mere research material is no way to show respect.

Finally, this proposal is unnecessary because adult stem cells and other alternatives are already achieving some of the goals for which embryonic stem cells have been proposed, and new clinical uses are constantly being discovered.[6]

In our view, human life deserves full respect and protection at every stage and in every condition. The intrinsic wrong of destroying innocent human life cannot be "outweighed" by any material advantage—in other words, the end does not justify an immoral means. Acceptance of a purely utilitarian argument for mistreating human life would endanger anyone and everyone who may be very young, very old, very disabled, or otherwise very marginalized in our society. However, even the Clinton Administration's bioethics advisors, who denied human embryos the moral status of "person," concluded that they could only be destroyed for research as a last resort, if no alternative course existed.[7]

It cannot be denied that these alternatives are available. To be sure, further study will be needed to determine their full potential. But to fund destructive embryo research now, alongside these morally acceptable alternatives, would be to deny any moral status at all to human embryonic life. For that is what we would do if there were no moral issue at stake. Funding embryonic stem cell research here and now will force all taxpayers to act as though they agree with the international chairman of the Juvenile Diabetes Foundation that human embryos have no more value or dignity than a goldfish.[8]

This view of the human embryo as a goldfish has apparently garnered support from some members of Congress who have generally opposed abortion. Their claim is that human life does not begin until placed in a mother's womb. Biologically, however, this is an absurd claim. An embryo's development is directed completely from within—the womb simply provides a nurturing environment. Scientists tell us it would be technically possible to nurture a human embryo in a man's body by abdominal pregnancy, or in a mammal of another species, or even (someday) in an artificial womb.[9] Upon being born could such a person morally be killed for his or her stem cells, because he or she never lived inside a woman's womb?

A subtly different argument has also emerged to try to justify using embryos from fertility clinics for destructive experiments. While human embryos ordinarily deserve respect, goes this argument, these particular embryos do not, because they "would be discarded anyway" by their parents. But this is, to say the least, fallacious reasoning. If parents were neglecting or abusing their child at a later stage, this would provide no justification whatever for the government to move in and help

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[3] See Fact Sheet, "The NIH Proposal for Stem Cell Research Is a Crime," www.usccb.org/prolife/issues/bioethic/states701.htm.

[4] Federal regulations on Protection of Human Subjects include protections for the human fetus, "from the time of implantation." 45 CFR §46.203 (c). Implantation generally begins about six days after fertilization, at the blastocyst stage of human development.

[5] "We believe that most Americans agree that human embryos should be respected as a form of human life . . ." National Bioethics Advisory Commission (NBAC), *Ethical Issues in Human Stem Cell Research* (September 1999) at 2.

[6] See Fact Sheet, "*Current* Clinical Use of *Adult* Stem Cells to Help Human Patients," www.usccb.org/prolife/issues/bioethic/adult701.htm.

[7] "In our judgment, the derivation of stem cells from embryos remaining following infertility treatments is justifiable only if no less morally problematic alternatives are available for advancing the research." NBAC, note 5 supra at 53.

[8] "The embryos that are being discussed, according to science, bear as much resemblance to a human being as a goldfish." Mary Tyler Moore, Testimony on behalf of the Juvenile Diabetes Foundation before the Senate Appropriations Subcommittee on Labor, Health and Human Services and Education, September 14, 2000.

[9] Testimony of Lee M. Silver, Ph.D., before the House Government Operations Subcommittee on Human Resources and Intergovernmental Relations, July 14, 1988; R. Rowland, *Living Laboratories: Women and Reproductive Technologies* (Indiana University Press 1992) at 288–9.

destroy the child for research material. We do not kill terminally ill patients for their organs, although they will die soon anyway, or even harvest vital organs from death row prisoners, although they will be put to death soon anyway. Federal law prohibits federally funded researchers from doing any harm to an unborn child slated for abortion, though that child will soon be discarded anyway (see 42 USC §289g). If people's value depends entirely on the extent to which other people "want" them, they have no inherent value at all. So on reflection, this argument ultimately reduces to the argument of "embryo as goldfish."

The argument also rests on a false premise. The embryos slated for destructive research under the NIH guidelines are those deemed to be "in excess of clinical need" by fertility clinics. This simply means that they are not needed or wanted by their parents for reproduction at present. Parents in this situation are routinely offered several options, including: saving the embryos for possible later use (by far the most frequently chosen), discarding them, or donating them to another couple so they can have a child. The NIH guidelines require that these parents be asked to consider donating their embryos for destructive cell harvesting at the same time that they are offered these other options.[10] Some couples who would otherwise have allowed their embryonic children to live—in their own family or another—will instead have them killed for government research. That is why the adoptive couples of some of these former "frozen embryos" have filed suit against the guidelines.[11]

We have presented our position on this issue at length in other testimony.[12] In the remainder of this testimony we would like to comment on recent developments, including new evidence that proponents of destructive embryo research have misrepresented or distorted the facts to serve their political goal.

NEW DEVELOPMENTS IN ALTERNATIVES TO EMBRYONIC STEM CELL RESEARCH

Since we testified before this subcommittee in 1999, startling advances have been made in adult stem cell research and other non-embryonic avenues for repairing or replacing damaged organs and tissues. The field of "tissue engineering" using adult cells has exploded as researchers move toward rebuilding ears, tracheas, and even hearts.[13] Adult stem cells have successfully treated hundreds of thousands of patients with cancer and leukemia; they have repaired damaged corneas, restoring sight to people who were legally blind; they have healed broken bones and torn cartilage in clinical trials; they are being used to help regenerate heart tissue damaged by a cardiac arrest.[14] Adult bone marrow stem cells were responsible for the first completely successful trial of human gene therapy, helping children with severe combined immunodeficiency disease to recover an immune system and safely leave their sterile environment for the first time.[15] Adult cells from a young paraplegic woman's own immune system, injected into the site of her spinal cord injury, have apparently cured her incontinence and enabled her to move her toes and legs for the first time—"generating hope for those with spinal-cord injuries around the world," as one news report observes.[16]

Finally, adult pancreatic islet cells from cadavers have been used to reverse juvenile diabetes in fifteen patients, and further human trials are being planned at several centers in the United States. At the annual meeting of the American Diabetes Association on June 24, researchers announced that all patients benefited from the transplants, and nine have remained "insulin free" for a median period of eight months—with some patients requiring no injections for up to two years.[17]

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[10] Parents must be asked about having their embryos destroyed for federally funded stem cell research "only *at the time* of deciding the disposition if embryos in excess of the clinical need." National Institutes of Health, note 2 supra at 51980 (emphasis added). Proponents seem to assume that the option of destructive research is to be offered after parents have decided to have the embryos discarded. Read strictly, the guidelines actually forbid clinics to do this.

[11] *Nightlight Christian Adoptions* v. *Thompson* (D.D.C. filed March 8, 2001).

[12] For past testimony, including our public comments on the NIH guidelines and our testimony before this subcommittee in December 1998 and January 1999, see: www.usccb.org/prolife/issues/bioethic/biotest.htm.

[13] J. D'Agnese, "Brothers with heart," *Discover*, July 2001 at 36–43, 102.

[14] For documentation see www.stemcellresearch.org, the Web site of Do No Harm: The Coalition for Americans for Research Ethics, especially "Current Clinical Applications of Adult Stem Cells" (www.stemcellresearch.org/currentaps.pdf) and "Letter to Ruth Kirschstein, Ph.D., Acting Director of the National Institutes of Health" (www.stemcellresearch.org/kirschstein.pdf).

[15] M. Cavazzana-Calvo et al., "Gene Therapy of Human Severe Combined Immunodeficiency (SCID)–X1 Disease," 288 *Science* 669–72 (28 April 2000).

[16] K. Foss, "Paraplegic regains movement after cell procedure," *The Globe and Mail* (Toronto), June 15, 2001 at A1.

[17] E. Ryan et al., "Glycemic Outcome Post Islet Transplantation," Abstract #33-LB, Annual Meeting of the American Diabetes Association, June 24, 2001. See: http://38.204.37.95/am01/AnnualMeeting/Abstracts/NumberResults.asp?idAbs=33-LB.

Hailed by experts as a "remarkable advance," this breakthrough has also received enthusiastic attention from Lee Ducat, founder of the Juvenile Diabetes Foundation (JDF). "There's still a lot to be learned, but this is the most optimistic I've been in 30 years," she says. "To take patients who are terribly ill and going in and out of shock and give them a normal life . . . this is an unbelievable result. They say they never knew what feeling normal is all about."[18]

Yet this good news has gone largely unnoticed by the current leadership of the JDF. Instead the organization is focused on diverting funds toward a misleading ad campaign to persuade Americans to support killing human embryos for their stem cells.

Neglect—even misstatement—of recent scientific data was also evident in last year's testimony before this subcommittee by the Christopher Reeve Paralysis Foundation. Mr. Reeve, on behalf of the Foundation, testified that adult stem cells are no substitute for embryonic cells because they cannot be "pluripotent" but are confined to a narrow range of specialization. Yet a few weeks after that hearing, researchers funded by the NIH and the Christopher Reeve Paralysis Foundation published a study indicating that adult bone marrow stem cells "may constitute an abundant and accessible cellular reservoir for the treatment of a variety of neurologic diseases." The first sentence of the published study states: "*Pluripotent* stem cells have been detected in multiple tissues in the adult, participating in normal replacement and repair, while undergoing self-renewal."[19] The authors cite eleven other studies in support of this observation. Their article, prepared under the aegis of Mr. Reeve's foundation, was received for publication in March 2000, before Mr. Reeve testified in April that adult stem cells cannot be pluripotent.

An author of that study, Dr. Darwin Prockop, told this subcommittee last year that the implications of his work should not be overstated and that he himself supports funding both embryonic and adult stem cell research. However, medical and patient groups have now tilted the pendulum so far toward outright denial of the facts about the promise of adult stem cell research that Dr. Prockop recently felt obliged to correct the record. Responding to an article that questioned the benefits of adult stem cells, he notes:

"More than 20 years ago, Friedenstein and then others grew adult stem cells from bone marrow called mesenchymal stem cells or marrrow stronal cells (MSCs). MSCs differentiate into bone, cartilage, fat, muscle, and early progenitors of neural cells. Human MSCs can be expanded up to a billionfold in culture in about 8 weeks. Preliminary but promising results have appeared in the use of MSCs in animal models for parkinsonism, spinal cord defects, bone diseases, and heart defects. Also, several clinical trials are in progress. In addition, there are promising results with other adult stem cells that perhaps we may yet learn how to grow effectively."[20]

Perhaps the most troubling and unwarranted fixation on embryonic stem cells to the exclusion of all other approaches has been exhibited by the Parkinson's Action Network (PAN). This group has declared that it actively opposes a new bill introduced by Congressman Chris Smith, which would authorize $30 million a year in new funding for stem cell research and establish a national stem cell bank for research and possible treatments (Responsible Stem Cell Research Act of 2001, H.R. 2096). While this bill places no restrictions on embryonic stem cell research—indeed, does not mention such research one way or the other—PAN believes that this much-needed additional funding for promising medical research must be rejected because it does not include stem cells obtained by destroying embryos. By this logic PAN would have to oppose all current NIH funding for Parkinson's research, which has never included funding for embryonic stem cell research.

NEW DISAPPOINTMENTS IN EMBRYONIC STEM CELL RESEARCH

In the past two years, initial enthusiasm over embryonic stem cells has been dampened in the scientific community by some sober realizations, even as patient groups organize public campaigns based on earlier assumptions.

First, these cells are not as easy to maintain in the laboratory as once thought. Researchers call them "tricky" and "more tedious to grow" than their mouse coun-

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[18] M. McCullough, "Islet transplants offer hope that diabetes can be cured," *Philadelphia Inquirer*, June 22, 2001 at A1.

[19] D. Woodbury et al., "Adult Rat and Human Bone Marrow Stromal Cells Differentiate Into Neurons," 61 *J. of Neuroscience Research* 364–70 (2000) at 364 (emphasis added).

[20] D. Prockop, "Stem Cell Research Has Only Just Begun" (Letter), 293 *Science* 211–2 (13 July 2001) (citations omitted).

terparts, as well as "really difficult" to direct toward more specialized cells.[21] The dream of "immortal" cell lines that will easily provide unlimited supplies of any kind of tissue remains a dream.

Second, a new study of problems in cloning suggests that embryonic stem cells are "surprisingly genetically unstable" in mice and perhaps in humans as well. This "may complicate efforts to turn the cells into cures," and interfere with efforts to produce all-purpose cell lines that could reliably become tissue of any desired type. "You may have to establish hundreds of lines to get the few you'd want to have," Dr. John Gearhart of Johns Hopkins University now says. Establishing hundreds of these cell lines could require destroying many thousands of human embryos, and replenishing them with thousands more when the original cell lines become too unstable for further use. Perhaps most troubling is the news that these researchers deleted from their final paper a reference to this problem, believing that any public acknowledgment of such setbacks has become too "politically sensitive."[22] We can only wonder how much of this kind of information is being withheld without detection. We have reached a stage in this discussion where, on the side supporting destructive embryo research, science is becoming subservient to politics.

Third, the chief advantage universally cited for embryonic stem cells—their ability to grow and differentiate into all the more than 200 kinds of cells and tissues in the human body—is proving to be a major disadvantage for transplantation into living bodies. For it is very difficult to make these cells stop turning into all kinds of cells and tissues. In recent studies, embryonic stem cells (or partially differentiated cells arising from them) "stayed in a disorganized cluster, and brain cells near them began to die."[23] Says bioethicist Glenn McGee, who supports of embryonic stem cell research:

"The emerging truth in the lab is that pluripotent stem cells are hard to rein in. The potential that they would explode into a cancerous mass after a stem cell transplant might turn out to be the Pandora's box of stem cell research."[24]

By contrast, though non-embryonic stem cells seem harder to direct to form tissues of different categories, they seem much more docile to their environment. Upon reaching a particular kind of tissue, they receive signals as to the kind of tissue needed and produce only that tissue. They may be "easier to manage," and therefore far safer for clinical use in humans, than embryonic cells.[25] After all, adult stem cells are already found throughout the human body, already provide a built-in repair kit for repairing and regenerating human tissue, and have already safely treated hundreds of thousands of patients. Understanding and stimulating this natural ability may be a far more promising avenue than efforts to harness and control cells that simply do not belong in an adult body in the first place—cells with a tendency to form tumors, in an apparent effort to turn back into a complete embryo.

The kind of exaggerated claims now made for embryonic stem cells have been seen in this Congress before. A decade ago it was fetal tissue from abortions that was hailed as the magic bullet that might cure diabetes, Parkinson's disease and many other conditions in a few years if only federal funds were provided. By the time such funds were approved in 1993, however, it was already becoming clear that fetal tissue from abortions would be largely useless in treating diabetes. Millions of taxpayers' dollars were diverted toward fetal tissue transplant trials for Parkinson's disease—and the final results were not only disappointing but "devastating," according to the New York Times. The implants "failed to show an overall benefit," and in 15 percent of the patients actually produced "nightmarish" symptoms as the immature cells produced dopamine in uncontrollable amounts.[26] The chief result of the campaign for fetal tissue research by some Parkinson's disease groups is that a significant number of Parkinson's patients may now be incurably worse off than before.

Will embryonic stem cells prove to be equally disappointing or even disastrous? No one knows. However, a tragic occurrence following one particular fetal tissue transplant for Parkinson's disease should give us pause. Some of the tissue placed

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[21] G. Vogel, "Stem Cells: New Excitement, Persistent Questions," 290 *Science* 1672–4 (1 December 2000) at 1674.

[22] R. Weiss, "Clone Study Casts Doubt on Stem Cells," *The Washington Post*, July 6, 2001, A1 and A9.

[23] G. Vogel, note 21 supra at 1674.

[24] E. Jonietz, "Innovation: Sourcing Stem Cells," *Technology Review*, January/February 2001, http://209.58.177.220/articles/jan01/innovation_jonietz_printable.html.

[25] G. Vogel, "Can Old Cells Learn New Tricks?", 287 Science 1418–9 (February 25, 2000) at 1419; L. Johannes, "Adult Stem Cells Have Advantage Battling Disease," *Wall Street Journal*, April 13, 1999 at B1.

[26] G. Kolata, "Parkinson's Research Is Set Back By Failure of Fetal Cell Implants," *The New York Times*, March 8, 2001 at A1, A12.

in this man's brain may have been from an earlier gestational age than is customary in American clinical trials—that is, it may have been more embryonic than fetal in nature. Within two years after the transplant this man died mysteriously—and an autopsy revealed that masses of "nonneural tissue" such as skin and hair had filled the ventricles of his brain and cut off his breathing. Researchers theorized that this tissue may have remained "pluripotent" and differentiated uncontrollably to cause the patient's death.[27]

At the very least, past experience argues in favor of greater humility than some researchers and organizations are now showing in their campaign for destructive embryo research. To quote two bioethicists who do not oppose such research on moral grounds, "much of the hype that surrounded the debate about the clinical value of fetal tissue implants was exactly that—hype. This ought to be kept in mind by those now engaged in the debate over stem cell research."[28]

THE SLIPPERY SLOPE IN ACTION

Finally, recent developments highlight a point made by opponents of embryonic stem cell research for years: Once our consciences are numbed to the moral wrong of using so-called "spare" human embryos for research, our society will move on to even more egregious abuses. The Jones Institute for Reproductive Medicine in Virginia has announced that it is using donated eggs and sperm to create human embryos solely to destroy them for stem cell research.[29] Moreover, Advanced Cell Technology (ACT) in Massachusetts has announced it is trying to make human embryos by somatic cell nuclear transfer (cloning) for the same purpose.[30]

In the past, this further step—that of creating life in the laboratory for the sole purpose of destroying it—was supported by the NIH, but widely condemned even by abortion supporters in Congress and editorial boards across the country. President Clinton refused funding for this approach, and the Washington Post editorialized:

"The creation of human embryos specifically for research that will destroy them is unconscionable . . . [I]t is not necessary to be against abortion rights, or to believe human life literally begins at conception, to be deeply alarmed by the notion of scientists' purposely causing conceptions in a context entirely divorced from even the potential of reproduction."[31]

Despite this strong consensus against creating embryos to destroy them, those actually involved in embryo research no longer see any serious ethical problem in it. Now the American Society for Reproductive Medicine (ASRM), which published the Jones study in its journal, says the study is "not inappropriate" and is in accord with ASRM's ethical guidelines. Some even argue that such research is morally superior to the use of "spare" embryos, because the egg and sperm donors understand from the beginning what the embryos will be used for.

Similarly, when ACT testified before this subcommittee in December 1998, it was virtually alone in insisting that success in embryonic stem cell research would require moving on to human cloning to make genetically matched tissues for each patient. However, the nation's leading for-profit group promoting embryonic stem cell research, the Geron Corporation, soon acquired the Roslin Institute in Scotland to combine its own expertise in embryonic stem cell research with Roslin's expertise in cloning.[32] The president of Geron recently testified to a House subcommittee that allowing the special creation of human embryos by cloning will be "essential" to the future of embryonic stem cell research.[33]

These groups have engaged in embryo research long enough to deaden all sensitivity to the fact that they are dealing with human life. If the federal government

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[27] R. Folkerth and R. Durso, "Survival and proliferation of nonneural tissues, with obstruction of cerebral ventricles, in a parkinsonian patient treated with fetal allografts," 46 *Neurology* 1219–25 (May 1996).

[28] A. Caplan and G. McGee, "Fetal Cell Implants: What We Learned," *Hastings Center Report*, May-June 2001 at 6.

[29] S. Stolberg, "Scientists Create Scores of Embryos to Harvest Cells," *The New York Times*, July 11, 2001 at A1.

[30] A. Regalado, "Experiments in Controversy," *Wall Street Journal*, July 13, 2001 at B1.

[31] Editorial, "Embryos: Drawing the Line," The *Washington Post*, October 2, 1994 at C6.

[32] L. Krieger, "Clone Coup: Geron Buys 'Dolly' Biotech Pioneer for Technology That May Have Worldwide Medical Use," *San Jose Mercury News*, May 5, 1999 at 1C.

[33] "Somatic cell nuclear transfer research is essential if we are to achieve our goals in regenerative medicine." Testimony of Thomas Okarma before the House Energy and Commerce Subcommittee on Health, June 20, 2001. During the question session at this hearing, Dr. Okarma made it clear that he was speaking of the use of this technology to create genetically tailored human embryos for research.

funds even a limited amount of research that relies on destroying human embryos, this deadening of consciences will occur on a wider scale and with government approval.

The Coalition for the Advancement of Medical Research, which favors federal funding of embryonic stem cell research, has argued that these developments actually show that the Bush Administration should proceed with the funding. To stop such abuses, goes the argument, the federal government must fund embryo research so it will have the authority to set limits.[34]

But the first groups to make this claim were groups that favor destructive embryo research, including groups closely associated with the Jones Institute's abuses. ASRM, which has given the ethical "green light" to the Jones study and published the results in its own journal, is an active member of the Coalition for the Advancement of Medical Research. So we are being told how to prevent special creation of embryos by the leading groups that favor and even perform it!

The argument that one must fund this research to regulate it is also absurd on its merits. The Jones study was done entirely with private funds, because for five years Congress has clearly prohibited funding of all destructive embryo research. If the federal government begins to fund some destructive research, it will be able to set standards for the research it chooses to fund, but the privately funded Jones study will remain untouched. In fact, such a policy change will signal that the government is moving in the Jones Institute's direction on this issue. It will soon become apparent that the government must fund research involving special creation of embryos for research—that is, must fund the very abuse it claims to oppose—in order to set standards for such research. Even then, those choosing not to obey such standards will simply conduct that part of their research with private funds—and encourage the federal government to catch up with their advanced thinking, as it already will have done on the subject of destroying "spare" embryos. Indeed, supporters of embryo research in Congress have already introduced legislation that could fund research using specially created "research embryos," to take this next step (Stem Cell Research Act of 2001, S. 723).

We know that destructive embryo research can be regulated or even prohibited without funding it. As noted earlier, nine states now ban all such research, whether publicly or privately funded.[35] The state of Virginia itself has banned the use of cloning to make human embryos for research, and is considering a response to the Jones Institute's project for making research embryos by in vitro fertilization.[36] And the Food and Drug Administration, without funding any part of in vitro fertilization, recently wrote to in vitro fertilization clinics engaged in new reproductive techniques to remind them that such technologies, albeit privately funded, are subject to federal regulation.[37]

CONCLUSION

Like the argument that human embryos are not members of the human race, arguments that destroying them is necessary for medical progress or that funding such destruction is needed to prevent broader abuse cannot be sustained. With these arguments out of the way we can return to the real issue at stake: Should the federal government subsidize—and force millions of morally opposed taxpayers to subsidize—research that requires the destruction of innocent human life? We hope that the President and Congress will answer that question in the negative, and will unite instead to support promising medical research that everybody can live with.

Senator HARKIN. Thank you, Mr. Doerflinger.
Dr. Usala.

STATEMENT OF ANTON-LEWIS USALA, M.D., FOUNDER, CHAIRMAN, AND CHIEF SCIENCE OFFICER, ENCELLE, INC.

Dr. USALA. Thank you, Senators.

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[34] Press Release, "Development of Stem Cells from Fertilized Eggs Created for Research Demonstrates Need for Oversight," Coalition for the Advancement of Medical Research, www.stemcellfunding.org/fastaction/news.asp?id=52.

[35] See note 3 supra.

[36] Code of Virginia, §32.1–162.21 and §32.1–162.22 (Enacted 2001); C. Timberg, "Va. to Examine Embryo Research," *Washington Post*, July 14, 2001 at B1.

[37] R. Weiss, "FDA to Regulate Certain Fertilization Procedures," *Washington Post*, July 11, 2001 at A2.

For the record, I would like to state that I resigned as chairman of my company in December and that the views I am about to express are my own as a medical scientist, not those of my company.

I appear before the subcommittee to discuss embryonic stem cell research and alternative technologies that are currently under development in the company I founded. Our focus was to develop a method to regenerate and replace damaged patient tissues as a treatment for various human diseases.

I developed a proprietary scaffolding based on the structure of embryonic tissue scaffolding, to which the adult cells can attach. This proprietary injectable scaffolding has developed apparent—that my company has developed, apparently enables regeneration of a specific kind of tissue called mesenchymal tissue. One of three embryonic germ layers, mesenchymal tissue gives rise to connective tissue, blood vessels, bone, cartilage, and parts of skin.

In pre-clinical animal studies, we have demonstrated regeneration of blood vessels and skin in animals suffering from chronic diabetic and surgical extremity lesions. We are currently nearing completion of our FDA-approved first human clinical trial with what I believe are exciting results. We have not yet submitted the final report to the Food and Drug Administration and the data has not yet been peer reviewed and I would like to make that point for the record.

However, photos of chronic diabetic foot ulcer wounds in some of the patients treated with a single injection of our scaffolding appear to show rapid, well vascularized tissue regeneration and closure of these ulcers within 2 to 8 weeks. These ulcers were refractory to multiple forms of therapy and were unhealed from between 2 and 12 years prior to our treatment.

Several years ago, children with diabetes came to the House and Senate to request lifting the ban on fetal tissue research. At the time, many at the NIH believed that the less differentiated fetal pancreatic cells would be a better source for human transplantation as they should be less immunogenic. This too was hailed as a medical miracle.

Subsequent studies, both in the United States and Europe, demonstrated this not to be the case. Successful transplantation studies in Canada using adult cadaveric pancreas cells have removed fetal tissue sources from the limelight.

Having diabetes 42 of my 43 years, I can bear witness to the fallacy of consensus medical thinking. As a child, I remember my physician telling my mother that multiple NIH-funded studies showed that blood sugar control did not make any difference into whether or not I would develop vascular complications. Indeed, when I was in medical school early in the eighties this same NIH dogma was being taught.

At 10 years of age, I reasoned that nature kept blood sugars within a normal range for a reason and I surreptitiously injected myself with fast-acting insulin at meals to prevent my blood sugar from rising. People and physicians who thought like I did were labeled as extremists. It was not until the early 1990's that reasonably well designed studies demonstrated that in fact blood sugar control is the single largest determinant as to whether a child will develop complications such as kidney failure and blindness. How-

ever, hundreds of thousands of children developed renal failure and died between 1960 and 1990 because of this medical consensus mistake.

As I testified last September before this committee, the mass of cells that begins the process of specific differentiation occurs very shortly after conception. The promotion of a specific and integrated genome pathway results in the beginning of that particular species of animal. The embryos that are fertilized in vitro differentiate and integrate their cellular signals in a specific way that are human. When they acquire rational thought and feeling is as yet debatable. When they are defined as human is not.

All societies are ruled by laws, even unjust societies. The difference between a just and an unjust society is the set of precedents the society chooses to use in establishing its laws. In my view the United States is a uniquely just society, being the first government in the history of humankind where the rights of the individual supersede the perceived right of the State. This is the foundation that was established by the first 10 amendments to our Constitution.

Should human embryonic stem cell research be funded, it will be the first time in U.S. history that the Federal Government has determined the best use for a human being. This would be a cataclysmic paradigm shift. The perceived right of the state will have superseded the right of the individual. Even during the horrific times of slavery, the Federal Government did not fund programs using human beings for state purposes, although clearly individuals did.

Enthusiastic medical consensus on a promising idea does not make any potential therapy a medical breakthrough, and a congressional subcommittee is probably not the ideal forum for discussing the scientific validity of one form of research compared to another. Existing regulatory bodies such as internal review boards and the Food and Drug Administration are better equipped to assess the validity and safety of such data.

However, I am grateful that this subcommittee has taken the time and effort to hear the scientific as well as the societal case regarding human embryonic research. It is one of only a few appropriate forums to link all of these arguments together to best serve the national interest on all levels.

PREPARED STATEMENT

In conclusion, the suffering caused by as yet incurable diseases can more quickly and with more certainty be alleviated by the multiple efforts that do not require a paradigm shift in our national character. Such a paradigm shift would necessarily result from Federal funding of human embryonic stem cell research.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF ANTON-LEWIS USALA

Senators, I appear before this subcommittee to discuss embryonic stem cell research, and alternative technologies that are currently under development in the company I founded. Our focus was to develop a method to regenerate and replace damaged patient tissues as a treatment for various human diseases. I developed a proprietary scaffolding, based on the structure of embryonic tissue scaffolding, to

which adult cells can attach. The hypothesis that we first tested in multiple tissue culture, animal, and toxicology studies, was that upon binding to this embryonic-like structure, patient cells would be signaled to promote areas of the genome that are normally only promoted during embryogenesis and early fetogenesis. During this time, cells that are not committed to becoming a specific kind of cell, explosively differentiate into specialized tissues. As they do, they make connections and are modulated to integrate with all surrounding cells in a manner that is species specific.

The proprietary scaffolding that my company has developed apparently enables regeneration of a specific kind of tissue called mesenchymal tissue. One of the three embryonic germ layers, mesenchymal tissue gives rise to connective tissue, blood vessels, bone, cartilage and parts of skin. In pre-clinical animal studies, we have demonstrated regeneration of blood vessels and skin in animals suffering from chronic diabetic and surgical extremity lesions.

Years are required for an idea to be tested first in the petri dish, then in controlled animal efficacy studies, then in safety studies. Years are required to build the infrastructure to safely and reproducibly build a product for human clinical trials. Immense amounts of time and money are required to efficiently put the pieces into place that will give the Food and Drug Administration confidence that the risks for patients in experimental clinical trials are worth the potential benefit.

My company is currently nearing completion of its first human clinical trial, with what I believe are exciting results. We have not yet submitted the final report to the Food and Drug Administration, and the data have NOT yet been peer reviewed. However, photos of chronic diabetic foot ulcer wounds in some of the patients treated with a single injection of our scaffolding appear to show rapid, well vascularized tissue regeneration, and closure of the ulcers within 2 to 8 weeks. These ulcers were refractory to multiple forms of therapy and were unhealed for 2 to 12 years prior to our therapy.

Yesterday, on the Today show, a segment was aired showing a mother injecting insulin into her four year old diabetic child. The mother stated she was extremely supportive of embryonic stem cell research if it could cure her child. It is not honest to bring before this Committee people such as myself, who have chronic illnesses for which there is no cure, as a valid argument for funding human embryonic stem cell research. There are many alternative paths; and if there is a legal or ethical reason not to conduct this research, public resources can be all the more effectively focused on those alternative paths.

There are private companies in human clinical trials using porcine derived neurons as a treatment for Parkinson's disease. The first project my company embarked upon also utilized porcine tissue sources as a treatment for diabetes. We showed remarkable pre-clinical success in transplanting porcine tissue into diabetic dogs, without immunosuppressive therapy, and maintaining the tissue without rejection. Others in Europe and New Zealand have conducted human clinical trials utilizing microencapsulated porcine tissue. Pre-clinical animal studies utilizing adult human stem cells have to date demonstrated at least as much efficacy as human embryonic stem cells, and the advantages of using embryonic stem cells is only theoretical at this point in time.

There is little data to support, or infer, that embryonic human stem cells have any advantages over adult human stem cells in medical research. As a scientist in the field of human tissue regeneration, it is clear to me that integrating functional new tissue, not simply healthy tissue, into a diseased area requires integration of hundreds if not thousands of signals. Several years ago, children and patients with diabetes came to the House and Senate to request lifting the ban on fetal tissue research. At the time, many at the NIH believed the less differentiated fetal pancreatic tissues would be a better source for human transplantation as they should be less immunogenic. This, too, was hailed as a medical miracle. Subsequent studies, both in the United States, and in Europe, demonstrated this not to be the case, and the successful transplantation studies in Canada, using adult cadaveric pancreatic cells, have removed fetal tissue sources from the limelight.

Having diabetes 42 of my 43 years, I can bear witness to the fallacy of consensus medical thinking. As a child, I remember my physician telling my mother that multiple NIH funded studies showed blood sugar control did not make any difference in whether or not I would develop vascular complications. Indeed, when I was in medical school in the early eighties, this same dogma was being taught.

At ten years of age, I reasoned that nature kept blood sugars within a normal range, and I surreptitiously injected myself with fast acting insulin at meals to prevent my blood sugar from rising (as occurs in patients without diabetes). People who thought like I did were labeled as extremists. It was not until the early 1990's that multiple reasonably well designed studies demonstrated that in fact, blood sugar

control is the single largest determinant as to whether a child will develop complications such as kidney failure and blindness. However, hundreds of thousands of children developed renal failure between 1960 and 1990 because of this medical consensus mistake.

We all agree that the diseases for which cures are sought through embryonic or adult stem research are responsible for a great deal of human suffering, as well as economic cost to the nation. According to the National Bioethics Advisory Commission, most of us also agree that human embryos are deserving of respect. It is for that last reason that these hearings are being held.

As I testified last September before this subcommittee, the mass of cells that begins the process of specific differentiation occurs very shortly after conception. The promotion of a specific and integrated genome pathway results in the beginning of that particular species of animal. The embryos that are fertilized in vitro differentiate and integrate their cellular signals in a specific way that are human. When they acquire rational thought or feeling is as yet debatable; when they are defined as human is not.

The real question before Congress is whether or not this research should be funded by the federal government. Whether it is scientifically valid is not an issue that Congress can resolve—for if there is no legal or ethical issue, it should be considered by the relevant regulatory bodies as any other approach is considered. However, the legal and ethical issues are paramount. As Dr. Frank Young, a former FDA Commissioner and physician scientist says:

"I believe that the only defensible position is that life begins at conception whether in the petri dish or the uterus. To destroy embryos for only potential benefits that are promised to suffering people before the work is done in animals is misleading, inappropriate and in my opinion utilitarian ethics. We do pre-clinical tests of medicines in animals rather than rush into humans to avoid mistakes as much as possible. Why rush into experiments or trials with ES before completing animal studies and exploring adult stem cells?"

As I said before this subcommittee in September, all societies are ruled by law, even unjust societies. The difference between a just and an unjust society is the set of precedents the society chooses to use in establishing its law. In my view, the United States is a uniquely just society, being the first government in the history of humankind where the rights of the individual supersede the perceived right of the State. This is the foundation that was established by the first ten amendments to our Constitution. Should human embryonic stem cell research be funded, it will be the first time in U.S. history the Federal government has determined the best "use" for a human being. This would be a cataclysmic paradigm shift. The perceived right of the State will have superseded the right of the individual. Even during the horrific times of slavery, the Federal Government did not fund programs using human beings for State purposes (although clearly individuals did).

Enthusiastic medical consensus on a promising idea does not make any potential therapy a medical breakthrough, and a congressional subcommittee is probably not the ideal forum for discussing the scientific validity of one form of research compared to another. Existing regulatory bodies, such as Internal Review Boards and the Food and Drug Administration, are better equipped to assess the validity and safety of such research data. However, I am grateful that this subcommittee has taken such time and effort to hear both the scientific, as well as the societal, case regarding human embryonic research. It is one of only a few appropriate forums to link all of these arguments together to best serve the national interest on all levels.

In my view, the suffering caused by as yet incurable diseases, can more quickly and with more certainty, be alleviated by the multiple efforts that do not require a paradigm shift in our national character. Such a paradigm shift would necessarily result from Federal funding of human embryonic stem cell research.

Senator HARKIN. Dr. Usala, thank you very much.

Now we will turn to Dr. Gibbons. Dr. Gibbons.

STATEMENT OF WILLIAM E. GIBBONS, M.D., CHAIRMAN, JONES INSTITUTE FOR REPRODUCTIVE MEDICINE

Dr. GIBBONS. Thank you. My name is William Gibbons. I am chairman of the Department of Obstetrics and Gynecology at Eastern Virginia Medical School, within which resides the Jones Institute of Reproductive Medicine. I am here today with Dr. Susan Lanzendorf, the lead scientist on the recently published work con-

cerning the experience of the Jones Institute with human stem cells. Dr. Lanzendorf and I would like to thank the committee for the opportunity to participate in the dialogue concerning the use of human stem cells.

I am a reproductive endocrinologist. Dr. Lanzendorf is a Ph.D. reproductive scientist. We are not here today to indicate that we have all of the answers regarding this very complex scientifically and ethically challenging process. The Jones Institute has initiated some studies involving human embryonic stem cells, research which we are hopeful may lead to the realization that the potentially staggering benefits of stem cell therapy to many patient conditions.

This project was initiated after multiple levels of input from bioethicists, clerics, lay leaders, and legal scholars. It was debated at all levels of our institution, including the multidisciplinary approval of the institutional review board at the Eastern Virginia Medical School.

Was there unanimity? No. Was there consensus? Yes.

In addition, we have followed the guidelines of committees which have included the late 1970's advisory panel to the Department of Health and Human Services, the ethics panel of the American Society of Reproductive Medicine, and the 1994 Special Panel to the National Institutes of Health.

The path chosen by the Jones Institute was done for its clarity of informed consent, psychological assessment of participants, and to optimize the medical success by focusing on a volunteer population that was not infertile and was younger than our infertile population, as oocyte and egg quality is dependent upon a woman's age.

PREPARED STATEMENT

To see the clinical benefits of this process, it is going to require tremendous resources, perhaps best coming from both the public and the private sector. Before Dr. Lansdorf speaks to her results, I would ask this powerful forum to allow the continuation of this controversial, but critically important, research.

Thank you. Dr. Lanzendorf.

[The statement follows:]

PREPARED STATEMENT OF WILLIAM E. GIBBONS

My name is William E. Gibbons, Chairman of the Department of Obstetrics and Gynecology at the Eastern Virginia Medical School, within which resides the Jones Institute for Reproductive Medicine. I am here today with Dr. Susan Lanzendorf, the lead scientist on the recently published work concerning the experience of the Jones Institute with stem cells. Dr. Lanzendorf and I would like to thank the committee for the opportunity to participate in the dialogue concerning the use of human stem cells.

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To see the clinical benefits from this process it is going to require tremendous resources, perhaps best coming from both the public and private sectors. Before Dr. Lanzendorf speaks to her results I would ask this powerful forum to allow the continuation of this controversial, but critically important research.

Senator HARKIN. Thank you, Dr. Gibbons.

Dr. Lanzendorf.

STATEMENT OF SUSAN LANZENDORF, Ph.D., EASTERN VIRGINIA MEDICAL SCHOOL

Dr. LANZENDORF. Thank you for this opportunity to discuss our work with human embryonic stem cells. As Dr. Gibbons has explained, I am a reproductive scientist and my main area of interest is fertilization and the study of early stages of embryo development.

In the mid-1990's it became clear that science was moving forward in the potential uses of embryonic stem cells. Embryonic stem cells were being produced in many different animal species and it was becoming clear that they may one day provide a means for curing numerous diseases. My colleagues and I joined many scientists around the world who began evaluating ways to study human stem cells.

Some scientists directed their efforts toward harvesting embryonic germ cells from aborted fetuses, evaluating them for their ability to develop into different cell types. Other investigators chose to initiate embryonic stem cell lines from human embryos obtained following infertility treatment.

In 1994 we also began evaluating methods for initiating human embryonic stem cell lines. We also looked at embryos donated by infertile couples as a source of study material. However, we found that few such embryos existed at our center. While it is true that many couples no longer wishing to store their embryos do request that they be destroyed, it is usually their wish that the embryos be discarded without further evaluation. Therefore, these embryos would not be available for embryonic stem cell research.

Another option that we evaluated was the use of donated gametes for the production of embryos, from which we could harvest the stem cells. The evaluation of this possible source was not entered into lightly and the debates and discussions that followed happened over a number of years. In fact, it was about 3 years from the time we began the discussion to the performance of the first egg retrieval.

The study published in Fertility-Sterility was solely investigational. It was our goal to evaluate the laboratory conditions required to produce and maintain human embryonic stem cell lines. The fact that the embryos used in these early studies were obtained from healthy, fertile volunteers most certainly aided us in our studies. These findings have also allowed us to modify our techniques and obtain institutional approval for further studies to in-

vestigate how human embryonic stem cell may one day cure diseases.

The use of donated gametes to produce embryonic stem cells was the path we chose to begin our investigation. I personally feel that this method is ethical in that the donors of the gametes specifically consent to what they are being used for and that the embryos that are produced were never done so for the purpose of creating an individual. However, I also understand that there are other avenues available for the production of human stem cells.

PREPARED STATEMENT

Over the past week I have been amazed at the number of individuals struggling with diabetes, spinal cord injury, and other conditions who have contacted by colleagues and me offering to donate their gametes and embryos to further this research. Regardless of how it progresses, we urgently request that resources be made available to continue the research and endeavors of the scientist community in the area of human embryonic stem cells.

[The statement follows:]

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gametes and embryos to further this research. Regardless of how it progresses, we urgently request that resources be made available to continue the research endeavors of the scientific community in the area of human embryonic stem cells.

Senator HARKIN. Thank you very much, Dr. Lanzendorf.

Now Dr. Krause.

STATEMENT OF DIANE KRAUSE, M.D., Ph.D., ASSOCIATE PROFESSOR, YALE UNIVERSITY

Dr. KRAUSE. Chairman Harkin, ranking member Specter, and members of the Senate Appropriations Committee: I am Dr. Diane Krause. I am an Associate Professor at Yale University School of Medicine, where I work on adult-derived stem cells. My objective here today is to describe why Federal funds need to be applied to embryonic stem cell research. I am speaking not only for myself, but also for other members of the scientific and medical community, and specifically on behalf of the American Society of Hematology, which has over 10,000 members united by their commitment to understanding and curing blood disorders.

Recently, my colleagues and I published data providing the strongest evidence yet that adult stem cells may be used to repair multiple organs. We showed that in mice adult-derived bone marrow cells make not only blood, as was expected, but also produce mature cells of the liver, the lung, the intestine, and the skin.

While I am very excited about this research, it is important that the subcommittee understand that adult stem cell research is not a substitute for embryonic stem cell research. I am deeply concerned that people seeking to end Federal funding for human embryonic stem cell research are using my data as justification for discontinuing this Federal funding. This interpretation is not only stunningly premature, but potentially undermines the development of adult stem cell therapeutic options. In fact, the progress made in studying adult human stem cells relies on what has been learned from embryonic stem cell studies.

I would like to discuss the importance of embryonic stem cell research and the need for the administration to allow Federally funded embryonic stem cell studies to proceed. It is my testimony that these two areas of research together will lead to effective and safe treatments for life-threatening diseases.

There are three main reasons why embryonic stem cells need to be funded.

First, embryonic stem cells are unique in that they can be grown in vitro, outside the body, and maintain the capacity to become any type of cell in the body. In contrast, adult stem cells have not yet been grown in vitro and it is not yet known whether adult stem cells have the same ability as embryonic stem cells do to become all cell types.

Second, in order for scientific discovery to continue rapidly in this field, both adult and embryonic stem cells will need to be studied and compared. At present, we can obtain far more information from embryonic stem cells, which are the experts in versatility, than from rare adult-derived cells.

Third, no one can predict which line of investigation will lead to development of effective and safe treatments for human diseases. In fact, it is likely that critical therapies for different diseases will derive from different research avenues. To eliminate one avenue

simply because the other has begun to show promise is to speculate on the basis of too little data on matters which may be life-threatening or life-preserving for large numbers of people.

I urge you to take into consideration the long-term objectives of embryonic stem cell research, to cure and eliminate life-threatening diseases. Any possible compromise, such as that attributed to the administration, that allows Federally funded research using only existing cell lines, is far too limiting for multiple reasons. Perhaps the most important reason is that scientists need to compare multiple cell lines in order to better understand the common factors that give embryonic stem cells their incredible versatility.

PREPARED STATEMENT

In closing, embryonic stem cell research should receive Federal funding because work on these cells is invaluable and work on adult-derived stem cells is just beginning. To close off one avenue because of premature assumptions about the other is to play odds with people's lives.

Thank you very much for providing me this opportunity to speak with you.

[The statement follows:]

PREPARED STATEMENT OF DR. DIANE KRAUSE

Chairman Harkin, Ranking Member Specter, and members of the Senate Appropriations Subcommittee: I am Dr. Diane Krause and I am an associate professor at Yale University School of Medicine where I work on adult stem cells. My objective here today is to describe why Federal funds need to be applied to embryonic stem cell research. I am speaking not only for myself, but also for other members of the scientific and medical community and specifically on behalf of the American Society of Hematology which has over 10,000 members united by their commitment to understanding and curing blood disorders.

My colleagues and I recently published data providing the strongest evidence so far that adult stem cells could be used to repair multiple organs. We showed that, in mice, adult-derived bone marrow cells make not only blood, as expected, but also produce mature cells of the liver, the lung, the intestine and the skin.

While I am very excited about this research, it is important that the Subcommittee understand that adult stem cell research is not a substitute for embryonic stem cell research. I am deeply concerned that people seeking to end federal funding for human embryonic stem cell research have inappropriately used my data as justification for discontinuing federal funding for embryonic stem cell research. This interpretation is not only stunningly premature, but potentially undermines the development of adult stem cell therapeutic options.

In fact, the progress made in studying adult stem cells relies on what has been learned from embryonic stem cell studies. Today I would like to discuss the importance of embryonic stem cell research and the need for the Administration to allow federally funded embryonic stem cell studies to proceed. It is my testimony that these two areas of research together will lead to effective and safe treatments for life-threatening diseases.

We all agree that it would be optimal if we could bypass this controversial issue of using embryonic stem cells by using adult derived stem cells exclusively. However, we also agree that it is important to develop treatments and cures for human diseases and progress toward this goal will be slowed considerably if embryonic stem cell work is inhibited!

There are three main reasons why embryonic stem cell studies need to be funded.

First, embryonic stem cells are unique in that they can be grown in vitro (outside of the body), and maintain the capacity to become any type of cell in the body. In contrast, adult stem cells have not yet been grown in vitro, and it is not yet known whether adult stem cells have the same ability as embryonic cells to become all cell types.

Second, in order for scientific discovery to continue rapidly in this field, both adult and embryonic stem cells will need to be studied and compared. At present, we can

obtain far more information from embryonic stem cells, which are the "experts" in plasticity, than from rare adult derived cells.

Third, no one can predict which lines of investigation will lead to development of effective and safe treatments for human disease. In fact, it is likely that critical therapies for multiple different human diseases will derive from different research avenues. To eliminate one avenue simply because the other has begun to show promise is to speculate on the basis of too little data on matters which may well be life threatening or life preserving for large numbers of people

I urge you to take into consideration the long-term objectives of embryonic stem cell research—to cure and eliminate life-threatening disease. Any possible compromise, such as that attributed to the Administration that allows federally funded research using only existing cell lines is far too limiting. Perhaps the most important reason is that scientists need to compare multiple cell lines in order to better understand the common factors that give embryonic stem cells their incredible plasticity.

In closing, embryonic stem cell research should receive federal funding because work on these cells is invaluable and work on adult derived stem cells is just beginning. To close off one avenue because of premature assumptions about the other is to play the odds with people's lives.

Thank you very much for providing me this opportunity to address you on this critical issue.

Senator HARKIN. Thank you very much, Dr. Krause.

Now we go to Dr. Hendrix.

STATEMENT OF MARY J.C. HENDRIX, Ph.D., PROFESSOR AND HEAD, DEPARTMENT OF ANATOMY AND CELL BIOLOGY, UNIVERSITY OF IOWA COLLEGE OF MEDICINE

Ms. HENDRIX. Thank you. Chairman Harkin, Senator Specter, and distinguished members of the subcommittee: I am Dr. Mary Hendrix and I am honored to be here today to present a scientific perspective on embryonic stem cell research. As a scientist conducting cancer research and as the immediate past president of the Federation of American Societies for Experimental Biology, or FASEB, I speak to you today on behalf of FASEB's 21 member societies and more than 60,000 member scientists.

First I would like to briefly summarize the current state of human embryonic stem cell research in the United States. The human embryonic stem cells that we are talking about are isolated from a very early embryo called the blastocyst, which is so small that it can fit on the tip of a sewing needle. The inner cell mass from which the stem cells are derived is composed of 30 to 34 undifferentiated cells. These embryonic stem cells of the inner cell mass cannot form a human being, not even when implanted into a woman's womb.

This scientist observation has sparked an emotional and profound debate about whether Federal funds should be used to support this new and promising area of research, and right now our leading medical institutions are prevented from conducting stem cell research, severely limiting the flow of information. There is great promise, as we have heard, in human embryonic stem cell research.

First, human embryonic stem cells are self-renewing. So far, the cell lines derived appear to have virtually unlimited replication capacity.

Second, human embryonic stem cells are pluripotent, that is they can differentiate into many diverse cell types that comprise the human body. Understanding how these particular cells develop will allow us to direct their differentiation into specific cell types and

tissues. We now know that the development is governed by the intricately choreographed interactions of hundreds of genes, and with this research we hope to realize the true potential of the fully sequenced genome.

Stem cells may also provide cures and therapies for many of the diseases that plague humanity. Let me just mention a few. Patients with Alzheimer's and Parkinson's disease might be treated by replacing dead cells with neurons grown from embryonic stem cells. The most hopeful near-term example of the promise of stem cell research is in type 1 or juvenile diabetes, where new pancreatic islet cells, cells that produce the insulin in the body, can be transplanted into diabetes patients.

In my own field of cancer biology research, stem cells hold great promise. Stem cells can renew themselves indefinitely and may shed new light on the uncontrolled growth of cancer cells. In the realm of gene therapy for cancer, if embryonic stem cell research is allowed to proceed it might allow us to engineer cells and tissues that are resistant to the most effective, but also the most toxic, cancer therapies. That would allow normal tissues to be protected while cancer cells are selectively destroyed.

Existing embryonic stem cell lines are a valuable resource, but they are insufficient to explore adequately the vast therapeutic potential of stem cell research. At this time we do not know precisely how many human embryonic stem cell lines are available for study and we do not know if these existing cell lines are genetically diverse enough. The scientific community, like the public, is divided on the issue of how many embryonic stem cell lines will be needed to address current and future scientific questions.

Whatever the needs may be, the NIH can provide the oversight necessary to regulate the ethical considerations involved in all aspects of this research.

I would like to conclude by saying, we at FASEB strongly support allowing human embryonic stem cell research to go forward under the pending NIH guidelines and, second, based on our current knowledge, while adult stem cell research is highly promising and should be pursued, embryonic stem cells have greater potential.

PREPARED STATEMENT

We are grateful to you, Mr. Chairman, and to your colleague Senator Specter for championing the opportunities to conduct human embryonic stem cell research. We hope it can be done in an open manner so that the public can see exactly what is going on.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF MARY J.C. HENDRIX

Chairman Harkin, Senator Specter, and distinguished Members of the Subcommittee, I am Mary Hendrix, and I am honored to be here today to present a scientific perspective on embryonic stem cell research. As a scientist conducting cancer research, and as the immediate past president of the Federation of American Societies for Experimental Biology or FASEB, I speak to you today on behalf of FASEB's 21 member societies and their more than 60,000 scientist-members.

THE CURRENT STATE OF RESEARCH

First, I would like to summarize the current state of human embryonic stem cell research in the United States.

In 1998, a milestone in biomedical research was achieved. We learned that cells isolated from the inner cell mass of a very early human embryo (4–5 days after fertilization), and grown in culture under special conditions, could develop into the many different cell types of the human body. This very early embryo (called the blastocyst) is so small that it can fit on the tip of a sewing needle. The inner cell mass within it, and from which stem cells are derived, is comprised of 30–34 undifferentiated cells. These embryonic stem cells of the inner cell mass cannot form a human being, not even when implanted into a woman's womb.

This scientific observation has sparked an emotional and profound debate about whether federal funds should be used to support this new and promising area of biomedical investigation. Right now, our leading medical institutions are prevented from conducting stem cell research, severely limiting the flow of information.

THE PROMISE OF HUMAN EMBRYONIC STEM CELL RESEARCH

There is great promise in human embryonic stem cell research, because we might learn how to grow specialized cells for therapeutic purposes. This is possible because of two unique attributes of these cells.

First, human embryonic stem cells are self-renewing. So far, the cell lines derived from the pioneering work of Dr. James Thomson of the University of Wisconsin have undergone more than 300 population doublings and appear to have virtually unlimited replication capacity based on the expression of certain cellular and genetic markers.

Second, human embryonic stem cells are pluripotent, that is, they can differentiate into many of the diverse cell types that comprise the human body. This capacity for replication, coupled with the property of pluripotency provides researchers an extraordinary opportunity. Understanding how these particular cells develop may allow us to learn how to direct their differentiation into specific cell types or tissues.

Embryonic stem cells might also provide part of the answer to the fundamental mystery of human biology: how does an early blastocyst develop into the multitude of cells that become the tissues, organs and limbs of an adult? We know now that this development is governed by the intricately choreographed interactions of dozens, even hundreds of genes. Stem cell research is allowing scientists to understand how genes interact during human development. With this research, we can realize the true potential of the fully sequenced human genome.

In addition to revealing the secrets of human development, stem cells may provide cures and therapies for many of the diseases that plague humanity. Let me mention just a few here.

NEURODEGENERATIVE DISEASES AND NEURONAL INJURY

Among the most heart-wrenching human afflictions are diseases in which cells of the brain and nervous system degenerate and die, for example, in patients suffering from Alzheimer's and Parkinson's diseases. In the case of Alzheimer's disease, dead and dysfunctional cells in the hippocampal and cortical regions of the brain might actually be replaced by transplanted, specialized neurons developed from embryonic stem cells. Similarly, Parkinson's disease, which is characterized by the death of dopamine-transmitting neurons, might be treated by replacing dead cells with neurons grown from embryonic stem cells.

Recent research performed in rodents suggests that pluripotent stem cells may help repair the damaged nervous system. In this very exciting research, paralyzed rodents with spinal cord injuries have regained some degree of mobility following transplantation of oligodendrocytes derived from mouse embryonic stem cells.

TRANSPLANTATION AND TYPE I DIABETES

The most hopeful near-term example of the promise of stem cell research is in type-I or juvenile diabetes. Using embryonic stem cells and our understanding of how they differentiate, we may be able to give patients new pancreatic islet cells, the cells that produce insulin in the body, and thereby provide a cure for juvenile diabetes.

CANCER

In my own field of cancer biology, stem cell research holds great promise. That special intrinsic property of stem cells, their ability to renew themselves indefinitely, may shed light on the similar uncontrolled growth of cancer cells. By under-

standing how embryonic stem cells are able to replicate themselves, we might be able to understand the cellular mechanisms by which tumor cells become immortal and grow out of control until they kill the patient.

In the realm of gene therapy for cancer, if embryonic stem cell research is allowed to proceed, it might be possible to "engineer" cells and tissues that are resistant to the most effective, but also most toxic, cancer therapies, so that normal tissues would be protected while cancer cells are selectively destroyed. By the same principle, it might also become possible to design cells that generate antibodies against cancer cells, effectively programming the patient's immune system to attack deadly tumor cells.

ADULT STEM CELLS HOLD PROMISE BUT HAVE DRAWBACKS

Let me conclude my discussion on the promise of embryonic stem cell research by addressing adult stem cells. I want to emphasize that embryonic and adult stem cell research are both extremely promising and should be federally supported. In fact, they are complementary to each other but may not be interchangeable. While adult stem cells may indeed hold great potential, our current understanding is that they have several major drawbacks.

First, it is difficult to identify and isolate adult pluripotent stem cells. Second, adult stem cells appear to be much more restricted in their ability to differentiate into different cell types in the body, and it remains to be proven whether adult stem cells can truly give rise to all cell types in the body. Finally, the ability of adult stem cells to replicate is not as robust as embryonic stem cells.

Mr. Chairman and Members of the Subcommittee, while it is possible that pluripotent adult stem cells may exist and that additional research might reveal their sources in the body, we have pluripotent embryonic stem cells now. The potential of adult stem cells remains only a hope, and that's why federally-funded embryonic stem cell research, which is far more likely to lead to new knowledge and therapies quickly, must be allowed to proceed.

THE NIH GUIDELINES FOR RESEARCH USING HUMAN PLURIPOTENT STEM CELLS

Mr. Chairman, having concluded my overview of the current state of human embryonic stem cell research, I would like to turn to the current NIH Guidelines for Research Using Human Pluripotent Stem Cells. Let me state from the outset that FASEB strongly endorses these NIH Guidelines. These draft guidelines were presented to the public and the scientific community for formal review in 1999, and the revised guidelines issued by NIH last year reflect the advice and ethical judgements of scientists and other concerned citizens.

Under the NIH Guidelines, research using pluripotent embryonic stem cells is eligible for Federal funding. This research can only be supported if the embryonic stem cells are derived without Federal funds and are certified to have been derived from embryos in excess of clinical need for in vitro fertilization procedures. Research on embryonic stem cells derived from fetal tissue may also be federally supported under the NIH Guidelines.

Please allow me to make an important point about the virtue of the NIH Guidelines: Federal funding means medical progress under Federal oversight. Scientists working under the NIH Guidelines and with Federal oversight will be allowed to conduct the research and provide the cures and therapies for which we all hope.

EXISTING STEM CELL LINES ARE INSUFFICIENT

Existing embryonic stem cell lines are a valuable resource, but they are insufficient to explore adequately the vast therapeutic potential of stem cell research. At this time, there are approximately 30 human embryo-derived cell lines available for study. We do not know if these existing cell lines are genetically diverse enough.

The scientific community, like the public, is divided on the issue of how many embryonic stem cell lines will be needed to address current and future scientific questions. Whatever the needs may be, the NIH can provide the oversight necessary to regulate the ethical considerations involved in all aspects of this research.

CONCLUSION

We are grateful to you Mr. Chairman, and your colleague Senator Specter, for championing opportunities for researchers to conduct human embryonic stem cell research in an open manner—with government support and oversight.

The public has every right to know exactly what type of human embryonic stem cell research is being performed in our country. For that to happen, the government must provide funding and the appropriate oversight for these new research opportu-

nities. In the absence of Federal support and oversight, this exciting line of research will occur only behind closed doors. To preclude such an approach is to delay the prospect of life enhancing biomedical breakthroughs.

Senator HARKIN. Dr. Hendrix, thank you very much.

Now we turn to Dr. Michael West, president and CEO of Advanced Cell Technology. Dr. West.

STATEMENT OF MICHAEL D. WEST, Ph.D., PRESIDENT AND CHEF EXECUTIVE OFFICER, ADVANCED CELL TECHNOLOGY

Dr. WEST. Thank you, Mr. Chairman and members of the committee. My name is Michael West. I am the president and CEO of Advanced Cell Technology, a biotechnology company in Massachusetts. Prior to Advanced Cell, I was the founder of Geron Corporation in Menlo Park, California, and beginning in 1995 organized an effort in collaboration with Jamie Thompson and John Gearhart to isolate the human embryonic stem cell and human embryonic germ cell.

It may be of surprise and interest to know that I hold a pro-life position and, consistent with that, believed at that time and still do that the effort to isolate embryonic stem cells and to use them in medicine is moral and is consistent with the pro-life position. I would like to explain why and to clarify some misinformation. I feel that misinformation is our enemy more than anything else.

To begin with, what are we so excited about with these embryonic stem cells? It has been mentioned frequently and in the report submitted by the NIH that these cells stand at the base of the tree of life, of cellular life, in that they can branch out, forming any cell and tissue in the body. So cells that at least to this date have never been made from an adult stem cell, like a beta cell for diabetes and so on, or dopamine for Parkinson's, can be obtained from these cells.

Not only can any cell type be made from these cells, but even complex tissues, which is quite amazing in the history of science and medicine. These cells will self-aggregate, for instance, into intestine. They could be used to repair damaged intestine in colon cancer, as an example.

Beginning in 1995, it became clear that we had a major unsolved problem, however. The problem is these are all cells that are not us. Our bodies would reject them as foreign. With the cloning of Dolly in 1997, it became clear that mankind in this decade had been given two enormous possibilities: one, to make any cell type for a person who is sick; second, the door is now open to find a way, an ethical and a carefully designed way, to give back a patient their own histocompatible, meaning their own cells that can be accepted by the body itself.

This is an enormous opportunity and gift to mankind. The question is how do we take this gift and translate it into something that we all can agree on is a good and ethical use of technology? An important part of this debate—and we have heard it several times today—is what is this thing called the blastocyst embryo?

I have a diagram here on the chart. An important part of this debate, first, is there is a constant misuse of information about what is a life or human life. Human cells are alive, we know this. We evolved from single cell organisms. These are living entities. So to say that there is human life in a sperm cell or an egg cell is cor-

rect. You could indeed adopt a sperm or an egg cell and bring in to show in testimony that we have created a human being from these cells.

But we agree a sperm or an egg cell is not a human life. With the development of a multi-cellular animal, which is a human being, from the fertilized egg, we have this first aggregation of cells called the blastocyst. These cells on the outside will become the placenta. The cells on the inside are the subject of debate. If put in culture, they are simply an embryonic stem cell. An important point: these cells—and this is I think a central issue for this committee and all of us to grapple with. These cells have not committed to becoming any cell of the body or indeed somatic cells at all. They can still become a sperm or an egg cell.

Second and very importantly, I think it goes to the heart of this issue: This blastocyst embryo has not individualized. It can become identical twins. If the intercell mass separates into two separate balls of cells, you will have identical twins that have, what is said, share the corionic sac, but have separate amniotic sacs. If two primitive streaks form no the intercell mass, you will have identical twins that share the same amniotic sac.

These are lessons from nature that teach us that not only are these cells not body cells of any kind, they have not even become an individual, and to ascribe to unindividualized cells the status of a person is a logical inconsistency.

We have heard references to the Bible and tradition is to help guide us moving forward into the future. There are two verses I would like to mention. One is in the book of Corinthians the Apostle Paul says: "When I was a child, I spake as a child, I understood as a child, I thought as a child. But when I became a man, I put away childish things."

I think it is important for us as the leading country in technology to have a mature, reasoned, and I think dispassionate debate of these issues. We have been given two talents of gold, to recall another biblical parable, two gifts to mankind which are of great merit: the cell that can form any cell tissue in the body and I think this rather remarkable and unexpected gift of being able to return a cell back in time, in the tiny time machine of nuclear transfer, to make these cells identical to a patient.

PREPARED STATEMENT

I would encourage the United States, as we have in the past in our exploration of space, for instance, to shrug off accusations that we are building a modern tower of Babel in reaching for the heavens and to touch the moon. We shrug off those fears and superstitions, and with good intentions and proper moral and ethical debate we bravely move into the future to try to find a way to alleviate human suffering.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF MICHAEL D. WEST

Mr. Chairman and members of the Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, my name is Michael D. West and I am the President and Chief Executive Officer of Advanced Cell Technology a bio-

technology company based in Worcester, Massachusetts. A copy of my curriculum vitae is presented in Appendix A.

INTRODUCTION

I am pleased to testify today in regard to the new opportunities and challenges associated with human embryonic stem (ES) cell and nuclear transfer (NT) technologies.

I will begin by describing the bright promise of these twin and interrelated technologies and then attempt to correct some misunderstandings relating to their application in medicine.

It may be useful to point out that I think of myself as pro-life in that I have an enormous respect for the value of the individual human life. Indeed, in my years following college I protested abortion clinics. My goal was not to say to women that they did not have the right to choose. My intent was simply to urge them to reconsider the destruction of a developing human being. Despite my strong convictions about the value of the individual human life, in 1995 I organized the collaboration between Geron Corporation and the laboratories of Dr. James Thomson and John Gearhart to isolate human embryonic stem cells and germ cells from living human embryos and fetuses. My reasons were simple. These technologies are entirely designed to alleviate human suffering and to save human life. They are, in fact, pro-life. The opponents that argue they destroy human lives are simply and tragically mistaken. Let me explain why this is the case.

Human ES cells

We are composed of trillions of individual living cells, glued together like the bricks of a building to construct the organs and tissues of our body. The cells in our bodies are called "somatic cells" to distinguish them from the "germ line" or reproductive cells that connect the generations. We now know that life evolved from such single-celled organisms that dominated all life some one billion years ago.

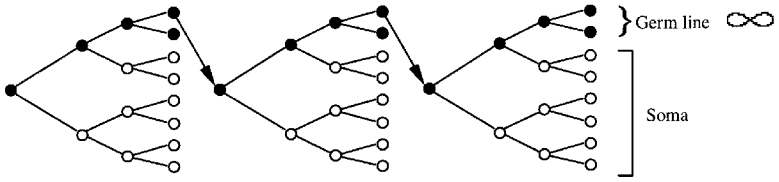

FIGURE 1. The Distinction Between the Life of Cells and the Life of and Individual Human Being in the Human Life Cycle. Biological, that is, "cellular life" began with the origins of life on earth. The beginning of the life of an individual human being is linked to the appearance of somatic cells, that is, cells committed to form the human body.

Therefore, in answer to the question of when life begins, we must make a critical distinction. Biological life, that is to say, "cellular life" has no recent beginnings. Our cells are, in fact, the descendents of cells that trace their beginnings to the origin of life on earth. When we speak of an individual human life, we are speaking of the communal life of a multicellular organism springing from the reproductive lineage of cells. The individual human life is composed of cells committed to somatic cell lineages. All somatic cells are all related in that they originate from an original cell formed from the union of a sperm and egg cell.

The fertilization of the egg cell by a sperm leads to a single cell called the "zygote". From this first cell, multiple rounds of cell division over the first week result in a microscopic ball of cells with very unusual properties. This early embryo called the "preimplantation embryo" has not implanted in the uterus to formally begin a pregnancy.

It is estimated that approximately 40 percent of preimplantation embryos formed following normal human sexual reproduction fail to attach to the uterus and are simply destroyed as a result.

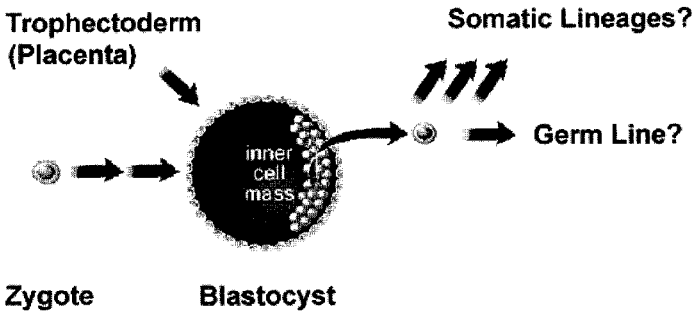

FIGURE 2. The Blastocyst Stage of the Preimplantation Embryo. At the blastocyst stage of the preimplantation embryo, the external cells called the "trophectoderm" are destined to attach to the uterus and form the placenta. The remaining cells, the Inner Cell Mass (ICM) are completely undifferentiated and have not committed to any somatic cell lineage.

From the above it should be clear that at the blastocyst stage of the preimplantation embryo, no body cells of any type have formed, or even more significantly, there is strong evidence that not even the earliest of events in the chain of events in somatic differentiation have initiated. A simple way of proving this is by observing subsequent events.

Should the embryo implant in the uterus, the embryo, at approximately 14 days post fertilization will form what is called the primitive streak, the first definition that these "seed" cells will form an individual human being as opposed to the forming of two primitive streaks leading to identical twins. Rarely two primitive streaks form that are not completely separated leading to conjoined or Siamese twins. In addition, rarely, two separately fertilized egg cells fuse together to form a single embryo with two different cell types. This natural event leads to a tetragammetic chimera, that is a single human individual with some of the cells in their body being male from the original male embryo, and some cells being female from the original female embryo. These and other simple lessons in embryology teach us that despite the dogmatic assertions of some theologians, the evidence is decisive in support of the position that an individual human life, as opposed to merely cellular life, begins with the primitive streak, (i.e. after 14 days of development). Otherwise we are left with the logical absurdity of ascribing to the blastocyst personhood when we know, scientifically speaking, that no individual exists (i.e. the blastocyst may still form identical twins).

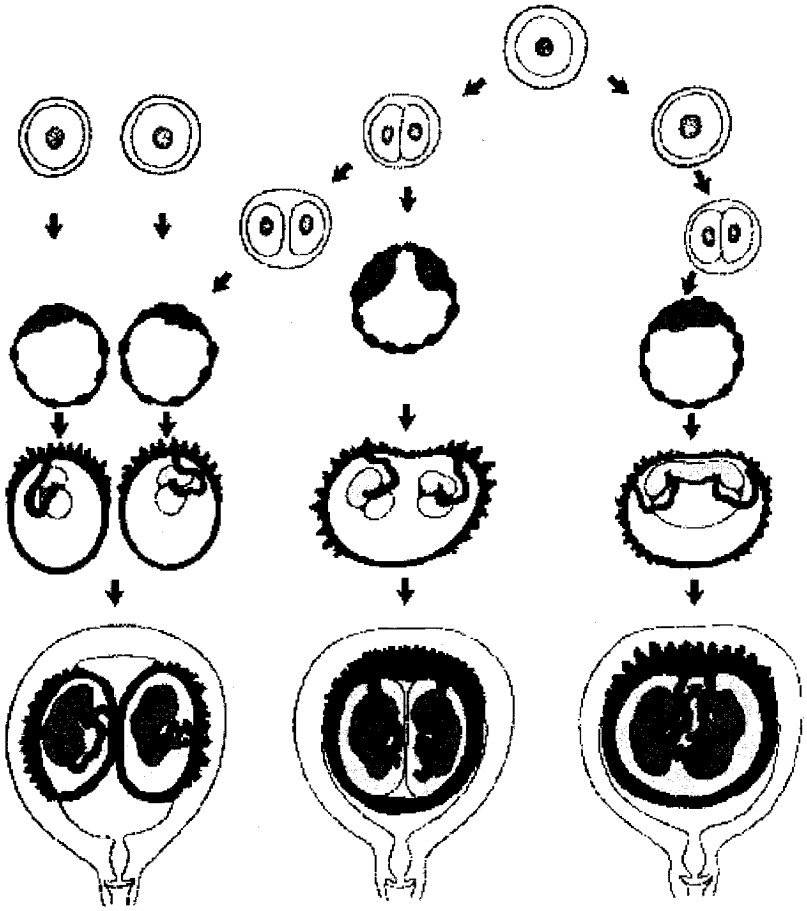

FIGURE 3. The lack of Individuation of The Blastocyst Stage Embryo. Lessons from nature indicate that the blastocyst-stage preimplantation embryo has not individualized. On the left fraternal or nonidentical twins form from independently-fertilized egg cells. Identical twins form from a single ICM breaking into two ICMS (center diagram) or by two primitive streaks forming on one ICM (right diagram).

Human ES cells are nothing other than ICM cells grown in the laboratory dish. Human ES cell technologies may greatly improve the availability of diverse cell types. Human ES cells are unique in that they stand near the base of the developmental tree. These cells are frequently designated "totipotent" stem cells, meaning that they are potentially capable of forming any cell or tissue type needed in medicine. These differ from adult stem cells that are "pluripotent" that is, capable of forming several, but only a limited number, of cell types. An example of pluripotent adult stem cells are the bone marrow stem cells now widely used in the treatment of cancer and other life-threatening diseases.

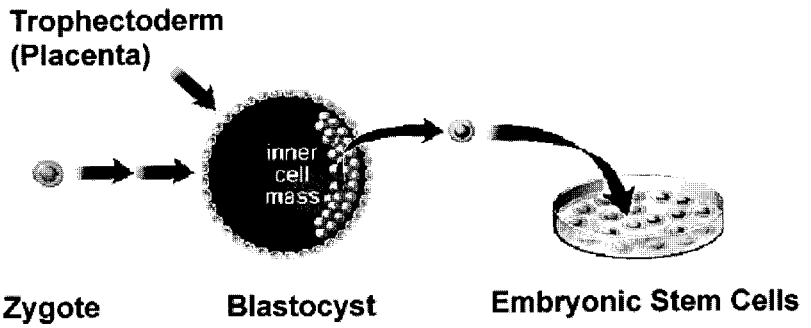

FIGURE 4. Human Embryonic Stem (ES) Cells are Inner Cell Mass (ICM) Cells Cultured in the Laboratory Dish. Human ES cells were first cultured for long periods of time in the laboratory by Dr. James Thomson of the University of Wisconsin at Madison.

Some have voiced objection to the use of human ES cells in medicine owing to the source of the cells. Whereas the use of these new technologies has already been carefully debated and approved in the United Kingdom, the United States lags disgracefully behind. I would like to think it is our goodness and our kindness that generates our uncertainty over these new technologies. Indeed, early in my life I might have argued that since we don't know when a human life begins, it is best not to tamper with the early embryo. But, with time I learned the facts of human embryology and cell biology. As the Apostle Paul said: "When I was a child, I spake as a child, I understood as a child, I though as a child: but when I became a man, I put away childish things." (I Cor 13:11) In the same way it is absolutely a matter of life and death that policy makers in the United States carefully study the facts of human embryology and stem cells. A child's understanding of human reproduction could lead to disasterous consequences.

With appropriate funding of research, we may soon learn to direct these cells to become vehicles of lifesaving potential. We may, for instance, become able to produce neurons for the treatment of Parkinson's disease and spinal cord injury, heart muscle cells for heart failure, cartilage for arthritis and many others as well. This research has great potential to help solve the first problem of tissue availability, but the technologies to direct these cells to become various cell types in adequate quantities remains to be elucidated. Because literally hundreds of cell types are needed, thousands of academic research projects need to be funded, far exceeding the resources of the biotechnology industry.

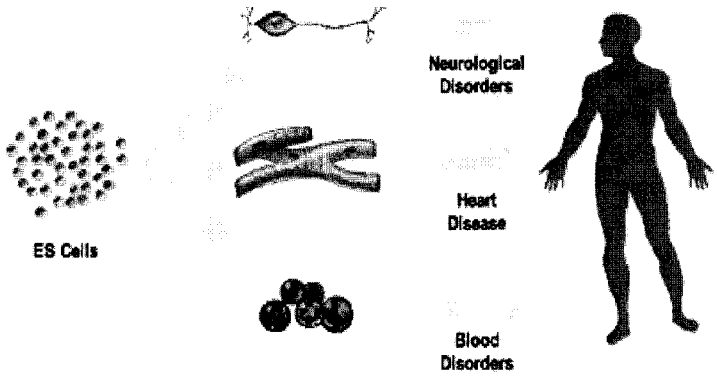

FIGURE 5. Using Embryonic Stem (ES) cells in human therapy. Human ES cells are immortal while cultured in the undifferentiated state and can theoretically lead to any cell or tissue type in the human body.

As promising as ES cell technology may be, it does not solve the second problem of histocompatibility. Human ES cells obtained from embryos derived during in vitro fertilization procedures, or from fetal sources, are essentially cells from another individual (allogeneic). Several approaches can be envisioned to solve the problem of histocompatibility. One approach would be to make vast numbers of human ES cell lines that could be stored in a frozen state. This "library" of cells would then offer varied surface antigens, such that the patient's physician could search through the library for cells that are as close as possible to the patient. But these would likely still require simultaneous immunosuppression that is not always effective. In addition, immunospuppresive therapy carries with it increased cost, and the risk of complications including malignancy and even death.

Another theoretical solution would be to genetically modify the cultured ES cells to make them "universal donor" cells. That is, the cells would have genes added or genes removed that would "mask" the foreign nature of the cells, allowing the patient's immune system to see the cells as self. While such technologies may be developed in the future, it is also possible that these technologies may carry with them unacceptably high risks of rejection or other complications that would limit their practical utility in clinical practice.

Given the seriousness of the current shortage of transplantable cells and tissues, the FDA has demonstrated a willingness to consider a broad array of options including the sourcing of cells and indeed whole organs from animals (xenografts) although these sources also pose unique problems of histocompatibility. These animal cells do have the advantage that they have the potential to be genetically engineered to approach the status of "universal donor" cells, through genetic engineering. However as described above, no simple procedure to confer such universal donor status is known. Most such procedures are still experimental and would likely continue to require the use of drugs to hold off rejection, drugs that add to health care costs, and carry the risk of life-threatening complications.

THERAPEUTIC CLONING

A promising solution to this remaining problem of histocompatibility would be to create human ES cells genetically identical to the patient. While no ES cells are known to exist in a developed human being and are therefore not available for treatment, such cells could possibly be obtained through the procedure of somatic cell nuclear transfer (NT), otherwise known as cloning technology. In this procedure, body cells from a patient would be fused with an egg cell that has had its nucleus (including the nuclear DNA) removed. This would theoretically allow the production of a blastocyst-staged embryo genetically identical to the patient that could, in turn, lead to the production of ES cells identical to the patient. In addition, published data suggests that the procedure of NT can "rejuvenate" an aged cell restoring the proliferative capacity inherent in cells at the beginning of life. This could lead to cellular therapies with an unprecedented opportunity to improve the quality of life for an aging population.

The use of somatic cell nuclear transfer for the purposes of dedifferentiating a patient's cells for purposes of obtaining undifferentiated stem cells has been designated "Therapeutic Cloning" or alternatively, "Cell Replacement by Nuclear Transfer". This terminology is used to differentiate this clinical indication from the use of NT for the cloning of a child which in turn is designated "Reproductive Cloning". In the United Kingdom, the use of NT for therapeutic cloning has been carefully studied by their Embryology Authority and formally approved by the Parliament.

ETHICAL CONSIDERATIONS

Ethical debates often center over two separate lines of reasoning. Deontological debates are, by nature, focused on our duty to God or our fellow human being. Teleological arguments focus on the question of whether the ends justify the means. Most scholars agree that human ES cell technology and therapeutic cloning offer great pragmatic merit, that is, the teleological arguments in favor of ES and NT technologies are quite strong. The lack of agreement, instead, centers on the deontological arguments relating to the rights of the blastocyst embryo and our duty to protect the individual human life.

I would argue that the lack of consensus is driven by a lack of widespread knowledge of the facts regarding the origins of human life on a cellular level and human life on a somatic and individual level. So the question of when does life begin, is better phrased "when does an individual human life begin." Some dogmatic individuals claim with the same certainty the Church opposed Galileo's claim that the earth is not the center of the universe, that an individual human life begins with

the fertilization of the egg cell by the sperm cell. Like previous vacuous pronouncements, this is simply not based in fact or, for that matter, without basis in religious tradition.

All strategies to source human cells for the purposes of transplantation have their own unique ethical problems. Because developing embryonic and fetal cells and tissues are "young" and are still in the process of forming mature tissues, there has been considerable interest in obtaining these tissues for use in human medicine. However, the use of aborted embryo or fetal tissue raises numerous issues ranging from concerns over increasing the frequency of elected abortion to simple issues of maintaining quality controls standards in this hypothetical industry. Similarly, obtaining cells and tissues from living donors or cadavers is also not without ethical issues. For instance, is it morally acceptable to keep "deceased" individuals on life support for long periods of time in order to harvest organs as they are needed?

The implementation of ES-based technologies could address some of the ethical problems described above. First, it is important to note that the production of large numbers of human ES cells would not in itself cause these same concerns in accessing human embryonic or fetal tissue, since the resulting cells have the potential to be grown for very long periods of time. Using only a limited number of human embryos not used during in vitro fertilization procedures, could supply many millions of patients if the problem of histocompatibility could be resolved. Second, in the case of NT procedures, the patient may be at lower risk of complications in transplant rejection. Third, the only human cells used would be from the patient. Theoretically, the need to access tissue from other human beings could be reduced.

Having a knowledge of a means to dramatically improve the delivery of health care places a heavy burden on the shoulders of those who would actively impede ES and NT technology. The emphasis on the moral error of sin by omission is widely reflected in Western tradition traceable to Biblical tradition. In Matthew chapter 25 we are told of the parable of the master who leaves talents of gold with his servants. On servant, for fear of making a mistake with what was given him, buries the talent in the ground. This servant, labeled "wicked and slothful" in the Bible, reminds us, that simple inaction, when we have been given a valuable asset, is not just a lack of doing good, but is in reality evil. There are times that it is not better to be safe than sorry.

Historically, the United States has a proud history of leading the free world in the bold exploration of new technologies. We did not hesitate to apply our best minds in an effort to allow a man to touch the moon. We were not paralyzed by the fear that like the tower of Babel, we were reaching for the heavens. But a far greater challenge stands before us. We have been given two talents of gold. The first, the human embryonic stem cell, the second, nuclear transfer technology. Shall we, like the good steward, take these gifts to mankind and courageously use them to the best of our abilities to alleviate the suffering of our fellow human being, our will we fail most miserably and bury these gifts in the earth? History and many thousands of suffering fellow human beings will stand in judgment of our response to this great challenge. I urge you to stand courageously in favor of existing human life. The alternative is to inherit the wind.

Senator HARKIN. Dr. West, thank you very much.

Again, thank you all very much for being here today and for waiting so patiently. I want to say that all of your written statements will be made part of the record in their entirety.

I just have a couple of questions. Dr. Skirboll, again I want to follow up on this question to make sure I understand it completely. Does it make any sense to allow Federally funded researchers to work with embryonic stem cells already derived, but not to allow those researchers to derive the stem cells in their own labs?

Dr. SKIRBOLL. I think if I understand your question, Senator, you are asking about Federal funding of derivation with that?

Senator HARKIN. Yes.

Dr. SKIRBOLL. I think there are several things that need to be considered with regard to Federal funding for derivation, questions that have actually not been thoroughly explored. There may well be intellectual property issues with regard to patenting and the patenting of the technology that may or may not allow for Federal

funds to go toward derivation. I am not an expert in that arena. I think I suggest that we would need to look at that more carefully.

Senator HARKIN. I will ponder that.

Dr. Hendrix, as the head of FASEB and as a distinguished researcher yourself, you know the science. As a federally funded researcher, if you decided to do research today using embryonic stem cells, but you were limited to using those lines now in existence, what problems would that present for you? Are there sufficient existing stem cell lines that they offer sufficient diversity? Are there patent issues?

We heard the discussion, you heard the discussion this morning, is it 30, is it 50, is it 100, is it 200. Do we have any idea at all how many lines that we think might be sufficient?

Ms. HENDRIX. Mr. Chairman, in the absence of formal oversight, we have no idea right now precisely how many cell lines are available for study. My concerns as a scientist—if I did not have the opportunity to understand precisely how these cell lines were derived, if I did not have the opportunity to derive them in my own lab, or if I did not know precisely the source of these precious materials, I would have a problem conducting an experiment and also interpreting the results of an experiment.

So to specifically answer your question, we do not know how many lines are available right now. We have heard there may be up to 30 lines available. We have heard from scientists such as Dr. Gearhart from Hopkins. He feels that we could use at least 100 cell lines and that would give us the genetic diversity that we would need to look at many different aspects from these cells.

But at this point we really do not know, and that is the honest answer. We do not know exactly how many lines are available for study and how many we will need to answer our current questions and our future questions.

Senator HARKIN. Would there ever be a point in time where we might know that? I mean, both Dr. Frist and others said earlier today that you do not need thousands and thousands and thousands of lines. But is it tens and tens or hundreds and hundreds, or what? I mean, how do we finally figure this out?

Ms. HENDRIX. If we were to consult a panel of experts in this area right now, the number that people may settle on may be a number such as about 100. However, until we actually are involved in the science of looking and examining those cell lines, we will not know if they are sufficient for all of our activities. One possibility where a template currently exists is that when scientists are funded by the Federal Government to develop research tools such as antibodies or animal models or discover new genes, they are obliged because of Federal funding to share those resources in publications with all other researchers.

Something we might consider and the panel might consider is if this research could be Federally funded, that researchers would be allowed to derive lines, and they must share them with others. This template already exists for other research tools.

Senator HARKIN. My time has run out. In my second round I just want to ask Dr. West a question about therapeutic claims, but I will get back to that.

Senator Specter.

Senator SPECTER. Dr. Skirboll, thank you for your work in this area. I note in the comment in the report that diseases that might be treated by transplanting human cells derived from stem cells include Parkinson's disease, diabetes, traumatic spinal cord, Duchenne's, muscular dystrophy, heart failure, and osteogenesis imperfecta. However, treatment for many of these diseases require that human cells be directed to differentiate into specific cell types prior to transplantation. The research is occurring in several laboratories, but is limited because so few laboratories have access to human stem cells.

That is a pretty flat statement that we need more stem cells to be extracted from embryos, right?

Dr. SKIRBOLL. I think what we were referring to there, Senator, was we need more research on stem cell lines to show that we can differentiate them into those many cell types that would affect those various diseases.

Senator SPECTER. Are there adequate stem cells available at the present time for NIH to do research without having derivation paid for by the Federal Government? Let us come right down to the nitty-gritty. I am disappointed that your report did not deal with that. That is the crucial issue. The last administration said you could pay for them once extracted, and legislation is pending to have Federal moneys pay for extracting them.

How about it? Is it not a fact, a good hard cold fact, that you need to have Federal funding to get adequate number of stem cells from the embryos if this research is to continue?

Dr. SKIRBOLL. Well, I think it is a fact that we need, as Dr. Hendrix just testified, I think it is a fact that we need more than the existing cell lines to do all the research that is pending. A lot of research could be conducted with the cell lines that exist. Let me be clear. But more cell lines by genetic diversity. They took the issues in cell lines, we do know whether cell lines are different in their ability to proliferate, in their ability to differentiate, all of the things that matter when we get to treatment.

Senator SPECTER. Well, how will there be an adequate number of stem cells if we do not get that massive Federal budget that this subcommittee has taken the lead on? You only had $12 billion a couple years ago. Now you have got more than $20 million.

Dr. SKIRBOLL. Yes, sir.

Senator SPECTER. We did not take the lead in providing that research funding for you not to do research, not to be scientists. Is there any conceivable excuse for NIH not to actively seek to get stem cells and have the Federal funding available to extract them from embryos?

Dr. SKIRBOLL. I think in the order of science, what we need access to is the stem cells to do the research. I agree with you there, Senator. I do not think NIH at this point has a position as to whether Federal funding for the derivation of the stem cells in order to get those cells into the laboratories of Federal investigators is necessary.

As I stated to Senator Harkin, I think there are some intellectual property and patenting issues that may or may not affect the ability of Federal funds to go toward that.

Senator SPECTER. We will take care of that. That is a red herring. We are not going to have any problem with the intellectual property rights. If necessary, we will legislate on that subject if they are out there profiteering.

But the concern I have is that your report is a quasi-political document when it does not tackle the question of Federal funding to extract stem cells from embryos. But I am not asking you for a political position. I am asking you a scientific question. You are the leader of this report.

Dr. SKIRBOLL. Yes.

Senator SPECTER. It is pretty apparent on the face of it that there are not enough stem cells to conduct the research necessary, and that we have given you all that funding. Maybe we ought to take the funding back if you are not going to use it for important scientific purposes.

Dr. Hendrix is frowning. But we did not give you that funding not to use it for important scientific purposes.

Dr. SKIRBOLL. I see your point, Mr. Specter.

Senator SPECTER. Okay. Let me go to a harder point. When was this report substantially completed, Dr. Skirboll?

Dr. SKIRBOLL. We delivered a draft of the report to the Secretary of Health and Human Services on the 19 of June, slightly less than a month ago.

Senator SPECTER. How many changes were made, except for editorial comments and punctuation and a little polishing, after June 19 when you submitted the report?

Dr. SKIRBOLL. Well, the report was submitted to the Secretary on the 19 of June. It was my understanding it was being reviewed in the Office of the Secretary. Only last week did I have the opportunity—and I think the Secretary has many obligations, many interests—to brief the Secretary on that report. Shortly after that briefing——

Senator SPECTER. Last week? You submitted it on June 19 and you had access to the Secretary during the week of July 9?

Dr. SKIRBOLL. 3 weeks, 3½ weeks after the report was submitted—you yourself agree it is a long report to review—I had an opportunity to brief the Secretary. After that briefing and, frankly, because of this hearing, we moved expeditiously, my office moved expeditiously, to move that report from its draft form, which looked significantly different than this, to the final report which is published and handed to you last night.

Senator SPECTER. Well, was it substantially completed in draft form?

Dr. SKIRBOLL. It was substantially completed in draft form, yes, sir.

Senator SPECTER. Well, we would like to have a copy of that draft report to compare it to what was finally completed. The Secretary wrote to me yesterday after I told him that I was displeased with his censorship and displeased with his not responding to the letter which Senator Harkin and I sent him on June 29 and then our efforts to look at the report, where two staffers had to look at one report over in your offices. Then I wrote him on July 17, and I did not get a copy until 9:45 yesterday, hardly in a position to be adequately prepared for this hearing.

But we are requesting of you a copy of that draft report, because the Secretary has represented to me that it was not completed until—let me not have any chance of misquoting. His letter to me late yesterday: "The report was not finalized until a few hours before I sent it to you." So we want to get to the bottom of that, to see what "finalize" means. You have said it was substantially complete, because we are not going to wait forever.

I know the Secretary is a busy man, and you give it to him on June 19 and he cannot take it up until the week of July 9. But some of us on this subcommittee have some other responsibilities as well. But as I say, we will get to the bottom of it.

But as to your work, I thank you.

Dr. SKIRBOLL. Thank you, Senator.

Senator HARKIN. Senator Hutchison.

Senator HUTCHISON. Thank you, Mr. Chairman.

I want to continue one of the earlier points that was made by Senator Specter, and that is the availability of adult stem cells. I am struck, just because of my personal knowledge, that we would never be in a position to have enough stem cells donated by adults because of the pain involved in extracting stem cells.

It seems to me that when you talk about adult stem cells being adequate, which is the argument being made by some, is not the availability always going to be in question because of the pain involved in extracting stem cells for someone to donate just to an unknown? Whereas donating blood is very common, very easy, painless, stem cell donations are not so, and the number of people willing to donate to a bank are very small.

So you have a situation where a patient does not have an appropriate family donor, which is certainly very common. Is there a question in your mind about continued availability of adult cells in numbers that would be adequate? I would open it to anyone who would like to answer. Yes, I would like Dr. Doerflinger and then if there is another answer.

Mr. DOERFLINGER. Thank you, Senator. Well, Senator, the current bone marrow transplantation using stem cells can be an arduous process. It involves taking bone marrow from ten different places on a person's body and that is a painful process. One of the recent advances in the NIH's own stem cell biology laboratory is a tremendous advance in culturing very small quantities of these bone marrow stem cells to the point where they can grow them an order of magnitude, ten times, maybe more. They are doing that in primates now and moving toward a clinical trial.

So that a bone marrow transplant, instead of having to use almost a liter of material, you only need one injection, one site, and a very small vial of material.

Another particularly promising source of stem cells that early indications are may be more versatile than adult cells are stem cells from umbilical cord blood and from placentas. Four million of each of those is thrown away now without being used after live births. There is no moral problem with them and they provide a very abundant supply.

I think one of the cutting edges now of research, though, is really going to be stimulating the stem cells that are resident in our own

bodies to do their job better and to home in on sites of damage, in which case you would not need stem cell banks at all.

Senator HUTCHISON. I would like to ask if there is another view, because I would like, in addition to knowing the answer to my original question—our Texas legislature has just set up a cord blood bank for the State that would do exactly as Dr. Doerflinger mentioned. It would be a bank from which anyone could come that did not have a proper donor.

But my question is this: Is that as effective as the stem cells from embryos about which we are speaking today? Dr. Krause?

Dr. KRAUSE. I think that the question and the first answer both signify a lot of misrepresentation and misunderstanding that is going on in the field. "Stem cell" is not a definition of anything. There needs to be a word in front of that what that stem cell is capable of doing. An embryonic stem cell is capable of forming any cell in the body. A bone marrow-derived stem cell until recently we thought only made blood. It might have additional possibilities. Cord blood stem cells are similar to those from the bone marrow in that we know that they can produce blood. We have no idea whether cord blood stem cells have the versatility of the bone marrow-derived cells that I showed were present or of those that are embryonic stem cells. We do not have any idea.

Cord blood is cord blood. Liver stem cells make liver. Lung stem cells make lung. Bone marrow stem cells make blood. The versatility that an embryonic stem cell has is unique. However, there are recent inklings of data, like that from my laboratory, that there might be rare adult-derived cells that have some degree of versatility.

It is not painful to obtain these cells, but we simply do not know how to obtain these cells. We have never grown them in culture. We do not know how to expand them. Everything is unknown. We need embryonic stem cell research because these are the experts at versatility to show us what to do with adult-derived cells. But we are mixing apples and oranges in here to say cord blood, bone marrow, and embryo stem cells are all stem cells.

Senator HUTCHISON. Well, if I could just finish this point, do you think there is a lack of availability of adult stem cells because of the pain involved at this point in donating? Second, is there a possibility that the cord blood could be as effective as the embryonic stem cells?

Dr. KRAUSE. To answer your first question, in terms of painful to donate, I think you might be thinking about donating your eggs, the gametes, because we do not know where the versatile, multipotent adult-derived stem cells live. So we cannot say that it is painful to get them. Perhaps they are available in the bone marrow, perhaps they are available in fat. We just do not know.

Senator HUTCHISON. Collecting them from the bone marrow is painful.

Dr. KRAUSE. But we do not know where they are.

Senator HUTCHISON. It is very hard to get people to do that for an unknown donee, is what I am saying.

Dr. SKIRBOLL. I think it is important to keep in mind that one of the major barriers with adult stem cells is getting them to proliferate in vitro so that you can get them to, even if they can dif-

ferentiate into other cell types that might be used in therapy, you still have to get enough cells to be used in treatment.

So your point being taken about how many and how many adult stem cells you might need in order to get the treatment, embryonic stem cells, as I stated earlier, replicate indefinitely in culture. The other important thing about stem cells taken from bone marrow is that they are not pure, they are a population. We do not know—we have not isolated a single adult stem cell.

We get back to this issue of using a stem cell for treatment in the heart. You certainly would not want a mixed population to be injected into your heart. I do not think the FDA would allow that, either. So this issue of purity and proliferation are extremely important. We are not there with adult stem cells.

Dr. KRAUSE. So to address your two questions, no, I do not think that pain is one of the limitations to obtaining adult-derived stem cells. It is more that we do not know where they are, how do you get them and how to grow them.

The second thing, in response to your cord blood question, is cord blood may have potential to do things other than making blood, but we have no idea.

Senator HUTCHISON. But you think we should pursue it?

Dr. KRAUSE. Absolutely.

Senator HUTCHISON. In tandem with the other possibilities.

Thank you, Mr. Chairman.

Senator HARKIN. Thank you, Senator Hutchison.

I said, Dr. West, I wanted to ask——

Senator HUTCHISON. Mr. Chairman, excuse me. I am sorry. Could I submit two pieces for the record from Dr. William Pierce who is making statements on the adoption of the embryonic stem cells? He is the former President of the National Council for Adoption, and I would like to submit those for the record.

Senator HARKIN. Sure. Without objection, that will be done.

[The information follows:]

PREPARED STATEMENT OF WILLIAM L. PIERCE, PH.D., SENIOR FELLOW, DISCOVERY INSTITUTE FOR PUBLIC POLICY [1]

Because of more than 30 years' experience in the child welfare field, 20 of which were as President of the National Council For Adoption, perhaps some comments on the current controversy over Federal funding for embryonic stem cell research and the recommendation that *"embryo adoption"* be widely from my vantage point will be helpful.

The debate over stem cell research is raging and one of the reasons is that in the pluralistic society of the United States there are profound theological and religious differences on issues directly related to the debate.

The most important difference of opinion, that surprises many, is between those who are identified as "prolife"—such as Sen. Orrin Hatch (R-UT) and Rep. Chris Smith (R-NJ). The difference of opinion does not surprise people like Rep. Henry A. Waxman (D-CA), the Ranking Member of the House Committee on Government Reform. Rep. Waxman made the point clearly at a hearing July 17 on stem cell research before his Committee's Subcommittee on Criminal Justice, Drug Policy and Human Resources, Chaired by Rep. Mark Souder (R-OH).

Rep. Waxman said: "In closing, I want to acknowledge that some people do differ in this area. Some people believe that a fertilized egg (whether it is inside a womb or inside a test tube) is the same as a human being. They also oppose IVF [in vitro fertilization] as it is generally practiced, as well as some or all methods of family planning. I do not question their sincerity. But I sincerely do not agree."

[1] This statement does not necessarily reflect the views of Discovery Institute. For more information, contact Discovery Institute's Washington, D.C., Office at 202–299–0055.

Neither does Sen. Hatch, who said in his testimony July 17 that ". . . I believe that human life begins in the womb, not a petri dish or refrigerator." Sen. Hatch's views reflect the beliefs of his church, the Church of Jesus Christ of Latter-day Saints, also known as Mormons. Sen. Hatch's Church does not "strongly discourage" IVF as, for instance, it does so-called "surrogate motherhood." Mormons leave the matter of IVF to the judgment of the husband and wife. Because Mormons do strongly discourage surrogate motherhood, it was no surprise when Sen. Hatch's statement mentioned that ". . . the embryo adoption issue could raise a whole host of new legal issues. There are also religious issues—for example, there are people, some in my own faith, who seriously question the notion of surrogate motherhood."

Rep. Chris Smith, by contrast, testified that "These littlest of human beings aren't potential life—but life with vast potential." Rep. Smith's views reflect the beliefs of his church, the Roman Catholic Church. The Roman Catholic Church strongly condemns IVF, based on the view that human life begins at conception, not implantation.[2] Nor are Roman Catholics alone in this belief. At the press conference held by the Family Research Council on July 16, the list of speakers was headlined "LIVING PROOF: HOW CHILDREN'S DRAMATIC STORIES SHOW LIFE BEGINS AT FERTILIZATION." The remarks of Ken Connor, President of the Family Research Council, reflect his religious beliefs. Connor used the words "embryonic human beings" in his statement and asked the question, "Are the risks to tiny human beings created by man-made conception and frozen storage acceptable?"

As Rep. Waxman pointed out, these differences of belief are at the heart of the debate over not just embryonic stem cell research but of IVF itself and the "excess" human embryos that are routinely produced under current IVF protocols. No amount of Congressional testimony or research by the National Institutes of Health will settle questions that are theological or religious.

Since science cannot settle for all Americans what is a question of religious beliefs, it is clear why one group of legislators and a corresponding group of witnesses strongly object to the use of their tax dollars to fund experiments on "tiny human beings," in the words of the Family Research Council. And it is equally clear why those who do not share those religious beliefs are pressing forward with the case to spend Federal funds on this research.

Given the profound differences of opinion about the religious content of the controversy, the debate can still take place around other issues. At the July 17 hearing, there were strongly contrasting viewpoints from the scientists present not only on IVF but on whether research needs to go forward at this time on embryonic stem cells and whether the U.S. government should be involved in such research.

The questions on IVF include matters such as the creation of "excess" human embryos and the issue of the length of time these embryos can be stored. Testimony to the effect that non-human embryos have been frozen for 25 years suggests that the question is not so much a matter of "excess" but rather of the costs of storage. Perhaps a temporary solution to part of the current problem would be to find ways to relieve people of the burden of paying seemingly high storage fees, so that there is no financial pressure to thaw the embryos. Let's put a hold on these frozen embryos since no further apparent harm would be done to them in the process.

IVF techniques themselves could be changed to provide that reproductive medical experts no longer extract more ova than can be safely fertilized and implanted, without freezing. Let's urge those contemplating IVF to take a different approach, one that may impact consenting adults rather than embryos who cannot give consent.

There is no question but that research on embryonic stem cells is going to go forward, if not in the United States, then in the United Kingdom and other countries. This fact should not stampede U.S. policymakers. It is not unique for one country to engage in actions that most other countries question, or condemn. One could easily recount examples not just from medicine, and not just from the Nazi era, but from other arenas of human activity. For instance, despite the fact that the United States outlawed human slavery more than 100 years ago, as did most nations, we are today confronted with slavery in at least one African country, Sudan. The point is: just because some other country main gain some purported advantage by engaging in questionable activities, that is no reason why U.S. policy should react in blind competitive activity. This is a reverse "brain drain" that cannot be stopped, given the freedom to travel and the nature of free enterprise. In the view of some of us, this is no loss because the researchers at least will not be conducting questionable experiments in U.S. laboratories.

Such research may even continue in the United States, under private funding. Much was made of this issue in the July 17 hearing, as if such research is inher-

[2] Disclosure: the author is an observant, practicing Roman Catholic.

ently suspect. No such outrage was expressed and no major negative results flowed from the competition between Federal researchers and privately-funded researchers to decode the human genome. This is not to say that ethically illicit research should go forward without the strongest appropriate objections being raised, whether funded by tax dollars or private sources, but rather to say that some of the objections raised appear disingenuous.

At the July 17 hearing, an alternative for frozen human embryos was discussed at length: so-called "embryo adoption." Although there seems to be no reason not to move forward with embryo adoption at this time, especially given the alternatives, there are many unanswered questions which need to be explored. Some of those questions were included in a Statement for the Record provided to Chairman Souder's staff in advance of the July 17 hearing. Copies of the statement are available by email by contacting pgidc@AOL.com.

Senator HARKIN. Dr. West, what you are trying to do—clear this up for me. What you are trying to do is to say that, while there may be some rejection possibilities of cell lines that might be developed for a certain illness, diabetes or whatever, that what you are trying to do is to say that by taking the person's own cells and—I am searching for that word because I am not a scientist—and doing something, that way you match them up perfectly.

Would you tell me again how you differ from what we are talking about in terms of embryonic stem cell research.

Dr. WEST. Well, there was this discussion that has been ongoing about do we have sufficient numbers currently of human ESL lines to allow research to go forward. Well, one would be a sufficient number to allow some research to move forward. More lines would be useful to allow more genetic background and diversity. So if there are differences in the genes of all of us, we are drawing different genotypes, different kinds of genetic backgrounds. That would be of some marginal benefit.

I think what may be confusing is some people when they are talking about large, very large numbers of these lines, they are thinking about we might want to bank away maybe 10,000 ESL lines to have sufficient genetic diversity so that we might be able then, for a patient that is in heart failure, to take cell line number 10,001 that most closely matches their own genetic background, so that with mild immunosuppression or less severe drug therapies they may be able to long-term accept those cells. So the idea of making large banks of these cells may be driving some of these estimates upwards.

What I was pointing out is that we really need to grapple with this opportunity that has been given to mankind by nuclear transfer. It teaches us that, as has been talked about with adult stem cells, all cells in the body, given the right environment, are completely plastic. We know an egg cell can return a cell back to an embryonic state. So you could conceivably see a day when we will be able to offer people who is the dream of transplantation medicine, to offer a patient of any type cells of any kind that are genetically matched to that patient so they do not have the risk of long-term immunosuppressive therapy, which causes cancer and other complications.

Senator HARKIN. So what you do is you just take the cell from, say, some cells from my body or cell from my body and you would have a somatic cell transfer into the egg, is that right? Is that what you do?

Dr. WEST. There are a whole host of opportunities here. The simple example which I think is easy to point to is that in animal cloning we simply take a skin cell and some other cell, put it in an egg cell whose DNA has been removed, and we can create a whole genetically identical copy of that animal. What that teaches you is a simple cell biology lesson. You have taken a skin cell back in time, back to this embryonic state, from which you could then also make the stem cells.

Would it have to be done that way? Perhaps. There are other opportunities which we could explore at a future point. Nuclear transfer points the way to a relatively straightforward path of solving transplantation histocompatibility. There may be other ways around that.

Senator HARKIN. Senator DeWine, do you have any questions?

Senator DEWINE. Mr. Chairman, thank you very much. I apologize, I had another meeting.

I wonder if I could ask the panel if you could give us some idea of how much private funding is currently going into human embryonic research. Anybody have any ideas? The question may have been asked and I apologize if it was.

Dr. WEST. For the private sector, I could speak to some extent on that.

Senator DEWINE. Could you maybe kind of break it out into how it is being used?

Dr. WEST. When you said embryonic research, did you mean embryonic stem cell research or embryonic research in general?

Senator DEWINE. I would like both if you could.

Dr. WEST. Embryonic research in general, of course, emcompasses the whole field of in vitro fertilization.

Senator DEWINE. Sure.

Dr. WEST. But on the stem cell front, it is extremely small. It is nearly microscopic. There are two companies in the United States focused on this, whose total expenditures are in the range of probably $10 to $15 million a year in this particular area—no, probably more than that.

Senator DEWINE. $10 to $15 million apiece?

Dr. WEST. In a year, total.

Senator DEWINE. $10 to $15 million a year.

Dr. WEST. In the United States in the private sector. The problem of course with that is that it sounds like a significant amount of money, but we are looking at a project to make hundreds of cell types in the human body. The budget there is in the billions of dollars, to adequately address the problem.

Senator DEWINE. Anyone else have another comment on that?

Mr. DOERFLINGER. I do know, Senator, that one wealthy donor recently left a legacy of $58.5 million to one institution, Johns Hopkins University, solely to do stem cell research. I think they are going to do a great deal of the embryonic variety. So there is certainly more than $10 or $15 million out there. This was just one institution in the private sector.

I dare say that if the patient groups and organisms that are spending their money on ad campaigns to force all the rest of us to pay for this would spend the money instead on the research, there would be a lot more available.

Senator DEWINE. I would assume that with the publicity, the current public focus on this, that the amount as well as the obvious potential for drug companies and other companies' research folks to eventually make money, I would assume that the amount of money spent on this is going to continue to grow very significantly. Does anyone disagree with that?

Mr. DOERFLINGER. I think, Senator, that if you are to depend—it is going to depend on what research shows. There have been some very recent indications that there are more problems with embryonic stem cells than people thought, in terms of genetic instability and tendency to form tremors, a pretty complete failure for the cells to work in diabetes mice. They only produced 2 percent of the insulin needed.

So if those things do not pan out, private investors, who are sensible about the use of their money, may pull out of the field.

Senator DEWINE. But conversely—we are sitting here. We do not know. You are the experts, I am not. But obviously, if the opposite is true and it does begin to pan out, we assume the money will follow; will it not, at least to some extent it will follow.

Dr. USALA. Senator, my company is a venture company-funded. Our evaluation is $20 million at this point. Right now there is not a lot of interest in private investment in stem cells. The research is far too early to suggest to those that invest in this kind of thing that it would make a medical product. To make a medical product takes years of basically research, which I think all the scientists here are very enthused to get into, but on top of that you have to go through the pre-clinical testing, the toxicology, everything else.

Anywhere along the way, there can be a problem that would prevent an exciting idea to becoming a medical therapy. So at this point I would say there is very little interest in the biotech venture community for investing in something like this.

Senator DEWINE. Anybody else?

Dr. SKIRBOLL. I think it is important to not put the sole emphasis here on issues of private funding versus Federal funding.

Senator DEWINE. But I am not. I am just, asking just asking a question that I did not know the answer to, just a question.

Anybody else? Yes?

Dr. USALA. I would say there is far more interest in private financing in other forms of tissue regeneration, like my company is undergoing, just because those are much closer, a lot, to clinical trials. So the prospect for therapies that do not have to go through this very long and risky from a financial backing point of view, the venture community is much more likely to supplement.

Senator DEWINE. Thank you very much.

Mr. Chairman, thank you very much.

Senator HARKIN. Thank you, Senator DeWine.

Again, I thank you all very, very much for your efforts on this subject, the time and expertise you have given to it. Thank you for being so patient this morning. Thank you for all your wonderful testimony.

ADDITIONAL SUBMITTED STATEMENT

The subcommittee has received a statement from Senator Kohl which will be placed in the record at this point.

[The statement follows:]

PREPARED STATEMENT OF SENATOR HERB KOHL

Thank you, Mr. Chairman. I commend you and Senator Specter for holding this hearing today, and I want to thank both of you for your tireless efforts during the past few years to educate the Senate and the public about stem cell research.

I realize that people on both sides of this debate have strongly held beliefs about whether or not embryonic stem cell research should go forward. This issue raises ethical and moral questions that cannot be taken lightly. During the past several years, I have listened carefully to both sides, and I have come to the conclusion that it is time for stem cell research to go forward, and it is time for the Federal government to play an active role in the conduct and oversight of that research.

Every day, my constituents from Wisconsin write, call, and visit my office and describe the terrible and debilitating and life threatening diseases they endure. These are families who are suffering from the ravages of Alzheimer's Disease, cancers, diabetes, Parkinson's Disease, spinal cord injuries and countless others.

These families rightly demand more Federal help and funding for biomedical research. They need cures now, and they want their government to pursue every ethical avenue to help them. It would be shameful to let these families continue to suffer, while we know full well that there is promising new research that could improve or save their lives.

Every year, Congress works toward its goal of doubling funding for NIH. This Subcommittee works hard to find the money to do it and I support this goal. But if we are serious about finding cures and helping our families, then how can we ignore one of the most promising avenues of research? How do we explain that to our families?

Of course, as this research moves ahead, I agree we must also be sure that it's conducted appropriately. Currently, stem cell research is conducted by privately-funded researchers and there is practically no oversight. In recent weeks, we have seen news accounts that raise serious ethical and moral questions about the way some stem cell research is being conducted. Federal funding and oversight would shed light on these practices and provide a framework to make sure stem cell research is done in a way that the American public can support.

I am proud that the early breakthroughs in stem cell research happened in my home State at the University of Wisconsin in Madison. It is clear to me that we must now go forward nationally, and we must do so with the active oversight of the Federal government to make sure that stem cell research is conducted in a moral and ethical manner.

I hope that this hearing will shed additional light on the pressing need for stem cell research. And I hope that President Bush comes to the same conclusion I did: that helping families with tragic diseases is the ethical and moral choice here.

SUBCOMMITTEE RECESS

Senator HARKIN. Thank you all very much for being here, that concludes our hearing.

[Whereupon, at 12:18 p.m., Tuesday, July 18, the subcommittee was recessed, to reconvene subject to the call of the Chair.]

STEM CELLS

WEDNESDAY, AUGUST 1, 2001

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 9:30 a.m., in room SD–192, Dirksen Senate Office Building, Hon. Arlen Specter presiding.

Present: Senator Specter.

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Good morning, ladies and gentlemen. The hearing of the Appropriations Subcommittee on Labor, Health and Human Services, and Education, and Related Agencies will now proceed. Senator Harkin, who is chairman, is managing the agriculture bill which is on the floor of the Senate, at the moment, so I have just been informed that he will not be able to be present.

We may have to abbreviate the hearing to some extent because of the agriculture debate. I filed an amendment yesterday on an issue regarding dairy compacts, and the floor action is always unpredictable when we schedule these hearings. As you might suspect, the Senate floor action takes precedence over hearings because it involves votes and the disposition of legislation. However, we will now proceed, and go as far as we can on the hearing.

We are going to take up today the questions of patent and ethical issues relating to human embryonic stem cells. This is the ninth hearing which this subcommittee will have held. When the news about the embryonic stem cells burst upon the public scene in November of 1998, the subcommittee held a hearing very promptly thereafter, in early December, and we have had a whole series of hearings on this very, very important subject.

In my judgment, there is no issue before the Congress more important than embryonic stem cells and the potential to cure or ameliorate diseases for millions of people. I believe that the tremendous funding which has been provided for the National Institutes of Health, where this subcommittee has taken the lead in adding $8.5 billion. We have in the budget an additional $3.4 billion more for fiscal year 2002, which will in effect double the NIH funding over a 5-year period or fiscal year 2003.

The Department of Health and Human Services general counsel has ruled that while Federal funding may not be used to extract stem cells from embryos, Federal funding may be used to research on stem cells once extracted. Senator Harkin and I introduced leg-

islation a long time ago which would free the prohibition against limiting Federal funding, and I think that is very, very important. There is an enormous momentum, in my opinion, in America today to proceed with stem cell research because of the phenomenal benefits which have been demonstrated on Parkinson's and spinal cord, and the potential on Alzheimer's and so many other ailments. The only thing I have not heard that stem cells can handle is the common cold, which is plaguing me at the moment, as you might have noticed.

STATEMENT OF MARIA FRIERE, Ph.D., DIRECTOR, OFFICE OF TECHNOLOGY TRANSFER, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Senator SPECTER. We will proceed now to call Dr. Maria Friere, and Dr. Carl Gulbrandsen. Would you step forward? The time allotted is 5 minutes, and we would ask you to remain within that time frame.

Dr. Friere is the Director of the Office of Technology Transfer at the National Institutes of Health, oversees the patenting and licensing activities for NIH, and is responsible for the development and implementation of technology transfer policies and procedures for the Department of Health and Human Services. She has a Ph.D in biophysics from the University of Virginia. We thank you for joining us, and we look forward to your testimony.

Dr. FRIERE. Good morning, Senator. I am here today to address how intellectual property considerations affect basic science and the future development——

Senator SPECTER. Senator Thurmond says, will you pull the microphone a little closer?

Dr. FRIERE. Are we better now?

Senator SPECTER. Yes, you are.

Dr. FRIERE. So I am here today to address how intellectual property considerations affect basic science and the future developments of products for public health. This morning, Senator, I will focus on three issues, how technology is transferred from the not-for-profit sector to the private sector, how this applies in the case of stem cell technology, and on the implications for basic research.

Let me start briefly by discussing how laws enacted over 20 years ago that encourage university and Government laboratories to commercialize their research. These are the Bayh-Dole act and the Stevenson-Wydler Innovation Act, including one of its amendments, the Federal Technology Transfer Act. In general, these laws allow Government laboratories and recipients of Government funding to take ownership to their inventions. They also impose certain obligations to promote utilization, encourage commercialization, and ensure public availability.

As we will hear in a few minutes, the University of Wisconsin provides us with a good example of how the Bayh-Dole act is implemented. Early work by Dr. Thomson on nonhuman primates such as rhesus monkeys was federally funded. In accordance with the law, the invention on the primate stem cells was disclosed to the NIH. The university filed a patent application with the U.S. Patent & Trademark Office, and the technology was licensed to Geron.

Because Federal funds were used, the Government retains a nonexclusive royalty-free license to the technology. This right is lim-

ited, however, to use by or on behalf of the Government. In contrast, when research is funded entirely by the private sector, as is the case with research on the human embryonic stem cells, the Government has no retained license, and it is strictly a private matter whether and under what terms new intellectual property is made available to others.

Let me point out, however, that while some patents may have very broad claims, it is usually not the patent that raises concern for the biomedical research community, but rather, the way in which the patent holder chooses to exercise its rights.

For example, the discovery may be a research material or a new procedure, primarily useful as a means to conduct further research. Such discoveries are known as research tools. These tools may be patentable, and they have economic value to the holder of the patent. In our view, however, the value to society is greater when such research tools are widely available to scientists. Therein lies the quandary, how best to achieve the balance between commercial interest and the public interest.

So how do issues of intellectual property relate to the research in stem cells? Well, as you may know, there are important patents that have issued on stem cells. I will not go into the details of these patents, as in a few minutes we will have the opportunity to hear directly from the patent holder. In general, however, the ability of scientists to realize the potential of this technology will rest in part on how the owners of the patents choose to exercise their intellectual property rights.

It is important to note that the NIH has limited authority over the patenting and licensing activities of our contractors and grantees, as mandated by the Bayh-Dole act. Therefore, with regard to the stem cell patents and patent applications, it would be most appropriate to address questions to the owners and licensees of this technology as to what terms and conditions will be required from those who desire to use these rights.

In our view, the license or material transfer agreement can be crafted to ensure that both research continue and commercial uses are preserved. In fact, the NIH has urged, and will continue to urge patent owners and exclusive licensees to ensure continuing availability of the technology under terms that do not limit basic research or encumber future products.

PREPARED STATEMENT

Mr. Chairman, I am grateful for the opportunity to discuss our views, and I would be pleased to answer any of your questions.

[The statement follows:]

PREPARED STATEMENT OF MARIA FREIRE

Mr. Chairman and members of the Subcommittee, I am Maria Freire, Director of the Office of Technology Transfer. I am pleased to appear before you today on behalf of the National Institutes of Health to address how intellectual property considerations affect basic science and the future development of products for public benefit.

Given the complexity of these issues, it is important to understand how the transfer of federally funded technology from the not-for-profit sector to the for-profit sector is accomplished. To do so, I will briefly discuss the successful process established by Congress in the 1980's that governs the commercialization of federally funded biomedical research.

THE BAYH-DOLE ACT, STEVENSON-WYDLER TECHNOLOGY INNOVATION ACT OF 1980, AND AMENDMENTS, INCLUDING THE FEDERAL TECHNOLOGY TRANSFER ACT OF 1986 (FTTA)

Over twenty years ago, Congress enacted a series of laws that encourage government-owned and government-funded research laboratories to pursue the commercialization of the results of their research. These laws are the Bayh-Dole Act of 1980 and the Stevenson-Wydler Innovation Act of 1980, including one of its amendments, the Federal Technology Transfer Act of 1986 (FTTA). The Bayh-Dole Act addresses intellectual property rights in federally funded grants, contracts and cooperative agreements, while Stevenson-Wydler and the FTTA address intellectual property of government laboratories. The goal of these laws is to promote economic development, enhance U.S. competitiveness and benefit the public by encouraging the commercialization of technologies developed with federal funding. Generally, these laws allow government laboratories and the recipients of government funding to elect to retain title to their inventions. They also impose certain obligations: promoting utilization, encouraging commercialization and ensuring public availability of these technologies.

I am pleased to say that the goals set by Congress under these laws have been achieved and that, in the biomedical arena, the impact of these statutes has been critical. In fact, many experts believe that the biotechnology industry was spawned from the close interaction between academia and industry. It is widely recognized that the Bayh-Dole Act and the FTTA continue to contribute to the global leadership of the U.S. biomedical enterprise, and governments around the world are emulating these laws in the hopes of promoting economic development in their own nations.

New products developed under this system benefit patients daily and provide hundreds of scientists with the tools required for further discovery in support of our public health mission. For example, inventions arising from the NIH intramural program alone have contributed to over 150 products on the market, including diagnostic kits, vaccines, therapeutic drugs and dozens of antibodies, cell lines and other research tools. Similarly, the transfer of technology arising from the NIH extramural program has contributed significantly to new products and fostered economic development.

To accomplish the transfer of technology, universities have relied on authorities granted to them by the Bayh-Dole Act. The Act permits the grantee to retain title to intellectual property developed with federal funds and to license its rights to for-profit entities. It should be noted that, as provided by the Act, the Government does not have any direct control over patenting and licensing activities related to discoveries resulting from NIH funded research.

Patents provide the right to exclude others from making, using, selling, offering for sale, or importing a new invention for the life of the patent. This is society's reward to the owner for teaching others how to make and use the invention claimed in the patent. In the biomedical field, patents are extremely valuable to companies, particularly small companies. They provide a means of securing investment income by establishing the company's preeminence in a particular area of technology. Parties interested in practicing an invention in which they have no ownership may obtain rights to the invention by entering into a licensing agreement with the patent owner. A license is a contract with binding commitments on each party, usually involving compensation. A license does not grant title to the invention. Licenses can be exclusive, when only one licensee is permitted to benefit from the use of the technology, or non-exclusive, when more than one licensee is permitted to benefit from such rights.

As this Subcommittee well knows, new drugs and vaccines are costly to develop, and companies are unlikely to invest in further research and development without some promise of future product exclusivity. When Congress gave federal grantees the ability to patent and exclusively license government-funded inventions, the private sector turned its attention toward publicly supported research as a new source of potential products. The value to the public resides in the generation of new drugs, vaccines, and medical devices. These activities have also stimulated economic development and the creation of new jobs in the United States.

Whenever federal funds are used to support a new discovery by contractors and grantees, the government has a non-exclusive, royalty-free right to use the patented technology by or on behalf of the government. This would allow the government laboratories and contractors the right to use the patented technology for further research. In addition, in dealing with this invention the federal grantee or contractor must ensure that the goals of the Bayh-Dole Act—utilization, commercialization, and public availability—are implemented.

When research is funded entirely by the private sector, the government has no statutory license, and it is strictly a private matter whether, and under what terms,

new intellectual property is made available to others for commercial or research purposes.

Mr. Chairman, as we have discussed with this Subcommittee before, it is not merely the existence of a patent that raises concern for the biomedical research community. The concern mostly arises when the patent holder chooses to exercise its rights through licensing or other contractual agreements in a manner inconsistent with the advancement of basic research. For example, many new inventions are not final products. The discovery may be a research material or a new method or procedure, primarily useful as the means to conduct further research. Such discoveries are commonly known as research tools. There is little doubt that many research tools may be patentable and that they are of economic value to the holder of these rights. There is also little doubt that the value to society is greatest when such research tools are made widely available to scientists.

For example, a license that provides complete exclusivity to a technology that is also a research tool may result in some product development in the short-term, but it will close off opportunities to advance science and develop other products in the long-term. The only way to maximize the benefit to the public is to ensure that both research use and the potential for commercial development are preserved.

The professionals working in the specialized field of biomedical licensing strive to promote a balance between commercial interests and the public interest. In those instances where a research tool can also become a therapeutic product, licenses can be, and are, carefully crafted by scope, application and field to allow use by the research community without destroying a company's commercial incentive to develop the product.

Careful licensing that preserves this balance, however, has not always been the case. The NIH has been concerned for some time about the potential adverse effects of restrictive licensing practices on access to research tools. In response to concerns from the scientific community, NIH has published guidelines on the sharing of biomedical research resources entitled "Principles and Guidelines for Recipients of NIH Research Grants and Contracts." This document helps ensure open sharing of research tools to maintain the robust research enterprise in this country.

STEM CELL RESEARCH

How do issues regarding intellectual property considerations relate to research on stem cells? The issuance of patents by the U.S. Patent and Trademark Office may not necessarily have an adverse effect on continuing research and often promotes the development of new therapeutics, diagnostics and research tools, including cells. If patent owners devise a licensing and sharing strategy that will allow basic research to continue unencumbered while preserving appropriate commercial value, they will help ensure that such research tools are broadly available to the research community. The terms and conditions on the use and the transfer of material, such as these cells, would be set forth in an agreement commonly called a Material Transfer Agreement, or MTA.

MTAs are vehicles used to transfer proprietary materials between and among the for-profit and not-for-profit sectors. Most MTAs are simple, 1- to 2-page agreements. MTAs can, however, impose obligations or restrictions that can stifle the broad dissemination of new discoveries, slow the technology transfer process and limit future avenues of research and product development. Examples of such obligations include so-called "reach-through" provisions that may: (1) give the provider of a material ownership of new inventions developed by the recipient; (2) require royalty payments by the recipient to the provider on inventions discovered by the recipient that are not covered by the provider's patent; or, (3) require the recipient to give the provider an option to exclusive rights to any new intellectual property arising from recipient's use of the material.

NIH's experience has shown, however, that conditions imposed by patent owners—whether in a license or an MTA—can be crafted to ensure both research uses and commercial development. For example, the NIH strategy is to negotiate non-exclusive licenses for its intramural technologies whenever possible. This allows more than one company to develop products using a particular technology, products that may ultimately compete with each other in the marketplace. We recognize that companies need an exclusive market to offset the risk, time, and expense of developing biomedical diagnostic or therapeutic products. However, companies do not necessarily need to achieve that position solely by exclusively licensing a government technology used to develop the product. Instead, companies are frequently able to add their own proprietary technologies to the invention licensed from the government to ultimately achieve some level of uniqueness and exclusivity for the final product.

If non-exclusive licensing does not provide enough incentive for the company to develop a product, and it often does not for a potential therapeutic application, NIH will award exclusivity for specific indications or fields of use, based on the license applicant's commercial development plans at the time of the application. NIH also provides for exclusive licensees to grant sublicenses to broaden the development possibilities when necessary for the public health. Finally, NIH insists on the continuing unencumbered availability of the licensed technology to the not-for-profit scientific community for further research.

Experience over the last 20 years has shown that to maximize public health benefit, the balance between exclusivity and access must be carefully maintained, and research uses of new technologies must be preserved. These concepts form the basis for the licensing policies of the NIH, as well as for the proposed guidelines for our grantees mentioned above.

Over the past few years, NIH has, however, faced situations in which the patent holder was willing to allow basic research to continue only under terms that were inconsistent with our research tools principles and guidelines. To resolve such a situation, NIH negotiated acceptable terms with the patent holder so that scientists could continue to use the tools for basic research while protecting the company's commercial rights. In fact, as part of these agreements, the terms and conditions were extended to NIH grantees, should they choose to take advantage of these more favorable terms.

The experience since the inception of the guidelines has been that, while the process between not-for-profit entities has been streamlined, there is still work to be done when transfer of tools happens between the for-profit and not-for-profit sectors. We are hopeful that continued dialogue between these two constituencies will eventually result in an understanding that would permit the research enterprise to continue to flourish without undue impediments.

Finally, it is important to remind the Subcommittee that the NIH has limited authority over the patenting and licensing activities of our contractors and grantees. Therefore, with regard to the stem cell patents and patent applications, it would be appropriate to address questions to the owners and licensees of this technology as to what conditions they may apply to those who desire to use the intellectual property.

SUMMARY

Congress has enacted legislation for recipients of federal funding that encourages the utilization, commercialization and public availability of federally funded inventions. Grantees and contractors have exercised the broad discretion awarded them by the law and sought to achieve these goals through the patenting and licensing of new inventions that arise through the use of federal funds. The government has only limited authorities over these activities. If the research is entirely funded by the private sector, the government has no statutory license and is not involved in patenting or licensing decisions. Exclusive licensing, without regard to research uses, can impede rather than enhance utilization and public availability of certain types of inventions, such as research tools. Strategic licensing can alleviate potential problems. Indeed, many grantees provide for the continuing availability of exclusively licensed subject matter to researchers in order to ensure progress of biomedical research. The NIH has urged, and will continue to urge, patent owners and exclusive licensees to ensure continuing availability of a technology under terms that do not limit basic research or encumber future products. The key to the use of a technology is in the manner in which holders of existing patents exercise their rights through licensing and other contractual agreements.

Mr. Chairman, thank you for the opportunity to provide this broad background on the effects of patents and licenses on the advancement of science and medicine.

Senator SPECTER. Thank you very much, Dr. Friere. We will have some questions, but first we will proceed to Dr. Gulbrandsen, managing director of the Wisconsin Alumni Research Foundation and president of WiCell Research Institute, a nonprofit subsidiary.

He received his bachelor's from St. Olaf, and J.D. from the University of Wisconsin, and Ph.D. in psychology from the University of Wisconsin Madison. Thank you very much for joining us, Dr. Gulbrandsen, we look forward to your testimony.

STATEMENT OF CARL GULBRANDSEN, Ph.D., MANAGING DIRECTOR, WISCONSIN ALUMNI RESEARCH FOUNDATION, PRESIDENT, WICELL RESEARCH INSTITUTE, INC.

Dr. GULBRANDSEN. Thank you, Mr. Chairman.

Mr. Chairman and members of the subcommittee, I am pleased to appear before you to discuss the role of the Wisconsin Alumni Research Foundation, or WARF, and the WiCell Research Institute in supporting the important research necessary to move the science of embryonic stem cells forward.

I want to thank Chairman Harkin and Senator Specter for their vision and commitment to the ES cell research. Your work on this issue has given hope to millions of Americans who suffer from degenerative diseases and has also provided inspiration for researchers in the laboratory.

WARF is an independent, nonprofit supporting organization for the University of Wisconsin Madison, and is the patent management organization also for the University of Wisconsin Madison. From its inception, WARF's mission has been to support scientific research at the university for the benefit of the university and the public.

WARF carries out its mission by licensing university inventions and returning the proceeds to fund further research at the university, but equally important to the money returned to the university is the fact that throughout its existence the inventions licensed by WARF have functioned to improve the condition of mankind.

WARF owns two issued patents covering primate embryonic stem cells, and has other applications pending. The first patent covers primate embryonic stem cells, including the human ES cell, and the method for deriving and maintaining those cells. The research underlying that patent includes research on nonhuman primates funded by NIH, and the patent carries the appropriate notice that the Federal Government has an interest in that patent. The second patent is specific to the human ES cell, and the research underlying that patent is entirely privately funded.

WARF has never used its patents to block research, and does not intend to do so with embryonic stem cell patents. WARF has granted both research and commercial licenses under its patents, and will continue to do so under terms that are fair to all concerned, including the general public. Our goal is to facilitate research and development of stem cell technology, not impede it. In that regard, WARF supports legislation to permit derivation of new cell lines, and would welcome the opportunity to license centers for derivation of ES cells under WARF's patents.

From the beginning, the distribution of the ES cells for research purposes was of critical importance to the university and WARF. In light of the complication of Federal law, the university asked WARF to establish a privately funded institute to support the distribution of and research on human ES cells.

In response to the university's request, WARF formed WiCell Research Institute as a nonprofit subsidiary of WARF. Dr. James Thomson is the scientific director of WARF, and Dr. Nancy Black, who is here with me, is the manager of WiCell. Excuse me, I misspoke. Dr. James Thomson is the scientific director of WiCell.

WiCell distributes human embryonic stem cells under a material transfer and license agreement. The fee charged to the researcher for the license is returned to the institute and helps defray but does not cover the cost associated with making embryonic stem cells widely available. The WiCell agreement provides a research license. Researchers are free to publish and patent their discoveries.

If the researcher or her institution wishes to commercialize a discovery made under the agreement, an appropriate commercial license may be required. It may be that such commercial rights must be obtained from WARF, or from WARF's licensee, Geron. If such rights are not required, the researcher or her institution may commercialize the discovery as they choose.

Geron is one of two commercial licensees under WARF's embryonic stem cell patents. Geron was instrumental in providing needed funding for the human embryonic stem cell research that led to the Thomson discovery. In return for that funding, Geron was granted certain exclusive and nonexclusive rights under the patents. Geron's exclusive rights are limited, are in the diagnostic and therapeutic fields, limited to six defined cell types.

WARF's license agreement with Geron contains development requirements. The development requirements give Geron the right to terminate the license granted to a commercial partner for lack of active development. To maintain its rights, Geron must develop commercially viable products.

It should be noted that Geron has no right to inventions made by researchers who receive ES cells from WiCell. Geron also has no right to distribute ES cells to third parties not associated with Geron. That right has been reserved for WiCell.

WiCell currently has one other commercial licensee who has licensed the right to conduct internal research under the ES patents and use the human ES cells. That licensee, Bresagen, Limited, has recently announced the derivation of four additional cell lines under license from WiCell.

PREPARED STATEMENT

WARF, WiCell, and the UW Madison believe in and are excited about the future of medicine utilizing the ES cell technology. Our goal is to see this technology widely disseminated and developed. We believe that our licensing practices reflect that goal. We hope that Federal funding will increase the number of researchers who work with ES cells, and that these researchers will bring the tomorrow of medicine closer today.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF CARL GULBRANDSEN

INTRODUCTION

Mr. Chairman and members of the Subcommittee, I am pleased to appear before you to discuss the role of the Wisconsin Alumni Research Foundation ("WARF") and the WiCell Research Institute ("WiCell") in supporting the important research necessary to move the science of Embryonic Stem Cells ("ES Cells") forward. Virtually every realm of medicine might be touched by this innovation. Because of this enormous promise, WARF and WiCell are committed to proceeding with this research and to providing scientists with ES Cells. Because of concerns over derivation and use of ES Cells, WARF and WiCell feel a special responsibility to conduct our mis-

sion ethically and legally. The absence of NIH funding and other federal restrictions are slowing the progress of research that could alleviate a great deal of human suffering.

I want to thank Chairman Harkin and Senator Specter for their vision and commitment to human ES Cell research. Your work on this issue has given hope to the millions of Americans who suffer from Parkinson's, diabetes, spinal cord injuries and heart disease. Your tireless efforts also provide inspiration for researchers in the laboratory attempting to turn the potential of ES Cells into real treatments and cures for diseases that until now were thought to be untreatable. Dr. James A. Thomson from the University of Wisconsin-Madison (the "UW-Madison"), the first researcher to isolate human ES Cells, testified at your first hearing and detailed the method of deriving the ES Cells and the tremendous potential of these cells for studying human development and birth defects. It is an honor to speak to the Committee today about the efforts of WARF and WiCell to promote ES Cell research and to make ES Cells widely available to researchers across the United States and throughout the world.

BACKGROUND ON WARF AND WICELL

The Wisconsin Alumni Research Foundation is an independent, non-profit, supporting organization for the University of Wisconsin-Madison (UW-Madison). Recently, WARF celebrated its 75th anniversary. From its inception, WARF's mission has been to support scientific research at the UW-Madison for the benefit of the UW-Madison and the public. WARF carries out its mission by licensing university inventions and returning the proceeds to fund further research at UW-Madison. But equally important to the money returned to the UW-Madison is the fact that throughout its existence, the inventions licensed by WARF have improved the condition of humankind. WARF's licensed inventions have cured rickets, treated bone disease and psoriasis; Warfarin or coumadin was patented and licensed by WARF and is still the major therapeutic blood thinner for vascular disease and stroke prevention; the UW solution, another WARF invention, is widely used to preserve organs for transplant; and most recently human embryonic stem cells promises regenerative therapies for previously untreatable conditions.

The UW-Madison is unique in its policies regarding faculty ownership of intellectual property. Researchers at UW-Madison are presumed to own the intellectual property rights to any invention discovered during the course of their employment, barring an obligation to assign the invention because of federal or industrial funding. If federal funding is used in the conception or reduction to practice of an invention, the researcher is required to disclose the invention to the UW-Madison and the provisions of the Bayh-Dole Act apply (35 U.S.C. 200 et. seq.). In that case, WARF is the designated patent management organization for UW-Madison and receives assignment of any federally funded invention. It is important to note that federal funds were not involved in the work of Dr. Thomson when he made the critical ES Cell breakthrough in 1998. In fact, federal law prohibited NIH funding of research on embryos, even those in excess of clinical need after in vitro fertility treatment.

Dr. Thomson, therefore, was not required to assign his invention to WARF. He could have patented the stem cell discovery in his own name and sold all the rights to a private company. It is a testament to Dr. Thomson that he voluntarily brought this important technology to us so that his discovery would be patented and licensed in a manner that would provide for wide distribution of the ES Cell and insure that the highest of ethical standards were followed.

From the beginning, the distribution of the ES Cell for research purposes was of critical importance to UW-Madison, WARF, and WiCell. In light of the complications of federal law, the UW-Madison asked WARF to support a laboratory that was free of federal funds to support distribution and research on ES Cells. In response to the UW-Madison's request, WARF formed the WiCell Research Institute as a non-profit subsidiary in October of 1999 to advance ES Cell research. WiCell's mission is two fold: (1) to provide ES Cells for research purposes and (2) to engage in research in the human ES cells utilizing the expertise of the UW-Madison community. Dr. Thomson is the Scientific Director of WiCell and Dr. Nancy Block is the General Manager.

To date, WARF has spent well over a $1 million to establish WiCell and for maintenance and distribution of the ES Cells. WiCell has already outgrown its physical facility and has plans for a five fold increase in lab space. This increase is necessary because of the tremendous interest by researchers at UW-Madison in working with ES Cells. WiCell exists because of the federal prohibition on embryo research. The federal prohibition has made it necessary to duplicate space, equipment, personnel

and utilities to carry out ES Cell research. Without such a prohibition UW-Madison would perform WiCell's research functions.

Recently, Dr. Roger Pederson, an early collaborator of Dr. Thomson, announced that he is leaving the University of California-San Francisco ("UCSF") for Great Britain due to the difficulties associated with performing ES Cell research in the United States. This happened only after UCSF tried unsuccessfully to accommodate federal restrictions within its campus. Who knows how many other investigators may follow that lead or may be reluctant to pursue a career in ES Cell research.

The Committee should know that the ES Cells that are currently available from WiCell do not meet the guidelines in the proposed NIH regulations. The present cell lines were derived from excess embryos that were created for reproductive purposes and not for purposes of research. They were, however, derived well before the guidelines were published. The current ES Cell lines do meet the spirit of the regulations but not the technical letter. WARF and WiCell are committed to deriving additional lines that will meet the NIH guidelines but we cannot promise a date by which new cell lines will be available.

PATENT POSITION

WARF has never used its patents to block research and does not intend to do so with its stem cell patents. WARF is the owner by assignment from the sole inventor, Dr. Thomson, of two issued patents in the area of ES Cells. The first, U.S. Patent No. 5,843,780, (the "'780 Patent") issued December 1, 1998 with claims to primate ES Cells. The '780 Patent covers any primate ES cells (including humans as primates) which: (i) are stable and capable of proliferation in culture, (ii) maintain a normal karyotype containing all chromosomes characteristic of the primate species, (iii) maintain the potential to differentiate into all three embryonic tissue types (endoderm, mesoderm, and ectoderm tissues), and (iv) will not differentiate when cultured on a fibroblast feeder layer. This is characteristic of all normal ES Cells. In addition, the '780 Patent covers a method of isolating an ES Cell comprised of the current known method for culturing ES Cells.

The second patent, U.S. Patent No. 6,200,806 (the "'806" Patent) issued March 13, 2001 and is a divisional of the '780 Patent (collectively the "ES Cell Patents"). The '806 Patent covers any ES cells with the same characteristics of those claimed in the '780 Patent but it specifically claims human ES Cells. Also, the '806 Patent claims the method for culturing ES Cells claimed in the '708 Patent but it again specifically claims the method for culturing human ES Cells.

It is anecdotally interesting to note that while WARF's ES Cell Patents currently cover the most basic characteristics and the current method of culturing ES Cells, a cursory search of patent databases reveals that there are 95 issued patents in the United States with "stem cells" in their title and there are at least 638 U.S. patents that incorporate "stem cells" somewhere in their claims. In addition, there are hundreds of additional related issued patents covering cell culture, growth factors, extra cellular matrices and cell differentiation. This is no different than the patent landscape in any other biomedical area of research. There is patent protection in almost every facet of our lives, from the cereal consumed in the morning, to the alarm clock set before bed at night. Scientific innovation in the United States is advancing faster than it ever has. Patents facilitate and enable this advance.

WARF does not believe the ES Cell Patents are a disincentive for researchers in any respect. WARF and WiCell are committed to making the ES Cells and licenses under the ES Cell Patents widely available to academic researchers and industry.

DISSEMINATION OF ES CELLS TO RESEARCHERS

WARF, through its subsidiary WiCell, is committed to making the ES Cells widely available to researchers, both academic and commercial, throughout the world. If federal funding is provided for ES Cell research, the process of distribution would continue at WiCell unchanged from present practice. WARF supports legislation to permit derivation of new cell lines and would welcome the opportunity to license centers for derivation under WARF's ES Cell Patents.

WiCell provides ES Cells for research purposes under its standard Materials Transfer & License Agreement ("MTA"). The MTA contains research restrictions as provided in the NIH ES Cell guidelines published last August and from the University of Wisconsin-Madison Bioethics Committee. The MTA requires a research plan and yearly reporting to enable WiCell to monitor proper use of the ES Cells. Researchers entering into the MTA are provided frozen ES Cells in two vials sent along with protocols to assist the researcher in culturing the ES Cells.

To date, WiCell has about 30 MTAs executed for the human ES Cells with academic and nonprofit research institutions. Currently, WiCell has approximately 100

additional MTAs in various stages of negotiation. WiCell anticipates the number of requests for human ES Cells will increase significantly when federally funded scientists are permitted to conduct research using the human ES Cells.

The MTA for ES Cells allows researchers to do research and patent and publish any discovery made using the ES Cells. In order to accomplish the goal of making the ES Cells widely available at a low cost to researchers without prolonged negotiation, WiCell provides its standard MTA for research use only. Commercialization requires an appropriate commercial license. That license may be obtained from WiCell, WARF or, in areas for which Geron has rights, from Geron. The arrangement separating research and commercial licenses allows WiCell to grant research licenses at a price below WiCell's cost of producing ES Cells lines.

GERON AND OTHER COMMERCIAL LICENSEES

WARF has two license agreements with commercial entities. The primary license is to Geron Corporation. The license agreement grants exclusive rights to therapeutic and diagnostic products for six cell types. WARF's license agreement with Geron contains development requirements. The development requirements give WARF the right to terminate the license granted to a commercial partner for lack of active development. To maintain its rights, Geron must develop commercially viable products. These products are those that so many hope will increase the capacity to cure conditions that are presently incurable. WARF believes that the development requirements are significant in pushing this vital technology forward for the benefit of the public.

There has been a suggestion and a concern that research conducted in an area that Geron has licensed exclusively only benefits Geron. WARF believes this suggestion is not valid but appreciates the concern. First, it should be emphasized that Geron has no rights to inventions made by researchers who receive ES Cells from WiCell. Second, as stated previously, such researchers or their institutions are free to patent inventions arising from research using the ES Cells. It may be that to commercialize an invention, a researcher will need to obtain rights from Geron. However, the converse is also true. If Geron wants to use an invention created through such research, Geron will have to license those rights from the researcher—presumably under reasonable commercial terms.

WiCell currently has only one other commercial licensee who has licensed the right to conduct internal research under the ES Cell Patents and using the human ES Cells. This licensee, Bresagen, LTD., has recently announced the deriviation of four additional cell lines under license from WiCell.

WiCell has and will continue to make research licenses on ES Cells available. Commercial licenses to make research, therapeutic and diagnostic products in any cell type other than Geron's six cell types are also available. If a company with a research license discovers a therapeutic or diagnostic product in the area of one of Geron's six cell types, the licensee may need a license from Geron to commercialize the invention. Geron has the right to sublicense in its areas of exclusivity and Geron has assured WARF and WiCell that it will do so on reasonable commercial terms.

WARF, WiCell and the UW-Madison believe in and are excited about the future of medicine utilizing ES Cell technology. Our goal is to see this technology widely disseminated and developed. We believe that our licensing practices reflect this goal. We hope that federal funding will increase the number of researchers who work with ES Cells and that these researchers will bring the tomorrow of medicine closer to today.

Senator SPECTER. Thank you, Dr. Gulbrandsen.

Dr. Gulbrandsen, how many entities, if you know, own patents on stem cells?

Dr. GULBRANDSEN. We did a preliminary search just recently, and I can tell you that I think there are over 65 patents that have stem cells in the title. The number of entities I think that are doing work in the stem cell area are at least in the half-dozen to dozen range in the United States.

Senator SPECTER. 65 patents and research entities in the half-dozen to dozen range, you say?

Dr. GULBRANDSEN. Yes.

Senator SPECTER. Is there any limitation on what someone may acquire by way of patent when you have something so fundamental

to medical research, and with such widespread application for humanity, to have it available as a restricted property right, an intellectual property right?

Dr. GULBRANDSEN. Well, I think the limitation under the patent law is that it be described in such a way that somebody can make and use it, and it has to be distinctly claimed.

Senator SPECTER. Someone can make it, use it, and what?

Dr. GULBRANDSEN. It has to be described sufficiently in the application that somebody can duplicate that invention, that they can make and use it, and then the claims are really limited to what is described in the application.

Senator SPECTER. So there is no limitation as to what kind of intellectual property right may be obtained through a patent, even if it has enormous implications for society, human welfare?

Dr. GULBRANDSEN. Well, under the patent law there have been limitations that have brought into play where the public interest is really in jeopardy.

Senator SPECTER. What are those limitations as you—let me finish the question.

Dr. GULBRANDSEN. I am sorry.

Senator SPECTER. As you articulate it, where the public interest is in question?

Dr. GULBRANDSEN. My recollection—and I teach patent law at the University of Wisconsin Madison. My recollection is——

Senator SPECTER. You teach patent law?

Dr. GULBRANDSEN. Yes—is that there is one case. In the Milwaukee sewage case—and this has to do not with what the Federal Government, or what the patent office issues as a patent, but whether the courts will enforce a patent, and they of course do have the right to not enforce a patent if, in the interest of public health and safety, enforcing that patent would jeopardize those interests, so in the Milwaukee sewage case, enforcing the patent meant that sewage was going to be dumped into Lake Michigan, and in that case the court would not enforce the patent.

Senator SPECTER. Do you know what court that was?

Dr. GULBRANDSEN. I think it was the Eastern District Court in Wisconsin.

Senator SPECTER. Well, do you think that kind of a generalization, that patent rights would be limited where public interest is involved, would be applicable where you have such enormous potential on the stem cells for alleviating so many diseases?

Dr. GULBRANDSEN. I think—certainly I am biased, Senator. I think that in the stem cell area that the opportunity for bringing these products to market to benefit mankind is going to be enhanced with the fact that WARF has patented this and is working very hard to distribute these cells to others to do research and that you do have an entity that is committed to serving the public good holding these patents.

Senator SPECTER. Well, intellectual property rights are very fundamental in our society, beyond any question. They are provided for in the Constitution. Where you have such an unusual situation as patents on stem cells—and the ramifications are very complicated. I do not know that they are yet fully understood as to

where you are going, and I appreciate your declaration of bias. You represent a patent holder. You have a right to be biased.

This subcommittee is concerned about how these techniques will be applied to cure diseases, and we would be looking for an exception that you state, where there is a public interest, and it may not be necessary, if there is licensing, and if there is an open attitude on the part of the patent holders to permit others to utilize them for the public interest, but if a tight hold is maintained for the profit motive, that is another matter.

What is your view on the issue, Dr. Friere, about limiting patent rights where there is an overwhelming, supervening public interest?

Dr. FRIERE. Well, Senator, that is of course a critical question and one that, as a public agency, we really take very seriously. We do sometimes, in fact, in the United States have patents issued that are very broad in scope, and have tremendous implications for these kinds of technologies.

In my experience, we have been able to work through by material transfer agreements or licensing agreements the issues of intellectual property such that you are able to maintain the research balance and the commercial balance. It is my hope——

Senator SPECTER. That has been your experience, but you have not had anything as dramatic as stem cells, have you?

Dr. FRIERE. No, not in stem cells.

Senator SPECTER. You did not look like you were old enough to have had experience with something as dramatic as stem cells.

Dr. FRIERE. No. We have had some experience, for example, with in vivo/ex vivo gene therapy in which we were issued a very broad claim on gene therapy, and that technology was licensed very broadly, after—it was licensed exclusively by us, and then it was made available very broadly to companies, so the system does have checks and balances in place, but you are correct, I have not had to deal with stem cells.

Senator SPECTER. Dr. Gulbrandsen, I have been advised by staff that any researcher who derives human embryonic stem cells in his lab would be infringing on WARF's patent. Is that true?

Dr. GULBRANDSEN. Yes.

Senator SPECTER. I am further advised that WARF has not indicated that it will license the right to derive stem cells in other labs, is that true?

Dr. GULBRANDSEN. No. It has indicated in both what I have said here this morning and in our written statement that we would be happy to license people to derive stem cells.

Senator SPECTER. Have you licensed people to do that?

Dr. GULBRANDSEN. Yes.

Senator SPECTER. At what cost?

Dr. GULBRANDSEN. This was a commercial entity, and the cost is proprietary.

Senator SPECTER. The cost is what?

Dr. GULBRANDSEN. The cost is a confidential matter between WARF and the commercial——

Senator SPECTER. Is there just one license which has been made available?

Dr. GULBRANDSEN. At this date there are two commercial licenses.

Senator SPECTER. Two commercial licenses where WARF has been paid for the licensing rights?

Dr. GULBRANDSEN. That is right.

Senator SPECTER. To what extent has NIH research been involved, Dr. Friere, which could be linked to the benefits or to the patents which WARF has obtained?

Dr. FRIERE. The original primate patent with the rhesus monkeys work by Dr. Thomson was federally funded, and we do have some rights to that original patent, as Dr. Gulbrandsen mentioned.

Senator SPECTER. Has Dr. Thomson—specify the relationship, if any, between Dr. Thomson and WARF.

Dr. FRIERE. Dr. Thomson is—well, I should actually have you answer the question, if he is one of your researchers.

Dr. GULBRANDSEN. Dr. Thomson is a faculty member at the University of Wisconsin Madison. He is a collaborator to WiCell, and he is the scientific director for WiCell.

Senator SPECTER. What is the relationship specifically between WiCell and WARF, Dr. Gulbrandsen?

Dr. GULBRANDSEN. WiCell is a wholly owned subsidiary of WARF.

Senator SPECTER. Well, would you elaborate, Dr. Friere, on what NIH has done with respect to funding Dr. Thomson which would give NIH some proprietary interest?

Dr. FRIERE. The NIH funded the very early work that Dr. Thomson did in monkeys. This was the work that allowed him to first look at this technology and, in fact, the original patent of the derivation of stem cells and of the actual cells was based on that primate work.

Senator SPECTER. Do you know how much funding there was from NIH?

Dr. FRIERE. No, but I can easily find out.

Senator SPECTER. Would you provide that to the subcommittee?

Dr. FRIERE. Yes, I will be happy to do that.

Senator SPECTER. And as you see it, does that give NIH an interest in what Dr. Thomson has developed?

Dr. FRIERE. Yes, by law, when we fund research, the Government retains a royalty-free, nonexclusive license to practice the invention on behalf of the Government.

Senator SPECTER. A royalty-free, nonexclusive license?

Dr. FRIERE. Yes.

Senator SPECTER. So you are saying that NIH would have a license to work on deriving embryonic stem cells?

Dr. FRIERE. We would have a license under the patent, if this was something that was permitted to do, we would have a license for Government purposes.

Senator SPECTER. You mean if Federal funding could legally be used to extract stem cells from embryos?

Dr. FRIERE. Right, and that means that we could use that, but only for Government purposes, and Government purposes are defined for work, for example, within the NIH and NIH contractors. It does not extend to our grantees.

Senator SPECTER. It does not extend to your grantees?

Dr. FRIERE. No.

Senator SPECTER. How do you distinguish between a contractor and a grantee?

Dr. FRIERE. A contractor is an award made for a specific Government purpose. A grantee is initiated by the researcher, so it is really a different system.

Senator SPECTER. Well, the contractor provision would give a fairly broad swath to what could be done with NIH funding.

Dr. FRIERE. I would have to look exactly into what that would allow us to do, Senator.

Senator SPECTER. Why the distinction between contractor and grantee?

Dr. FRIERE. That has always been the way that Government rights have been interpreted, have been interpreted to limit the rights to the contractor.

Senator SPECTER. Well, would you provide the subcommittee with the specifics on that?

Dr. FRIERE. I will be happy to.

Senator SPECTER. We may be involved in a very high finance issue here, where the semicolons turn out to be very, very important.

Dr. FRIERE. I will be happy to do so.

Senator SPECTER. Dr. Gulbrandsen, would you agree with what Dr. Friere said?

Dr. GULBRANDSEN. Yes, I would, and I would say again that WARF supports the establishment of centers for derivation of stem cells and is eager to license those centers.

Senator SPECTER. And you are prepared to license other laboratories which seek to derive human embryonic stem cells?

Dr. GULBRANDSEN. Yes.

Senator SPECTER. But at a price.

Dr. GULBRANDSEN. Well, at a price that is fair.

Senator SPECTER. But confidential.

Dr. GULBRANDSEN. That is right.

Senator, I might add that with respect to WARF's patents I think the evidence is that WARF has acted responsibly with respect to its patents, and we have also put a tremendous amount of effort in moving this whole program forward. The research that has been done at Wisconsin in the embryonic stem cell area is really quite remarkable, and the research done by Geron is also quite remarkable, and so you know, we are not sitting on these patents.

We are using these patents, and we are licensing them, and I would like to emphasize that Geron does not have the exclusive rights to these patents, and we are going to be looking at licensing others.

Senator SPECTER. You do not have exclusive rights to the patents. Who else has rights to the patents?

Dr. GULBRANDSEN. What I am saying is, Geron does not have total exclusivity with these patents. They have exclusive rights in certain defined areas, but there are many other areas that are available for licensing and WARF intends that this technology gets developed to benefit humankind.

Senator SPECTER. Well, are you saying that there are others besides WARF which have patent rights in the field?

Dr. GULBRANDSEN. No, not in the human embryonic stem cell area.

Senator SPECTER. So WARF has the only patents in the human embryonic stem cell area?

Dr. GULBRANDSEN. That cover the human embryonic stem cell that I am aware of. I assume that Johns-Hopkins has patents covering the human—what do they call it, the embryonic germ cells. I am assuming that Johns-Hopkins has filed patents on that.

Senator SPECTER. Well, this subcommittee is going to be looking at the specifics, and Dr. Friere, I would like you to provide the materials which I have asked for, and any other materials which would bear upon potential NIH rights to have research done because of the contribution which you made to Dr. Thomson.

[The information follows:]

You asked for clarification of the distinction between a grantee and a contractor and their respective right to use patented technology under grants and contracts.

Contracts are used when the principal purpose of the instrument is to acquire (by purchase, lease, or barter) property or services for the direct benefit of the Government. 31 U.S.C. 6303. Grants are used when the principal purpose of the relationship is to transfer a thing of value to the recipient to carry out a public purpose of support or stimulation instead of acquiring property or services for the direct benefit or use of the Government, and substantial involvement between the Government and the recipient in carrying out the activity is not contemplated. 31 U.S.C. 6304. In accordance with the Bayh Dole Act, 35 U.S.C. 200–212, the Government has a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any invention conceived or first actually reduced to practice in the performance of a grant or contract for the performance of experimental, developmental, or research work.

The government use license obtained from recipients of Federal funds may be used by the government for its own purposes, which have been determined to extend to government contractors, but not to grantees. As noted, grants are an assistance mechanism, where the grantee receives financial support for a particular activity, rather than a mechanism for the government to accomplish its own ends by setting the scope and performance of the work to be performed. Chapter 10 of Principles of Federal Appropriations Law, 2nd ed., U.S. General Accounting Office, provides additional guidance (p. 10–6): "Grant needs, by definition, are not needs for goods or services required by the Federal government itself. The needs are those of a nonfederal entity, whether public or private, which the Congress has decided to assist as being in the public interest." We are aware of no Federal court decisions directly interpreting the scope of the government's license under Bayh-Dole.

Senator SPECTER. Dr. Gulbrandsen, the subcommittee would appreciate it if you would identify to the extent you can other parties who have patents on intellectual property rights.

Dr. GULBRANDSEN. Certainly.

Senator SPECTER. And give us supporting data, to the extent you can, as to the positions that you have taken which have made this information available to others, and your general practices which, as you articulated, you consider to be responsible. We would like to take a close look at it, because it may be that the Congress will need to legislate in this area. I do not know.

[The information follows:]

WARF has never used its patents to block research and does not intend to do so with its stem cell patents. WARF is the owner by assignment from the sole inventor, Dr. Thomson, of two issued patents in the area of ES Cells. The first, U.S. Patent No. 5,843,780, (the "780 Patent") issued December 1, 1998 with claims to primate ES Cells. The '780 Patent covers any primate ES cells (including humans as primates) which: (i) are stable and capable of proliferation in culture, (ii) maintain a normal karyotype containing all chromosomes characteristic of the primate species, (iii) maintain the potential to differentiate into all three embryonic tissue types (endoderm, mesoderm, and ectoderm tissues), and (iv) will not differentiate when

cultured on a fibroblast feeder layer. This is characteristic of all normal ES Cells. In addition, the '780 Patent covers a method of isolating an ES Cell comprised of the current known method for culturing ES Cells.

The second patent, U.S. Patent No. 6,200,806 (the "806" Patent) issued March 13, 2001 and is a divisional of the '780 Patent (collectively the "ES Cell Patents"). The '806 Patent covers any ES cells with the same characteristics of those claimed in the '780 Patent but it specifically claims human ES Cells. Also, the '806 Patent claims the method for culturing ES Cells claimed in the '708 Patent but it again specifically claims the method for culturing human ES Cells.

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WARF does not believe the ES Cell Patents are a disincentive for researchers in any respect. WARF and WiCell are committed to making the ES Cells and licenses under the ES Cell Patents widely available to academic researchers and industry.

Senator SPECTER. We are on very unusual ground here when we talk about stem cells, and I congratulate what has been done by your organizations, Dr. Gulbrandsen, and the University of Wisconsin. We think it has been tremendous, and you have advanced scientific causes tremendously, and I do not in any way question your responsible approach to what is going on.

We would just like to get a handle on the details, because we had a hearing a couple of weeks ago. A representative of HHS made a representation that the patents would obstruct NIH research, and that is why we convened this hearing on that aspect so that we could get involved in the details.

Dr. GULBRANDSEN. Senator, I appreciate that. I do not believe the patents will obstruct either the research or the commercial development, and we are more than happy to work with your office as we are happy to work with NIH. We consider NIH a very good partner at the University of Wisconsin, and I think we all want the same goal. We want to see this technology used to benefit humankind.

Senator SPECTER. That is the common object.

Well, I am told Dr. Friere, that you are stepping down from your post at NIH to become CEO of a nonprofit company dedicated to finding a cure for tuberculosis. Why did you choose a nonprofit company when profits appear to be so plentiful?

Dr. FRIERE. Senator, I have a not-for-profit streak in me.

Senator SPECTER. Well, you fit in very well with Congress in that event.

Dr. FRIERE. Thank you.

Senator SPECTER. And they are lucky to have you, Dr. Gulbrandsen. You are both a Ph.D. and a J.D., you teach patent law and you make all the discoveries. That is a pretty good combination, pretty hard to beat. Nobody around here to my knowledge, not even Dr. Frist, can compare with that, but perhaps Senator Frist can.

Thank you very much, and we will take about a 2-minute recess, and will then convene the second panel, if the witnesses will come forward.

Dr. GULBRANDSEN. Thank you.

Senator SPECTER. Thank you.

We will reconvene. Thank you very much for coming, gentlemen.

Let us start with Dr. Nigel Cameron, who is executive chair of the Centre for Bioethics and Public Policy. Educated at Cambridge and Edinburgh, Dr. Cameron founded the International Journal of Ethics and Medicine, and has authored a series of books on bioethics. I might just point out that Dr. Cameron has a somewhat different perspective. We have made these hearings balanced so that all points of view would be expressed.

Senator Sam Brownback has been a frequent witness here, as have others, and my views on stem cell research are fairly well-known, but the subcommittee wants to hear from all points of view, and have it as balanced as possible so that there can be as thorough a discussion for the public as possible.

So we are glad you came, Dr. Cameron, and the floor is yours. There is a 5-minute time limit, let me repeat, and we would like to observe that. Dr. Cameron, proceed.

STATEMENT OF NIGEL M. DE S. CAMERON, Ph.D., EXECUTIVE CHAIR, THE CENTRE FOR BIOETHICS AND PUBLIC POLICY, LONDON, ENGLAND

Dr. CAMERON. Thank you very much, Senator. I do appreciate that welcome, and the invitation. Part of the problem we face in this discussion is to identify what the issue is in which we are engaged in debate, and it seems to me very plain that the issue is this, whether we should be using members of our own species, our own kind, homo sapiens sapiens, in whatever stage of biological existence, for a purpose that is other than the good of the individual concerned, whether we should sanction the use of ourselves as experimental subjects.

Let me offer four brief observations on our dilemma. First, until recently, it was widely agreed that human embryos should never be manufactured in order to be destroyed through experiment, however worthy the experiment. This principle, for example, is enshrined in the one international bioethics treaty, the European Convention on Biomedicine and Human Rights, and was memorably captured some years ago in a ringing editorial in The Washington Post.

The creation of human embryos specifically for research that will destroy them is unconscionable, yet the Jones Institute has now brazenly announced that they have done just that, and the debate seems to be moving on.

The problem, of course, is the challenge of consistency. May a line be drawn that will permit experimentation on clinically spare embryos, a line that will stand in the face of mounting commercial and clinical opportunity? This is, of course, the compromise that has been floated in various quarters, most notably and most seriously by Senator Frist.

The level of support for embryo cloning to order in the Greenwood-Deutsch bill and now the timely ocular proof of the Jones Institute suggests the final naivety of such well-intentioned policy

hopes, since in the minds of most of those who lead the call for spare embryo research, there is only a modest distinction between spare embryo research and the new Jones approach, a distinction which falls far short of the kind of language captured by the Post in its use of a term like, unconscionable.

Second, I do not propose to get involved in the extensive debate about the relative merits of embryonic and adult stem cell work. Plainly, some and perhaps all of the good things prophesied to come from the one may come from the other. It is ironic, and to my mind to be regretted that this debate has sometimes seemed to be central to our discussion of the ethics of embryonic stem cell work, as if somehow showing that there was another way to get these benefits somehow decided the moral questions. Moral questions, it seems to me, need to be decided on their own merits.

Third, I do believe that in this discussion we are in danger of losing sight of the middle ground in the assessment of the early embryo. That is to say, this is not a rerun of Roe. This is not essentially a debate about the implications of our stance on the abortion issue.

It is by no means necessary to take the view, moreover, that the early embryo is a full human person, however we define that term, in order to be convinced that deleterious experimentation is improper, indeed, the deeply held, widely held until very recently, view that creating embryos for the purpose of destructive research indicates a strong, intuitive commitment of persons, many of whom are not traditionally pro-life, that the early embryo deserves profound respect. We seem to be moving on also from that view.

Fourth, let me share my dismay at the degree to which this debate has sometimes degenerated into an iteration and reiteration of the potential benefits of this kind of experimentation, as if those who oppose public funding for what they consider unethical research are either ignorant of or heedless toward disease and its sufferance, and it does seem to me that the use of celebrities as an alternative argument is an unfortunate attempt to short-circuit the moral assessment of means by the crass assertion of ends.

PREPARED STATEMENT

At the heart of our conception of civilization lies the notion of restraint. There are things that we will not do, whatever benefit they may bring, things we shall never do, though the heavens fall. As we stand at the threshold of the biotech century, we could hardly confront a decision that is more onerous, since the promised benefits from this technology, as from many other potentially unethical technologies, may be great, if that is, of course, simply to focus the moral question. It has become alarmingly hard to insist that whatever the potential benefit of a particular course of action, the means must be patently ethical. Human dignity, Mr. Chairman, is finally indivisible.

Thank you very much.

[The statement follows:]

PREPARED STATEMENT OF NIGEL M. DE S. CAMERON

My name is Nigel Cameron. I have worked for 20 years in bioethics, founded the journal Ethics and Medicine in 1983, and am currently involved in bioethics projects in both Europe and the United States. It is a privilege to be invited to testify today.

Two great questions confront the human race at the start of the biotech century. The second, presently only on the horizons of our thinking and yet of incalculable import, will focus our growing capacity to design, determine, transform ourselves and our nature; the incremental progression toward the so-called "post-human" future. The first question is the one that confronts us today: whether we should use members of our own kind, Homo sapiens sapiens, in whatever stage of biological existence, for a purpose that is other than the good of the individual concerned; whether we should sanction the use of ourselves, in however early a form, as experimental subjects whose final end is destruction.

Let me offer four observations on our dilemma.

First, it seemed until recently to be widely agreed that human embryos should never be manufactured simply in order to be destroyed through experiment, however worthy the experiment. This principle is, for example, enshrined in the European Convention on Biomedicine and Human Rights, the one international bioethics treaty; and was memorably captured some years ago in a Washington Post editorial in the ringing phrase: "The creation of human embryos specifically for research that will destroy them is unconscionable." Yet the Jones' Institute has brazenly announced that they have done just that. And as Charles Krauthammer's recent pro-stem-cell research piece notes, the cloning debate has focused the same issue. The chorus of support for Greenwood-Deutsch has been fed precisely by a scientific-industrial community eager to clone and destroy embryos for scientific-industrial purposes.

The problem, of course, is one of drawing lines; the challenge of consistency. May a line truly be drawn that will permit experimentation on clinically "spare" embryos, a line that will stand forever and in the face, we may expect, of mounting commercial and clinical opportunity that argues for their creation to order? That is of course the compromise that has been floated in various quarters, most notably and seriously by Senator Frist. The level of support for embryo cloning-to-order in Greenwood-Deutsch, and now the timely "ocular proof' of the Jones Institute, suggests the naivete of such policy hopes, since in the minds of most of those who lead the call for "spare" embryo research only there is only a modest distinction between this politic option and the Jones way. It is a distinction that falls far, far short of what the Post designated "unconscionable." It is not, as we might put it, that we believe that further dominoes will fall; they are falling all around us. For the logic of the experimental abuse of "spare" human embryos depends ultimately on so meager a valuation of the embryo itself that their creation-to-order is inevitable. If the embryo is at base object and not in any sense subject, what is to prevent it? It is reported that one celebrity recently announced here on the Hill and in defense of embryonic stem-cell research that the embryo is of similar moral standing to a goldfish.

Second, I do not propose to get drawn into the extensive debate surrounding the relative merits of embryonic and other, typically adult, stem-cells. Plainly, some and perhaps all of the good things that are prophesied to be the fruit of embryonic stem-cells may be attained using adult cells or other means. It is ironic, and to be regretted, that this debate has sometimes seemed to hinge on whether adult stem-cell work is likely to be as fruitful as the embryonic kind, as if the moral question, while of some weight, could be discounted by a certain evaluation of likely relative clinical outcomes. This is a profound moral debate about what we will and will not do to our own kind, for whatever alleged benefit.

Third, I believe that we are losing sight of the middle ground. By that I mean that it is by no means necessary to take the view that the early embryo is a full human person in order to be convinced that deleterious experimentation is improper. There are many possible grounds for such a view—that we do not know if the embryo possesses full human dignity and should therefore be prudent; that the embryo possesses the potential to be a full human person and that such inbuilt potentiality entails profound respect, a view widely held and deeply threatened in this debate; or that membership in our species is enough to distinguish the human embryo from all other laboratory artifacts. Indeed, the widely held view that embryos should not be specially created for experimental purposes itself reveals a strong if undefined disposition to protect the embryo from abuse.

Fourth, let me share my sense of dismay at the degree to which this debate has sometimes degenerated into an iteration and reiteration of the potential benefits of this kind of experimentation, as if those who oppose public funding for what they

consider unethical research are either ignorant of or heedless toward disease and its sufferers. The celebrity argument is a sham, an attempt to short-circuit the moral assessment of means by the crass assertion of ends. It is an embarrassment to the cause of ethics in public policy.

For the question we face is distinctly ethical in character. At the heart of our conception of civilization lies the principle of restraint: that there are things we shall not do, shall never do, even though they may bring us benefit; some things we shall never do, though the heavens fall.

As we stand on the threshold of the biotech century, we could hardly confront a decision that is more onerous, since the promised benefits from this technology may be great. Yet that is of course simply to focus the moral question. If there are things that we should not do, it is easy for us to refuse to do them when they offer no benefit. When the benefit they offer is modest, the choice is still not hard. The challenge to morals and to public policy lies precisely here, where the benefits seem great. Yet it is here also that our intuitive respect for the early embryo requires us to pay a price. In a culture fixated with the satisfaction of its needs and the healing of its woes, it has become hard even to say that we shall never, for whatever benefit, experiment on our own kind? Shall we do evil, that good may come?

STATEMENT OF ARTHUR CAPLAN, Ph.D., DIRECTOR, CENTER FOR BIOETHICS, UNIVERSITY OF PENNSYLVANIA

Senator SPECTER. Thank you, Dr. Cameron. We turn next to Dr. Arthur Caplan, director of the Center for Bioethics, University of Pennsylvania, professor of molecular and cellular engineering, and professor of philosophy, B.A. from Brandeis, Ph.D. from Columbia. Thank you for joining us, Dr. Caplan, and the floor is yours.

Dr. CAPLAN. Thank you, Senator. It is a pleasure to have this opportunity to testify to the committee and to a fellow Pennsylvanian.

I think in some ways I, too, am going to follow Dr. Cameron's lead. I am not going to spend any time today in my brief remarks going over the benefits, be they from celebrities, or be they from scientists, or be they simply from patients who are suffering with disability or disease. I think we can concede that stem cell research is promising. I think there may be a long road to travel to deliver on that promise, but nonetheless, it seems to me the promise is there, and that can be conceded regardless of discussions about possible alternative strategies.

What I would like to do is focus instead on a couple of ethical points about how I would frame this debate. I have been following it closely, in fact, since I first came before this committee about 9 months ago, I think, to talk about this issue, and like Dr. Cameron I, too, have been a little bit put off by some of the tone of the debate. I think people who are arguing for respect for human life are commanding a moral position that is deserving of careful listening. I appreciate the committee soliciting all opinion, but at the end of the day, I think the framework being articulated is not correct.

It would be wrong for sure, morally, to say that we can benefit people who are in need, or future generations, by killing some people today. There is no doubt that a principle we should not break is that we should not murder to benefit. As the Senator knows, this has been a major issue in a related area that he and I have had a chance to talk about, organ donation. We know that we can benefit by making kidneys and livers and hearts available from deceased persons, but we also know that we must not hasten death, cause death, or in any way be involved with death, bringing it about, in order to do the benefit.

On the other hand, people die from many tragic reasons, and we do try, then, to approach individuals and see whether they wish to

make something good happen out of these tragic circumstances. There may be suicides, there may be murders, there may be child abuse. There are all kinds of conditions that sadly produce the availability of cadaver organs.

I believe that in this debate there is a moral equation that does not hold, and that is that embryos are either persons, or to be treated as human beings from the moment of conception. I think factually this is not the case. I think that what we are talking about and what most Americans believe is that we have something that is a potential or possible person in the right circumstances. In a dish, in a freezer, that potentiality will go nowhere.

If we look at the circumstance of embryos, and if we look at what our biologists are telling us about understanding the genetics involved in development, we know that many embryos are not ever going to become persons, no matter what we did to them. It is why infertility treatment is so difficult.

The fact that embryos may have genetic errors, if you will, blueprint problems, and many do, and that increasingly, as women age, those are more manifest, making fertility impossible after one reaches their fifties, is an indication that not all embryos have potentiality, so one premise I would put before you and the subcommittee to ponder is that not all embryos do have the potential to become human beings. We know this.

Second, when we store, freeze, and put them aside, it is often because in the opinion of physicians, these particular embryos are not likely to become persons, and the longer they are kept frozen and stored somewhat diminishes that potential even further.

That means that what we are talking about to begin with is not, if we propose to destroy embryos, necessarily killing. We are talking instead about, if you will, the destruction of potential, possible persons. We are also talking, if you will, about the destruction of many things that have no possibility of becoming persons.

If I am to make a trade-off, then, the other principle I have to follow is, do we make things with the intent of destroying them, or have we a situation where for good motives, people trying to have children, for good reasons, people wanting to have babies, these entities are created and exist, but are no longer wanted. As the Senator is well aware, there is something like 100,000 of these, at a minimum, around the United States. Their fate is never to become children.

I see that as somewhat analogous to the situation with transplant. No one set out to make this situation occur. It is a byproduct of our ignorance and inability to successfully help people who want to have children. We overproduce embryos. They are left behind, and they are ultimately going to be destroyed.

If we grant, then, that not all embryos have the potential to become persons, then not all embryos are persons, and that we have, if you will, an enormous number of embryos that never will become persons, and trying to make some good happen from the reality of the existence of those stored embryos, which abound, leads me to one last observation.

We are talking here about research that will involve embryonic stem cells, but we are talking also about research that is relatively new, that relatively few people can do. I have to report to the Sen-

ator that in trying to figure out—and you will see this in my written testimony—what number of embryos are we talking about for the next few years to demonstrate the feasibility of this research, I would estimate, if 15 researchers worked with five embryo cell lines, we might be talking about something less than 200 embryos out of 100,000 frozen that their fate is destruction, or permanent storage. It seems to me the moral equation comes out in favor of those who are real, here and now, with real needs and real disabilities and real problems. That promise should be delivered on.

So I would argue, using those facts, and the moral principle that making something good happen out of the reality of something unfortunate exists, the surplus, absolute huge number of embryos that already exist, if we are in a situation, what we are talking about then is possibility of potentiality that will never be actualized, I think it is a trade that this committee should pursue aggressively in order to bring benefits to the American people.

Senator SPECTER. Thank you very much, Dr. Caplan.

STATEMENT OF GLENN McGEE, Ph.D., ASSISTANT PROFESSOR OF BIOETHICS, PHILOSOPHY AND HISTORY AND SOCIOLOGY OF SCIENCE, UNIVERSITY OF PENNSYLVANIA

Senator SPECTER. We turn now to Dr. Glenn McGee, assistant director for education and assistant professor of bioethics, philosophy, history, and sociology at the University of Pennsylvania, editor-in-chief of the American Journal of Bioethics, B.A. from Baylor, and Ph.D. from Vanderbilt. Thank you for joining us, Dr. McGee, the floor is yours.

Dr. MCGEE. Thank you very much for inviting me, Senator, and for the opportunity to testify before the subcommittee.

As a scholar of bioethics, ethical issues and human cloning and stem cell research in particular, my role today——

Senator SPECTER. Tell me for the record how your laptop is working here. It does not appear in the printed text. I think it would be of some interest if anybody ever reads this record.

Dr. MCGEE. I am not sure I follow the question.

Senator SPECTER. Your mechanism for presenting your presentation. What is it, and how are you using it?

Dr. CAPLAN. He has got a battery-driven laptop.

Senator SPECTER. Dr. Caplan has clarified it totally. You may proceed, doctor.

Dr. CAMERON. It is not potential, it is actual.

Dr. MCGEE. That is right, and it has rights.

My role today as—I would like to construe it as to briefly discuss the question of self-regulation in human embryonic stem cell research. Like my colleague, Dr. Caplan, I have authored a number of articles about stem cell research ethics in general, and participated in a number of ethical debates within the FDA Panel on Molecular and Genetic Devices, on which I serve, but from August of 1999, when I was invited to join the ethics advisory board of Advanced Cell Technology, one of the companies that works in the area that we are discussing today, until October of 2000, I was active in a relatively new form of discussion and debate about ethics, and that is the corporate ethics advisory approach.

Although I am a proponent of stem cell research, and have argued in print that stem cell research, including research involving

embryos, should be permitted and funded, in October I reluctantly resigned from my role at Advanced Cell Technology for two very specific reasons.

First, I have concern over corporate decisions in stem cell research in particular not to share all of the information about ethically relevant activities in stem cell research with the ethics advisory board that is convened to help the company, or in due course to share the full amount of information available with the public so that public debate can be developed, and second, because I was concerned about what I viewed as the excessive pursuit of intellectual property in stem cell research.

To be clear, I am not opposed in principle to the creation of embryos for research using nuclear transfer, or to research that uses stored or made embryos. I believe that at some point in the future there may be significant therapeutic benefits to be derived from what is being termed therapeutic cloning, and I worked with the British Government in 2000 on what became their policy of carefully monitored nuclear transfer research.

But what I am concerned about today is the danger that industry self-regulation in the area of nuclear transfer may not be easily ameliorated by Federal funding. It seems to me extremely problematic that the early stem cell research currently underway has been driven in the main by small business, because at this early stage the only real resources that small stem cell companies can hope to build up are patents.

If stem cell research is tied up at this stage by patents and licensing agreements, even if those patents are held by universities who trade them in fair and honest ways, the effect will be to hamper and slow research, but moreover, it will tax any Federal dollars for stem cell research in what I think you could argue is an unacceptable way.

At this point, one could offer any number of percentages, but arguably as much as 30 to 50 percent of Federal funding for stem cell research might flow directly or indirectly to small stem cell companies through the fees that they are allowed to assess to any funded researcher.

More importantly, I am concerned about the risks of allowing a small biotechnology company, whether inside or outside the university, to control and license stem cell technologies. This is aggravated, moreover, by the fact that the companies with the most valuable portfolio of stem cell patents are also companies that, it has recently been reported in the media, are tiny operations with little capital or strategic flexibility.

Whether or not there is Federal funding of therapeutic cloning, it seems to me there must be much more oversight over nuclear transfer technologies and specifically over the control of these technologies by a few people in small business.

Perhaps it is because small companies are so innovative and important in the overall scope of stem cell research that at least two stem cell companies created ethics advisory boards to help them deal with the kind of controversy that corporate-driven basic research would necessarily create. I can only relay my own experience on such a board, which I think is in some ways instructive.

In my time on the ethics advisory board of Advanced Cell Technology, I do not believe that the relatively new mechanism of corporate ethics advisory boards performs the role of self-regulation effectively. I was concerned that ethics advisory boards, including the one on which I served, which many in industry have now pointed to as a way to promote ethical practice, will not be able to work in an objective way, or in the broader societal interest.

My concern is not that ethicists are bought by companies, or about research conducted within companies to determine whether or not ethical problems exist. Indeed, both of these are to be, I think, considered separately. Instead, I am concerned that ethics boards and their chairs are being asked by these companies to play roles that are, in my view, not appropriate to the ideals of bioethics or, more importantly, of science in the public interest.

Their roles have shifted, at least in my own experience, from the original conception of an ethics advisory board in its Government capacity, which is a research body convened to evaluate the activities of the organization and publish those to peers, into a very different role, that of lobbyists or public relations. In my view, industry self-regulation through boards thus serves neither the interests of the companies nor the interests of ethics.

Stem cell corporate ethics advisory boards are attractive to ethicists precisely because, in the world of stem cells, you cannot study the research without understanding how it is conducted. In my view, this was an important reason to participate in this research and in this way.

But whatever good intentions the company may have in terms of providing that kind of access, the usefulness of ethicists working in companies on ethics advisory boards is at least in part the fact that their papers and statements on behalf of the company have the effect of insulating the company against criticism from other ethicists, who will not be comfortable attacking their peers, whose work is coming out of such a vulnerable position.

Briefly, a final point. I think that in order for the ethics advisory board as a mechanism for self-regulation to work, it would have to do several things, and to do them openly. First, to foment public discussion and debate, to hold open meetings that are well-publicized in advance, to name its members.

Second, to advance discussion of corporate research in the bioethics community before companies begin their work, not afterwards.

Third, to insist on full knowledge of corporate activities, including disclosure of any experiments that might receive ethics scrutiny. In my case, I found out about one very controversial experiment the day after it was released from embargo. The ethics advisory board had not been notified that cell technology was working on, for example, cloning a gauer.

Fourth, to be open about the affiliations, responsibilities, and expertise, or partisanship of any members of the committee.

Fifth, to be fully funded by the committee not just an unfunded declaration.

PREPARED STATEMENT

And finally, to discuss only those issues about which it has written or debated, and to insist on rigorousness about that role.

I think that ethics advisory boards are the best model industry has offered for self-regulation, and in my own experience, working in a number of different capacities, including my single experience on an ethics advisory board, I think we will find that this is insufficient.

[The statement follows:]

JOINT PREPARED STATEMENT OF ARTHUR L. CAPLAN AND GLENN MCGEE

We are very pleased to have the opportunity to address this subcommittee on the subject of stem cell research. One of us has had the privilege of speaking on this subject at an earlier hearing and since that time we have followed with keen interest the thoughtful efforts by this subcommittee to address the complex moral, regulatory and scientific issues associated with stem cell research.

As some of the members of this subcommittee know, we have tried for many years to wrestle with the question of the morality of using cells from fetal and embryonic sources for medical research. In thinking through the ethics of such research activity it is our view that ethical principles and values, which have broad support in our society, ought to guide the initiation and direction of such research.

In the case of embryonic stem cell research in particular, it is not morally acceptable to decide that embryonic stem cell research will be done and then set off in search of those experts, values and principles that will support such a policy. Unfortunately, that appears to be what has happened with respect to some of the ethical analyses that private companies who wish to engage in fetal or embryonic research. Moreover, while we are in no way opposed to companies seeking ethical advice and input from many sources we do not see these activities as in anyway a substitute for or an alternative to government interest and responsibility for stem cell research and research in related areas such as therapeutic cloning. In our view we should try and understand what the relevant facts are about embryonic stem cell research. Then an effort must be made to see whether there are ethical values and principles that command broad consensus relevant to this issue. Then, having ascertained the facts about the proposed research and the values that we as a society are trying to adhere to with respect to undertaking research or therapy involving stem cells or cloned embryos it should be possible to offer an evaluation about whether Federal support should be offered, whether it is ethical to undertake the research at all regardless of funding source, what limits should be placed on research if any and what role the government should take in providing oversight and accountability to these activities.

THE FACTS ABOUT EMBRYONIC STEM CELL RESEARCH

In asking whether it is ethical for the Federal government to support research on embryonic stem cells it is important to be clear about what is being undertaken. Research on embryonic stem cells requires the destruction of human embryos. There is no avoiding that fact. This single fact makes embryonic stem cell research ethically troubling. One does not have to be a member of the "pro-life" community to understand that destroying human cells that have the potential to become human beings represents an action that requires ethical justification.

Why undertake research on embryonic stem cells? The answer is that these cells show great promise as a source of cell lines and tissues that could be used to repair or replace damaged cells, tissues and organs in fetuses, babies, children and adults who have a variety of ailments and diseases. Many of the ailments that plague humankind are caused by damage to our cells and tissues. Parkinsonism, juvenile diabetes, traumatic brain injuries, spinal cord injuries, Canavan's disease, sickle cell disease and cystic fibrosis are but a few such disorders. Since many human cells and tissues do not have the capacity to regrow or rejuvenate or can only do so at a very slow rate it would be a boon in the battle against disease and disability to have a source of cells that could be grown to be transplanted into damaged areas of the human body and once there perform the requisite functions necessary for human health.

Some critics of embryonic stem cells research have acknowledged the potential benefit of conducting research which could provide a source of transplantable cells for all manner of diseases and disorders but they say there are alternatives to using

embryonic stem cells for this purpose. Adult stem cells, such as those that are used by the body to replace damaged skin or muscle or to continuously rejuvenate our blood cell might be able to be transformed into cells lines that can make the kind of bounty of cell types that might be possible to obtain from embryonic stem cells.

The fact is that no one can be sure what research on adult stem cells will produce in terms of being able to manufacture cells to repair cells in those with diseases because this research is very much in its infancy. It is absolutely true that embryonic stem cell research is also so new that it can only accurately be described as promising. But, there is no way that anyone can know today if research on adult stem cells will prove capable of making the kind of universal cell types that researchers hope to create from embryonic stem cells. Adult stem cell research is neither an alternative to nor a substitute for embryonic stem cell research. If the goals are to repair broken, damaged or dying cells in human beings than both lines of research must be pursued.

One other fact becomes important in trying to formulate an ethical assessment of the morality of Federal support for embryonic stem cell research—embryonic stem cell research is at best a promise. Almost no sustained work has been done in this area. While there are private companies and clinics that are eager to pursue this avenue of work they have not published or made public any information that should lead anyone to think that therapies are in the offing. Nor has any of the work on embryonic stem cells done in the public sector using animal models done anything more than show potential for therapies. The facts are that relatively few scientists have done relatively little research using human embryonic stem cells.

That said, it becomes very important to make clear the number of embryos that would be utilized should the Federal government decide to support embryonic stem cell research. In talking with scientists and veterinarians who know quite a bit about stem cell research it has become clear to me that there are no more than thirty researchers who might seek Federal support for research using human stem cells in the next few years. If one presumes that the Federal science agencies, mainly the NIH, were to give grants for fifty percent of the proposals received (a generous estimate) then there would probably be an average of 15 researchers conducting research with human embryonic stem cells a year for the next three years. If each one of these scientists were to use on average five human embryos for each study then the debate about Federal funding of human embryonic stem cell research is a debate about the utilization of less than one hundred human embryos a year for three years.

There are some other facts that are equally relevant about human embryo stem cell research. There are four ways to get embryonic stem cells—from newly created human embryos made specifically for that purpose, from newly created human embryos made in order to help infertile couples have children, from frozen human embryos and from human embryos that have been created through the process of cloning following the steps used to create Dolly the cloned sheep. And each source is currently being utilized or could easily be utilized.

At least one clinic, the Howard Jones Institute at Eastern Virginia Medical Center in Norfolk has reported that it has publicly stated that its scientists have made human embryos solely for the purposes of stem cell research. A few infertility programs that I have contacted have told me that they offer couples who are seeking infertility treatment the option of putting any embryos that will not be implanted for the purpose of reproduction the option of donating them for the purposes of research. At least one private company has stated that it has made human embryos by the process of cloning to use for procuring human embryonic stem cells. And a number of researchers have indicated an interest in utilizing human embryos that have been stored and remain unclaimed for many years as a source of stem cells.

There is one fact that is not at all clear and that is what is created when human DNA from an adult cell is used to make a clone. While some believe that starting a clone is equivalent to making a human embryo, others do not. We have referred to this puzzle as the "what is in the dish dilemma". Our view is that there is no certainty that a human clone at the embryo stage can turn into a viable human being. There is evidence from the animal world to suggest that the chances of being able to do that are poor. It is also the case that if the cloned human embryo is not put into a human uterus then it cannot become a human person.

We are troubled by the idea of making therapeutic clones solely for research purposes since we are not really sure what it is that is being created. Without such certainty and in the absence of any agreement about what this new technology creates it is difficult to argue that it makes sense from the point of scientific research to ban this modality of acquiring stem cells for research or therapy. Before any legislation is enacted to prohibit, fund or encourage therapeutic cloning it would seem very prudent to have a committee or commission established to formulate an answer

to the question of what moral standing should be accorded to human embryos made by nuclear transfer cloning techniques. While some may want to have a ban now on he grounds that the creation of any such clones is equivalent to the creation of human embryos more sustained deliberation may lead us to conclude that these "starter" clones lack the capacity to become human beings and as such may turn out to be a less ethically contentious source of stem cells for research.

ETHICAL VALUES AND PRINCIPLES

In 1996 Caplan wrote an article with George Annas and Sherman Elias in the New England Journal of Medicine in which we argued that research involving embryos was ethical if the embryos used for research were taken from those stored and frozen in the United States and other Nations. In taking this position we argued against the view advanced by various scholars and Federal panels that the source of human embryos did not matter. We believe this ethical position was correct then and remains correct today. The facts associated with human embryo stem cell research to demonstrate the feasibility of using stem cells for therapeutic purposes are consistent with the moral principles involved in restricting the source of such cells and tissues to frozen embryos left behind by the tens of thousands at infertility clinics in this country and other countries.

Before arguing for this position, we want to say that Americans should also understand that those who believe that all research on the human embryos are deserving of nothing short of respect. It is a sad fact about the tone of our ethical debate on this issue and on all matters pertaining the to the handling of embryos and fetuses we all too often find ourselves engaged in interactions which insult, deprecate or dismiss out of hand the moral concerns of those with whom we disagree. We understand the moral position that holds that all human life is sacred and that it is wrong to sacrifice one human life to save another or help another. We believe this is not what is required with respect to human embryo stem cell research but the moral sentiment underlying the position is absolutely sincere and is deserving of both a full hearing and praise for the moral value it articulates.

The values and principles that seem operative in thinking about what to do concerning the facts of stem cell research are that we should not kill in order to advance the welfare of those in need, we should not commercialize or commodify the process of procreation and human reproduction, we should accord all human cells and tissues respect by controlling how they are used and what can be done to them and with them and we must weigh seriously the health care needs of those who have diseases and disabilities carefully against the value of respect according to cells, embryos and the procreative process.

We believe that in weighing the balance of values and principles that human embryos and cloned human embryos are at most potential or possible human beings. They are not human beings from the moment of conception. Nor are they in any sense persons from the moment of creation or conception. Many embryos cannot become persons due to errors in their biology. Most human clone embryos most certainly lack the capacity to become human beings. And without being put into a uterine environment no embryo, regardless of how it is created or where it is obtained, can have its potentiality actualized.

We believe that in weighing the needs of children and adults who are paralyzed, demented or dying the needs of those are actual persons has greater moral standing than the potentiality inherent in embryos or clones. Thus, given the relatively small number of human embryos that would be required to establish the feasibility of human stem cell therapy, given the position that killing a potential or possible human being is not the same as murder, given the fact that medicine must, sadly, sometimes do harm in order to do good, given the potential for benefit in the form of assistance to real, living babies, children and adults we favor government sponsorship of a limited amount of human stem cell research. The best way for this work to proceed would seem to be to utilize embryos already in existence rather than to create news ones solely for the purposes of research. Without more consensus on the metaphysical status of cloned human embryos it makes better moral sense to proceed with research on embryos already in existence that are destined for destruction or never to be used for the purposes of procreation.

Senator SPECTER. Thank you very much, Dr. McGee.

STATEMENT OF MICHAEL D. WEST, Ph.D., PRESIDENT AND CEO, ADVANCED CELL TECHNOLOGY

Senator SPECTER. We will turn now to Dr. Michael West, president and CEO of Advanced Cell Technology, a biotechnology com-

pany based in Worcester, Massachusetts, he has a master's degree from Andrews, Ph.D in cell biology from Baylor College of Medicine, and this is his third appearance before this subcommittee. Thank you very much for joining us, Dr. West.

Dr. WEST. Thank you, Mr. Chairman, and members of the subcommittee. I have submitted my written testimony, so if I may, I will just make a few salient points.

Senator SPECTER. Your written testimony, as well as all other written testimony, will be made a part of the record in full.

Dr. WEST. Thank you. I would like to then summarize three major points, first just to briefly address I think maybe some useful points of science, and then secondly, on patent law, and then third on ethics, if I may.

First, on the scientific front, I think it is useful to point out that mankind occasionally is given gifts, things that can greatly advance the human condition. I think we have been given two in just recent history. The first we have talked about at some length already this morning, the human embryonic stem cell.

The opponents of the technology point out, or try to point out that we do not need this technology, these cells are not unique. There are other cells that do what these cells do. This is a misstatement of fact. The human embryonic stem cell is unique in at least two regards. One, it stands at the base of the developmental tree of cellular life. It can become any cell in the human body. As we say, it is totipotent. It has total power. This is unprecedented and a unique property for these cells.

As an example, the cells can even assemble into a complex tissue, such as a complete intestine, with all the cells of an intestine. No other cell has ever come even close to this in the history of medicine.

Besides the ability of these cells to become any cell in the human body, they have a second and equally important property. They have a property we call cellular immortality. This means that, unlike all the cells in the human body ever cultured to date, they can grow indefinitely. They stay young in a way that our reproductive cells stay young, making babies that are born young.

Cells that result from these cells would be predicted to be young, having their full replicative life span ahead of them, so for an aging population, which is increasingly a focus of our national concern, these technologies, because this technology in particular, embryonic stem cells, because of all these unique properties, may be uniquely poised to address a very large health concern for the United States and the rest of the world.

A second gift we have been given is this miracle we call cloning, or nuclear transfer. Nuclear transfer was a surprise to science. It tells us that a cell from our body, even an aged cell, can be taken back in time, in a little time machine—it is only big enough to hold a single cell, but it can take a cell back in time to an embryonic state, where that cell can then, as I just pointed out, become any cell in the body, but it also can be rejuvenated in the process, giving an aged patient back young blood cells, for instance, or young skin cells to help with geriatric skin ulcers.

So in summary, on the science side we have been given a great opportunity. How do we best implement this for the benefit of humanity?

On the legal front, opponents of this new technology point out that there should be no patents, or challenge the patentability of the technologies. It is important to point out that we have several basic assumptions I think we are operating from on the legal front, and forgive me for opining on law. I am not a lawyer, I am a scientist and a businessman, but in 1980, the Supreme Court decided the *Diamond* v. *Chakrabarty* case, saying that life forms are patentable inasmuch as they involve human intervention.

Maybe the most salient case goes back to a very early U.S. patent by Louis Pasteur. He patented in a very comparable way to the human embryonic stem cell patent a composition on living cells unaltered except for their isolation. He patented the isolated yeast cell, free of organic pathogens, useful in manufacture, one of the first U.S. patents issued in the field of biotechnology.

Historically important portal technologies do not interfere with commercial development products that can help people who are sick. We can look, for instance, at recombinant DNA, which was managed by Stanford University. Although patented, it was freely available, and has generated now the majority of the current biotechnology industry, which has clearly benefitted mankind.

Clearly an issue is availability, free availability for academic researchers in particular. In that regard, I would just like to point out to the committee, when I first approached WARF in 1995 about sponsoring research in this area, the first words out of WARF's mouth were exactly to that point, nonexclusivity, free access, to their credit.

Senator SPECTER. Would you repeat that, Dr. West? What were the first words out of WARF's mouth?

Dr. WEST. Out of WARF's mouth to me, as a corporate officer, when I approached them to sponsor this research, to obtain the human embryonic stem cells with private money, I requested an exclusive license, which is not unusual. Indeed, I would say the vast majority of such arrangements grant exclusivity.

Senator SPECTER. You asked for an exclusive license, and what was the response?

Dr. WEST. No—they refused, and what they stated was that they would be glad to talk about nonexclusive licenses, but they felt that as a matter of policy these cells should be licensed nonexclusively and be freely available, because of the potential breadth of the technology.

In the interests of time here, I will just point out, on the ethics front, one quick point. Much of the debate about these technologies is about human life. It is critical to understand that I think the differences of opinion are about human cellular life. All cells in the human body are alive. Many of us do not want to agree with this, but we evolved from single-celled animals. These are living entities. When a scientist talks about life, or human life in a dish, he does not mean a human life. It is a fundamental distinction which goes to the heart of the debate.

So in summary, I think even the critics of these new and emerging technologies will admit, teleologically, these technologies have

the potential to save millions of human lives. I think this is an issue of grave concern, and should cause us to pause.

PREPARED STATEMENT

Yesterday's vote by the House, with 2 hours of debate, I think was not a good indication of the relative graveness of this issue, and I would respectfully request that the Senate, the greatest deliberative body in the world, would take this issue with a great deal of caution and a careful deliberation. As a leader of world technology, I think it is the responsibility of the United States, it is our challenge, indeed, it is our duty to do so.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF MICHAEL D. WEST

Mr. Chairman and members of the Subcommittee, my name is Michael D. West and I am the President and Chief Executive Officer of Advanced Cell Technology, Inc., a biotechnology company based in Worcester, Massachusetts. A copy of my curriculum vitae is presented in Appendix A.

INTRODUCTION

I am pleased to testify today regarding human embryonic stem cell and nuclear transfer technology and their applications in medicine. I would like to first speak to the potential benefits of this emerging science, and then speak to some of the questions and concerns that have been voiced.

THE POTENTIAL BENEFITS OF ES AND NT TECHNOLOGY

Human Embryonic Stem (ES) cells are unique in the history of medical research for at least two reasons. First, they alone are totipotent stem cells. By stem cells, we mean cells that can branch out like the stems of a tree, becoming other cell types. By "totipotent" we mean to say that they stand near the base or "trunk" of the developmental tree and so are capable of forming any cell or tissue type needed in medicine. In addition to forming any cell type, they are unique in their ability to self-assemble into complex multicellular tissues such as intestine, full thickness skin, kidney tissue, and so on. They differ in this respect from adult stem cells that are "pluripotent"—that is, capable of forming several, but only a limited number, of cell types. One can think of adult stem cells as limbs further out on the branches of a tree. While able to branch out in several different directions, only the trunk of the tree branches out into every leaf and limb. An example of adult pluripotent adult stem cells are the bone marrow stem cells now widely used in the treatment of cancer and other life-threatening diseases.

The second distinguishing feature of ES cells is the ease with which they can be purposefully modified in a precise manner. This precise genetic modification is designated "gene targeting". The enhanced ability of ES cells to be modified with precision likely opens the door to many hundreds of clinical applications making human cells of any kind, genetically modified in any way to "heal" mutations in genes, something never before possible in medicine.

These two unique characteristics of human ES cells open the door to manifold novel therapeutic strategies. It may not be an exaggeration to state that the combination of the ability to precisely genetically modify these cells by targeted modifications and the ability to make any cell type may have as profound an application in medicine as the ability to arrange electrical components has made in the electronics industry.

To attempt to name every disease that potentially could be treated using this technology would require a larger report. Here are just a few examples. Neurons could be manufactured to treat degenerative diseases such as Parkinson's and spinal cord injury. Gene targeting to find and "heal" mutations could be used to manufacture neuronal stem cells for childhood retardation from diseases like Rett syndrome. Heart and skeletal muscle cells could be used for heart failure and age-related skeletal muscle wasting, and targeted genetic modification could be useful in muscular dystrophy. Blood forming cells would be useful in bone marrow grafting after cancer treatments, and anemias. Precision genetic modification could lead to better thera-

pies for inherited blood cell disorders such as sickle cell anemia and infectious diseases such as AIDS.

I would argue that the debate over the number of human ES stem cell lines approved for Federal funding largely misses the point. Human ES cells obtained from IVF preimplantation embryos are not identical to the patient, that is they are "allogeneic". We should expect that such cells derived from the 20–60 approved lines would be rejected by the patient's immune system. The primary purpose in funding human ES cell research is not just the pure pursuit of human knowledge, but rather to accelerate the delivery of novel therapeutics to afflicted people. We must address from the beginning how we are going to make these cells useful in transplantation.

THE USE OF NUCLEAR TRANSFER IN MEDICINE

The recent success in the cloning of animals from body cells demonstrates that the transfer of a body cell into the environment of an egg cell can "reprogram" it back to an embryonic developmental state. We have recently demonstrated that such technology actually rebuilds the replicative lifespan as well, suggesting that "young" cells can be derived from "old" cells. This is a profound development and perhaps the ideal solution for making real the longstanding dream of transplantation medicine; namely, to be able to offer any patient, even an aged patient, young healthy embryonic stem cells of from which any kind of cell could be make all of which would be their own cells, not expected to be rejected by their immune system.

Nuclear transfer offers an important solution of the problem of tissue rejection. Every year many thousands of people die for the inability to liver, kidney, or other tissue with the right constellation of markers to allow it to accepted by the body as self. It is estimated that three thousand people a day die from degenerative disease potential addressed by therapeutic cloning. This new procedure would begin with the patient donating living cells to a physician, who would then reprogram them back to a totipotent state using the cloning procedure. This is called therapeutic cloning, to distinguish it from reproductive cloning which is designed to clone an entire human being. Therapeutic cloning does not involve the cloning of a human being, it involves the medical use of cloning to make living cells. The cells and tissues made from these cloned stem cells would be expected to be grafted stably for the life of the patient without immunosuppression.

RESPONSES TO CONCERNS AND OBJECTIONS

(1) The preimplantation embryo is a human life and to use therapeutic cloning is to "clone and kill".

Answer. In the first few days following the fertilization of an egg cell by a sperm cell, there develops a microscopic ball of cells called a preimplatation embryo. This embryo is destined to die unless it implants in the uterus to form a pregnancy. Indeed, it is estimated that 50–80 percent of these preimplantation embryos naturally formed in a woman's body never implant and therefore die, naturally. Prior to day 14, the preimplantation embryo has no body cells of any kind, and, in fact, has no cells even committed to somatic cell lineages. Indeed, the embryo has not individualized. Once this ball of cells attaches to a uterus, one or even two or more individuals can form from it. It is therefore proper to say that it is not yet an individual. At ACT, we neither allow cell development beyond day 14, nor do we implant the cells in a uterus.

(2) Therapeutic cloning is merely theoretical; there is no reason to suggest it will work.

Answer. There are published reports of success of therapeutic cloning research in at least two mammalian species; namely mice (1–2). While never performed in a human, the animal data suggests that therapeutic cloning has great promise. The National Academy of Sciences has formally recommended in a report titled "Stem Cells and the Future of Regenerative Medicine" as follows:

"Recommendation: In conjunction with research on stem cell biology and the development of potential stem cell therapies, research on approaches that prevent immune rejection of stem cells and stem cell-derived tissues should be actively pursued. These scientific efforts include the use of a number of techniques to manipulate the genetic makeup of stem cells, including somatic cell nuclear transfer."

(3) Allowing therapeutic cloning would cause a "slippery slope" effect, whereby regulating human reproductive cloning would not be possible.

Answer. In reality the procedures to clone a human being are well known in the scientific literature. The widespread use of therapeutic cloning would not significantly increase the likelihood of the success of an effort to clone a human being. In addition, laws can easily be written to allow one and prohibit the other as repro-

ductive cloning requires the transfer of a cloned preimplantation embryo into a uterus.

(4) Therapeutic Cloning will lead to "embryo farms".

Answer. Therapeutic cloning guidelines could easily be constructed to limit development to less than 14 days as is the current practice with in vitro fertilization.

SUMMARY

In conclusion, nuclear transfer and human embryonic stem cell technology offer novel pathways to develop lifesaving therapies that will impact the lives of millions suffering from such diseases as Parkinson's disease, diabetes, arthritis, heart disease, kidney failure, spinal cord injury, liver failure, skin burns, blood cell cancers, to name only a few. The gravity of this issue calls for a compassionate, reasoned, and dispassionate debate. History will judge us harshly if we as a society fail to recognize and deliberate carefully upon a medical technology that could so powerfully alleviate the suffering of our fellow human being.

Senator SPECTER. Thank you, Dr. West.

Dr. Cameron and Dr. Caplan have a joint issue on the core concern, with Dr. Cameron being opposed to research on stem cells, and extracting stem cells from embryos, and Dr. Caplan raising the counter factors, and by saying that many of these embryos cannot produce life, and they are going to be either destroyed or permanently frozen.

Dr. Cameron, what is your response to that basic point, that for physiological reasons, many of these embryos cannot produce life, or will be destroyed? Why not use them to save lives?

Dr. CAMERON. Well, Senator, one or two reflections. One is, Dr. Caplan in fact kept using the term person. I may have used the term once, but I am making no case here that the early embryo is a person. A person is a legal concept. It is also a complex philosophical complex. My point is that the early human embryo is a member of the human species. Plainly, it is undifferentiated. I mean, plainly, it has yet to go through a whole series of transformations to become——

Senator SPECTER. The early embryo is a member of the human species?

Dr. CAMERON. That does seem to me a matter which is common to our understanding of the biology here, and in that context, plainly, certain embryos will not flourish, either because they are deformed, or because they are prevented from being in the maternal in utero environment in which they would flourish.

But mortality is a universal principle, and it is no comment on the dignity of any human individual that every human individual will die, and so it seems to me that for us to afford the earliest, youngest members of our species a dignity in which they are placed beyond the bounds of destructive experimentation is a fundamental component in our civilized vision of human dignity.

Senator SPECTER. So you characterize the embryo, even if it has no potential to develop into a baby, a child, not in the womb of a woman, but as a member of the human species in that form, and therefore you think morally it is inappropriate to extract the stem cells. That is the essence of your concern.

Dr. CAMERON. It is the essence of my concern, and I make one further comment, Senator. We use the word potential very freely in this discussion, and it can mislead us, because there are several different senses of potentiality, and my understanding—I am not a biologist, but my understanding is that every advance we have in

modern genetics has clarified our understanding that the potentiality is in-built. Given a lack of malformation, given an appropriate environment, the embryo will, indeed, go on to become someone who is palpably one of us.

Senator SPECTER. But if you have malformation—you say, two factors, the absence of malformation and the environment, the womb of a woman, and if you have malformation, then what?

Dr. CAMERON. Well, if you have—I mean, as every case of disease and deformity, death will come sooner, but the continuity is stronger than every discontinuity.

Senator SPECTER. So you think even with malformation you have a human specie which ought to run whatever course nature gives it.

Dr. CAMERON. Indeed, sir, and we have, of course, accepted principles for human experimentation and also for the use of human cadavers, involving consent issues and so on. It seems to me that the earliest members of our species need to fit within that framework of ethical understanding.

Senator SPECTER. And in the absence of an environment, the womb of a woman, still you say, let nature take its course, or whatever happens to that form of human species?

Dr. CAMERON. I am not happy that we bring into being human embryos who do not have the prospect of a maternal environment, but given that we do bring into being for all sorts of good, and now bad, reasons, it seems to me they need to be treated with a dignity which relates to who they are in themselves, and not to the context in which we place them.

Senator SPECTER. Dr. Caplan, I am sure you have some observations on our discussion with Dr. Cameron just now.

Dr. CAPLAN. Well, I would not refer to frozen embryos as potential members of the youngest members of our species. I still believe that they are possible members, but in actuality, what has been stored because it did not look right, what has been kept for more than 4 or 5 years, which most of these 100,000 embryos have now been, has no chance of having its potentiality actualized.

Senator SPECTER. No chance of——

Dr. CAPLAN. No one that I know of who operates an infertility clinic would say, if you want to have a baby, I am going to get a 5-year-old frozen embryo that probably was put aside because it did not look right, and make that the basis for my attempt to give you a child.

Senator SPECTER. Well, all right, not a baby, but Dr. Cameron has a very—has a different definition of the human specie. How do you deal with that ethically?

Dr. CAPLAN. I would distinguish between a blueprint and a house. I think that embryos carry instructions. They tell us things about how a house might be built. They tell us things about what sorts of ways to arrange the parts and the wood and the nails and the roof and so forth, but they are not houses.

So from my point of view, when we are talking about potentiality, when we are talking about possibility, what embryos become are instruction manuals, and we can actualize them, we can put them in the environment in which the other requisite components will then be manipulated to make something, but basically

what I would say is, it is more akin to a situation where you have possibility, as a blueprint inherently might, in the right circumstances, be used to turn into something like a house or a building.

And then if you say, but your blueprint is damaged, and it is deteriorating because you have not used it, and you have kept it in a circumstance when it is going to lose some of its information, and when it was actually made it came from someone who unfortunately produced embryos that were somewhat deficient, I think the potentiality is wavering, so I do not accept the idea that those entities are members of the human species membership.

Senator SPECTER. Dr. West, on therapeutic cloning, can the entity created be implanted in the womb of a woman and produce a baby?

Dr. WEST. That is a very large question, and certainly, I think——

Senator SPECTER. What kind of question?

Dr. WEST. It is a very large question you have asked. I think if you asked it in more specific subsets, is it possible to clone a human, so is it possible to make a cloned preimplantation embryo and put it into the uterus of a woman and create a pregnancy, we think it is possible. It has never been done.

Some species, despite repeated attempts, have not yet been cloned, and so we do not know how easy it would be to obtain a human pregnancy.

Senator SPECTER. You say some species have not been cloned. We have had Dolly cloned, the sheep.

Dr. WEST. Right, but I mean——

Senator SPECTER. Anything else cloned?

Dr. WEST. Well, it took years to clone a pig, despite repeated efforts, although that now has been cloned as well.

Senator SPECTER. A pig?

Dr. WEST. Pigs, yes.

Senator SPECTER. P-i-g, pig?

Dr. WEST. Pig, as in oink, oink, pig.

Some species have been more difficult. It is purely speculation as to how easy it would be to take a pre-implantation—cloned, as we say, reconstructed——

Senator SPECTER. Run through the stages of therapeutic cloning which could lead to the cloning of a person.

Dr. WEST. Right, so the most straightforward would be simply to recapitulate the work in the cloning of animals for therapeutic purposes. This is the context that is normally described, but then I will briefly mention the various shades of gray, and I think this is the part of the debate that needs to be carefully considered.

The first would be, the lessons from cloning is, you take a skin cell, put it inside of an egg cell whose DNA has been removed. The egg cell, like the computer, initializing a computer disk says, you are not a skinless cell. You are back in an embryo, you are young again. You get a pre-implantation embryo, as is made in IVF, but in the case of cloning we call these reconstructed embryos, and placed back into a uterus, and the embryo is healthy. You would then get implantation, and then individuation in the beginning of a cloned animal, with kidneys, heart, liver.

So what this teaches us is, there are a pathway to take a skin cell, take it back in time, and then make the specific cells and tissues. The way we would envision doing it using that model, is, we take a patient that has diabetes, take a skin cell from them, use a donated human or potentially nonhuman egg cell to reprogram the cell, making the pre-implantation embryo, making embryonic stem cells from that embryo, and then making all these cells and tissues for the patient. That is model one.

But then there are at least a half-dozen other possibilities, some of which would not create an entity that I think most rational people would call an embryo, as evidenced by the fact they could not create a pregnancy.

Senator SPECTER. Dr. West, let me give you the staff articulation of your company's research. Women were paid for egg donations and signed inform consent forms stating that their specimens would be used for research purposes. Scientists remove the nucleus, the genetic material from the donated egg, and insert genetic material from the skin cell of the patient, thereby creating the first cell of an embryo that is genetically identical to the patient. That constitutes the therapeutic cloning. Researchers can then coax the embryo to divide to become the cells of a heart, liver, or any other organ, and could be transplanted into the patient without a concern for rejection.

Now, it is noted this has not yet been performed successfully, but is that the way you would clone an identical person to the woman who has donated the egg?

Dr. WEST. That is a way, a very simple-minded one. There is other variations on this theme. Let me point out one very briefly to exemplify the numbers of possibilities in front of us, which have not been publicly discussed.

Another technology would be to do the reverse procedure, to take bits of an egg cell, so take an egg cell, which I think everyone agrees is not a human life, to take an egg cell, remove its DNA, and then take small packages of the cytoplasm, the substance of the egg cell, which is capable of reprogramming a cell, and put those packages of protein, cytoplasm, on top of the patient's skin cell to take them back to an embryonic state in a way that would not create an embryo.

So this is just one example of a host of possibilities, and to say that we are going to in a blanket way, and I think an unprecedented way, ban a whole field of medical research is unwise.

Senator SPECTER. Well, if you come back to the cloning of a person, is the way that I described from my staff's summary a way realistically—I know it has not been done, but the potential for cloning a person who would be identical to the woman who gave the egg?

Dr. WEST. Identical to the donor of the somatic cell, which is I think what you meant to say. The egg, the person who donated the egg would not be the clone, necessarily. The egg is a means of reprogramming a body cell, like a skin cell, so it is the person——

Senator SPECTER. You say cloning is not necessarily identical to the donor.

Dr. WEST. The donor of the genetic information, which goes into the egg cell, would be the individual cloned.

Senator SPECTER. Would it be identical?

Dr. WEST. It would for all practical purposes be an identical twin. The purists point out that there are slight differences.

Senator SPECTER. Do you think that there ought to be a statute prohibiting that?

Dr. WEST. When this came up for a vote in the Senate in 1998 I testified to a hearing in the House on this, and I stated publicly I thought there should be a law against the cloning of human beings. Like all areas of science and medicine, you start realizing the suffering of patients, and I have softened somewhat on that position, but I think most of us in the field believe that there is this mountain of opportunity in medicine to have this in any way interfered with by this phantom of human cloning——

Senator SPECTER. Well, do you still believe there should be a prohibition against cloning a human being?

Dr. WEST. I think I would lean in that direction, although even there I would argue we should be slow-going. Reproduction is an important part of human life, and there are couples that cannot reproduce any other way. I would support such a——

Senator SPECTER. Dr. Cameron, I am pretty sure of your answer, but state it for the record.

Dr. CAMERON. I am pleased to state it is yes. It seems to me that cloning a human being is something which should never have been allowed to happen. Certainly, there is such a wide consensus that we do not want a human baby born, but back of that, of course, we now have the possibility of industrial production of human embryos for research using the cloning technology.

And since my original homeland of Scotland, I come from a few miles away from where Dolly was cloned, I feel a sense of curious pride in that extraordinary event, and yet have deep, deep apprehension as I see the technology being applied to our own kind.

Senator SPECTER. Dr. Caplan, cloning people, what is your view?

Dr. CAPLAN. Well, I think we should absolutely prohibit human cloning simply on the grounds that the animal data shows us that we would be doing something very unsafe and very dangerous. The toll in terms of stillborns, deformed animals in the cloning process—and to answer your earlier question—of cows, pigs, bulls, mice, has been terrible, and it would basically amount to unethical human experimentation, simply on the grounds that you would risk killing somebody if you were able to do it.

I might add one other point here. I am not sure human beings can be cloned. I know the media loves to speculate about that, and in many ways if you listen to popular discussion people believe it has already been done, or it will be done soon. There is every reason to think that some of the problems using bull DNA from body cells, and the handshake problems between egg and DNA may make it impossible to clone ourselves.

So I would say ban it. I am not sure that it is possible, but the way I think it could be prohibited and controlled is to simply say, you may not put any cloned human embryo into a woman's uterus, or attempt to try and grow it for the purposes of reproduction.

Senator SPECTER. It is 11:00. We are going to have to take a very short break, just about 2 or 3 minutes.

Dr. McGee, what are your views on human cloning?

Dr. MCGEE. Well, I find myself in agreement both with Dr. West and Dr. Caplan in that I think it is clearly a——

Senator SPECTER. How can you be in agreement with both of them? Dr. West said he's leaning, Dr. Caplan's opposed. We are going to come back to Dr. West to see the degree of leaning.

Dr. MCGEE. Let me think about that, but I think it is clear that the question as to whether or not there should be a prohibition on clinical reproductive cloning of a human, an in vitro fertilization clinic making a human clone is somewhat a detraction. I mean, there is no evidence that——

Senator SPECTER. A detraction?

Dr. MCGEE. A detraction.

Senator SPECTER. A detraction.

Dr. MCGEE. Yes. I think it is clear that it would be extraordinarily difficult to do it, and that the mounting debate on that question has really drawn attention away from stem cell research, which is the much, much more important and likely development in the short-term future.

Moreover, I think as was discussed the first time this was brought up——

Senator SPECTER. There is no doubt that the arguments for stem cell research, those who propose it are quickly in the sound bite dialogue of Sunday morning talk shows, has moved over to cloning. Then you move from therapeutic cloning to cloning people, and you start to get on very dangerous ground politically. It would be pretty hard to get stem cell research if people are equating it with cloning, but that is why it is important to have clarification. We may spend more time at this hearing than the House of Representatives did before having 400-plus people vote on it. But go ahead, Dr. McGee. Where do you stand?

Dr. MCGEE. I think I agree with you. I guess my position is that I believe it is not—I think it is not a bad idea to ban reproductive human cloning because of the obvious safety concerns and the continuing national debate about whether or not it is appropriate.

Senator SPECTER. It is not a bad idea.

Dr. MCGEE. I think, though, that because there is no imminent danger of a human clone being produced, media attention to the contrary, as Professor Caplan suggested, that it might be better to concentrate, as you have this morning, on how to describe what it is that is being done in stem cell research.

I mean, this notion of a therapeutic clone is a misnomer, in my opinion, and what we are really talking about, as Dr. West pointed out, is what you call what you have made when you use nuclear transfer. Professor Caplan and I have called this from time to time the what's-in-the-dish problem. That is, if you, as Dr. West just suggested, organize the bulk of an egg around an adult cell, you will have produced what many embryologists would call an embryo. Some might not.

The question is, who is to define that, and it is not a simple, scientific problem. It is clearly one that is very complicated, and I do not think Dr. West is right in saying that every rational person would agree that nuclear-transfer-derived embryos are not embryos at all.

Senator SPECTER. Well, you lost me on your last answer. Do you want to repeat it?

Dr. MCGEE. I think the problem to be discussed about therapeutic cloning is the problem of how to responsibly respect the view of those——

Senator SPECTER. Are you saying that therapeutic cloning cannot be differentiated on a bright line from human cloning?

Dr. MCGEE. Yes. I think—well, I think there is one clear bright line, and it is the one Dr. Caplan identified. That is, something is or is not implanted in a uterus.

Senator SPECTER. Well, what is your view on therapeutic cloning?

Dr. MCGEE. I think it would be very difficult to define it, and the reason for that is because what is at stake in the debate about funding, as I understand it, funding stem cell research, is when you have an embryo, not when you have a clone, and so many of the technologies that are being developed in small companies right now, members of ethics advisory boards for those companies, for example, have been quoted to the effect that they are not making embryos, that they are really making, to quote one chair of an ethics advisory board, an activated egg, and I think it is very difficult—I think it is unfortunate that that is being captioned as a problem for industry.

Senator SPECTER. Dr. Caplan, what is your view on therapeutic cloning?

Dr. CAPLAN. I think we should absolutely prohibit any insertion of a clone into a human uterus, that any attempt to produce or derive cloned human cells for reproduction should be prohibited. I think we should not at this time prohibit therapeutic cloning for research purposes. I think that that avenue should be left open.

Senator SPECTER. Define therapeutic cloning, what you think should be permitted.

Dr. CAPLAN. I think we should at the present time allow scientists to transfer DNA from body cells into nucleated eggs of human beings, allow them to start to grow those entities to see what happens. I do not think we know very much about their potential. I do not think we know very much about what they can offer. I think that anyone who would put such a creation inside a human being, a woman, to try and turn that into a person, should be prohibited and restricted from doing so.

And as my colleague Dr. McGee was saying, we know from Dolly that we can transfer DNA from your skin, from your lip, into an egg, a human egg from which the DNA has been taken out, and we can put that DNA in, but there are other ways to make DNA and egg material come together. That is what Dr. West was also starting to talk about. I would allow that research for the time being under very tight control, very tight regulation, to make sure that no one ever attempted to undertake human reproduction using any of these techniques.

Senator SPECTER. They have just rung the bell for a vote, so I think it might be a good idea if we moved to the final subject on the agenda, and that is the issue which was joined by Dr. McGee and Dr. West on this business about the advisory board.

Dr. West, what do you think about Dr. McGee's enumeration of standards for an ethics advisory board?

Dr. WEST. Well, I appreciate Dr. McGee's concerns. What I attempted to do back in the mid-nineties, when I initiated this work in this area with Geron first, and then later now Advanced Cell, was put in place, ethics advisory boards in both cases, to advise us, where we were blindsided to provide support in charting the course through these uncharted waters, and we purposely—I have historically invited people, without knowing their perspectives, people who were opinionated, who had the power of the pen—I did not feel in the corporate concern we could give them veto power, because there are certain fiduciary duties corporations have, but we gave them the power of the pen.

Senator SPECTER. Dr. West, let us move toward the core of the controversy that you had with Dr. McGee. I would like to do it in a more leisurely way, but once the votes start it is very hard to reconvene. Dr. McGee, what were your specific objections that led you, as I understand it, to resign from the ethics advisory board of Dr. West's company?

Dr. MCGEE. Well, the straw that broke the camel's back for me was that I was involved in discussion, public discussion about the cloning of an endangered, rather distinct animal, the gauer, by Advanced Cell Technology. I did not know at the time I was discussing the question about this animal cloning project with a number of members both of my profession and of the media that Advanced Cell Technology had done the work. They kept it secret even from the ethics advisory board, despite the fact that this was very important, and very controversial work.

Senator SPECTER. Dr. West, is it true that it was kept secret from the ethics advisory board?

Dr. WEST. No. The chairman of our ethics advisory board, Ryan Green, did know. I apologize to Glenn. I simply felt that the cloning of an endangered animal was a humane and good use of technology, and it did not occur to me that that was a matter of urgent concern for our EAB, and so we did not discuss it with every member of our EAB, and that was wrong.

Senator SPECTER. How many members of the ethics advisory board, Dr. McGee, are there?

Dr. MCGEE. Well, as I noted in my comments, Senator, I think that is part of the question, because ethics advisory boards do not operate with any kind of disciplinary or professional or Federal or State standards. They operate in very different ways, and so the Advanced Cell Technology ethics advisory board's membership is kept secret, so I honestly do not know how many members there are, or their identities.

Senator SPECTER. Dr. West, how many members?

Dr. WEST. Nine, currently.

Senator SPECTER. Dr. Caplan, I am advised that you had served on the Advanced Cell Technology scientific board, and what was your experience there?

Dr. CAPLAN. Well, I served for a limited time. They did not choose to call upon me for any comment or advice, so I left. It was not out of any disagreement, disappointment. I just felt they were

not using the board, so I decided that that was not a good use of my name or time.

But I should add that I support the idea of ethics advisory boards. I think they are good when companies try to create them. I do not, however, personally believe that they are a substitute for Government oversight. They are commendable. It is great to get opinion. It is nice to have input. It is a nice thing, but I see them as no substitute for what this subcommittee is trying to accomplish.

Senator SPECTER. The staff reports to me were that you resigned from the ACT scientific board because you were not consulted. You felt you were being used as a front man. Is that an accurate characterization?

Dr. CAPLAN. There is a danger of having your name out there when you are not consulted, so I was worried about that.

Senator SPECTER. Response, Dr. West.

Dr. WEST. Only that we invited Dr. Caplan to be on our scientific advisory board, and he left before we had convened a scientific advisory board meeting.

Senator SPECTER. But as to the experience you had with Dr. McGee, you say you should have consulted him. That was an error on the part of the company.

Dr. WEST. Yes. We feel that cloning can be used to save endangered animals without bringing them into captivity, so you can literally take a cell from an animal in the wild and we thought this was a humane use of technology, and it frankly did not occur to me that it was a priority issue for our ethics advisory board, but they certainly should have been notified, and that was an oversight on our part.

Senator SPECTER. Now, Dr. West, what is your view as to Dr. Caplan's contention that there ought to be governmental regulation?

Dr. WEST. Well, in the corporate sector, of course, we always worry about such regulations, both because we like to go out and change the world and do not like to be slowed down, and of course secondly there is the issue of undue intervention in the business sector as a matter of principle.

Given the importance of this area, however, we are far more interested in helping people who are sick and seeing this technology fully utilized, and I think there is a great eagerness, at least on our part, to find a pathway to benefit people who are sick.

Senator SPECTER. So you think appropriate governmental regulation would be warranted?

Dr. WEST. Absolutely.

Dr. CAMERON. Senator, could I add a comment here, please?

Senator SPECTER. Sure.

Dr. CAMERON. It does seem to me that one matter common to a number of us here is the enormous importance of developing a regulated regime.

The huge changes taking place in the last 10 years with the privatizing of major areas of bioscience out of the public domain, out of the major universities, into corporations, means that the use of ethics advisory boards as private, essentially public relations advisory opportunities for companies, perhaps well-intentioned, but

that is the net effect of having these names on their letterhead, can be quite misleading, and certainly is no substitute for the development of a regulatory regime which will build public confidence in what the biotech industry is seeking to do.

This seems to me to be crucially important. We have to have transparent ethical frameworks leading to regulation within which these activities are carried on.

Senator SPECTER. The time has almost expired on the vote, so I am going to have to excuse myself, and there are some other issues that I want to take up, so we will stand in recess, and I will return as fast as I can, hopefully within 15 minutes.

We will resume.

Dr. West, I have just been advised that you were explaining during the break about a patent which you had obtained.

Dr. WEST. I am sorry, would you remind me? I am sorry, I do not remember, which patent?

Senator SPECTER. It only happened 5 minutes ago.

Dr. WEST. I know, I am sorry. Which patent?

Senator SPECTER. Do you want the question to be more specific?

Dr. WEST. A patent which we have obtained?

Senator SPECTER. I will try to find out more of the details. I just got a thumbnail on it.

Ms. TAYLOR. You were explaining to a reporter where you would take an egg, an unfertilized egg, crack open that egg——

Dr. WEST. Oh, I am sorry, yes. You said patent you had obtained, and that confused me. We have a patent application pending on an alternative to the traditional way of thinking about the medical uses of cloning.

The alternative is, you know, it is turning the arrow in reverse. When we talk about nuclear transfer, which is the scientific term used for cloning, we are referring, again, to recapitulate, an egg cell, remove its DNA, and then we do nuclear transfer. We take the genetic information from, typically, a body cell and put it into the egg cell, and that is why it is called nuclear transfer.

What occurred to our scientists is, it may be possible to do the reverse, turning the arrow in the other direction and doing O plasmic transfer so—but this is still largely theoretical, and the reverse would be taking the proteins in the egg cell that do the work of reprogramming, packaging them up in like, let us say, water balloons, and dropping them on a patient's cell, so it is the reserve transfer, it is plasmic transfer of O plasm, being the material of the egg cell.

That would lead to, we believe, undifferentiated cells in a flat layer on a dish, which although may be embryonic in the sense that they express the genes of the early embryo, would not have the architecture of an embryo, would not create a pregnancy if put into a uterus.

Senator SPECTER. Let us come back to the issue as to governmental regulation. Dr. Caplan, what do you think a statute should provide by way of regulation?

Dr. CAPLAN. Well, I think the key features to look for in terms of overall oversight of therapeutic cloning stem cell research are first, openness and transparency. I think that one of the problems we have is that much of the commercial work is done in private.

It is up to the company to release it. We already encountered some issues about price and availability of license, the earlier comments.

Senator SPECTER. What should be done in the regulation as to price or availability of patents?

Dr. CAPLAN. I think basically the regulation should drive to maximize the availability of the good from these techniques by making sure that prices are reasonable and affordable and, most particularly——

Senator SPECTER. Well, how can you do that?

Dr. CAPLAN. Well, most particularly by no charge to persons who are doing research, pure research without intent to commercialize or manufacture.

Senator SPECTER. Well, this, of course, is my field, not so much yours.

Dr. CAPLAN. Yes.

Senator SPECTER. I do not know that you can legislate to somebody who has a property right that there will be no charge.

Dr. CAPLAN. Well, I think if the goal is simply to undertake work for scientific knowledge, we would want to make sure that without that commercial intent, then that information should be broadly available.

I might add, Senator, you recall with the human genome the same issues were raised about patenting genes, making them available for research purposes, so I will defer to your vast expertise much more than mine about what can be done. What I would like to see happen is roadblocks to basic research taken down or minimized.

The second thing I would like to see is some guarantee that we do not have any embryos at the present time manufactured. I think what the Jones Clinic did in making embryos for production is not necessary, is wrong. I would like to see regulatory oversight there about where material comes from.

I would also like to see regulation, if you will, that makes sure that we do not have redundancy in research, so that if we are going to try and use these resources carefully and respectfully, we use them in the best hands, that we make sure that the peer review is absolutely solid on the science end, and that we are not allowing for unnecessary duplication, if you will. We want to try and keep what has to be done to a minimum.

I think the last area of regulation that concerns me is that we take a long, hard look at present at what our patent policy should be in this area. We have got some claims made. Fair enough. There are other techniques emerging. Some of what Dr. West is talking about may move around certain patents that allow certain therapeutic cloning techniques to take place, but I would like to see the NIH role clearly established and articulated, so that a public interest is served in terms of not holding up the potential of stem cell research.

Senator SPECTER. What would you like to see this legislation say as to the NIH role?

Dr. CAPLAN. Hold any new patents, control them, basically make them available, that its funding is going to be contingent on availability.

Senator SPECTER. Dr. Cameron, anything you would suggest on legislation?

Dr. CAMERON. Well, it seems to me my position would be that in this area we should seek to protect the early embryo from this sort of treatment.

I must say, I was—perhaps I could ask Dr. Caplan to clarify. Was he actually saying that the early embryo was not a member of the human species? This seemed to be the entailment of his remarks earlier, which I thought was somewhat extraordinary.

Dr. CAPLAN. Yes. I do not think they are persons, and I think membership in the human species gives them an equivalence to adults, to you and me, that I do not accept.

Dr. CAMERON. I would certainly take the view that we should protect the early embryo, but in the context, and part of the problem with our having discussions in this way now, is that we need also to be grappling with the much wider issues involved in biotechnology, and with the privatizing of the biosciences.

I mean, there has been almost no discussion in this context of where interests lie, of the way in which, for as what ACT is saying, in speaking about helping patients, they are also, of course, speaking about helping their stockholders, and there are huge financial interests at stake in this industry which make it a very urgent matter for there to be a comprehensive regulatory regime which the industry has so far proved very effective at discouraging.

Senator SPECTER. Dr. Cameron, thank you very much.

Dr. CAMERON. Thank you very much.

Senator SPECTER. Yes. Dr. Gulbrandsen, do you agree with what Dr. Caplan said about free licensing for science? Why don't you pull your chair forward.

Dr. GULBRANDSEN. What WARF has tried to do, Senator, is make the embryonic stem cell as freely available for research purposes as we can. We thus far have distributed this stem cell to over 30 researchers in institutions around the world. We have ongoing negotiations with about 100 additional material transfer agreements that are close to finalizing, and those will be provided to researchers.

Senator SPECTER. Are they provided to researchers without cost?

Dr. GULBRANDSEN. They are provided to researchers with a one-time-only fee of $5,000, to try and help cover expenses. It does not begin to cover our expenses. WiCell is truly a not-for-profit organization. We are not making any money, and we have spent a lot of money on WiCell, and the purpose of that is to distribute this material.

Senator SPECTER. How about WARF? Is WARF making money?

Dr. GULBRANDSEN. WARF has not made any money from WiCell or from the material transfer agreements that have been distributed. These have been made available below cost, and we will continue to do that.

Senator SPECTER. Let me just cover one other subject. When Dr. West testified about what you had sought on a license from WARF, would you amplify what your answer was to that?

Dr. WEST. Well, in 19—I believe it was 1995, I approached first the scientist in Wisconsin, Jamie Thomson, and then WARF, about the possibility of sponsoring research in an attempt to obtain the

human embryonic stem cell based on Dr. Thomson's expertise in deriving these cells from nonhuman primates, and as is typical in biotech, in fact nearly universal, is universities and companies can come to an understanding that if the university—sorry, if the company puts forward, for the company what is a lot of money, maybe hundreds of thousand of dollars for a speculative project, that the company would be rewarded with an exclusive license for the life of the patent.

Unlike all of my previous experiences, maybe 20 or 30 licensing arrangements with universities, WARF from the very beginning refused, so having stayed 2 or 3 days in a hotel in Madison, I left at that time without an exclusive license.

Senator SPECTER. Why was a nonexclusive license insufficient for you?

Dr. WEST. Why was it insufficient?

Senator SPECTER. Yes.

Dr. WEST. Well, the concern is, of course, in biotech you need to be able—despite the cynicism about profit-making, you know, biotech is a very speculative business. Profits being maybe 10 years away, hundreds of millions of dollars in the red before you can make a profit. Investors want to know you have some insurance against unfair competition, so exclusivity is critical.

Given the importance of the technology, I was willing to accept a nonexclusive arrangement. That has subsequently been amended.

Senator SPECTER. You did get a nonexclusive arrangement.

Dr. WEST. Originally. The agreement between the university and Geron was subsequently amended after I left Geron, and I could not speak to the current arrangement.

Senator SPECTER. Dr. Gulbrandsen, what was WARF's thinking on the rejection of the request for an exclusive license?

Dr. GULBRANDSEN. Again,the concern was wide availability of this material for research purposes, and not being able to commit ourselves at this time that an exclusive license would be an appropriate way to move forward with this technology.

Senator SPECTER. How did Geron fit into that, exactly?

Dr. GULBRANDSEN. I am not quite sure I understand what your question is. Geron provided the—when Dr. Thomson had succeeded with the rhesus monkey embryonic stem cells, Geron arrived and said, can you repeat this type of research with a human embryonic stem cell, and we were unable to use any Federal dollars for that, and so Geron provided critical funding at a critical time.

Senator SPECTER. Anybody care to add anything?

Well, thank you all very much. We are certainly on the frontier here, or maybe a little beyond.

Dr. GULBRANDSEN. Senator, I would like to add one other comment.

Senator SPECTER. Sure.

Dr. GULBRANDSEN. And that is, I do not believe in any way that patents have impeded anything here. The greatest impediment in this research has been the lack of Federal funding, and if we had Federal funding, we would see this research advance much quicker than it is right now.

Senator SPECTER. Well, there are many of us who are working on that very hard——

Dr. GULBRANDSEN. Thank you very much.

Senator SPECTER (continuing). Trying to get that accomplished. We have added $8.5 billion to NIH, and we are going to come up to, I think, $12 billion in fiscal year 2002, and there is a lot of interest, and I think NIH has done spectacular work. There are fascinating horizons on stem cells, and I am aware, as Dr. Cameron has articulated, of ethical concerns, and I think it has been a very pointed discussion between Dr. Cameron, Dr. Caplan, Dr. McGee and Dr. West, and also between Dr. West and Dr. Gulbrandsen.

It has been an interesting hearing, and I think a productive hearing, and I think we have exceeded the 2-hour debating time which the House undertook before voting on this measure.

SUBCOMMITTEE RECESS

Thank you all very much for being here, that concludes our hearing.

[Whereupon, at 11:53 a.m., Wednesday, August 1, the subcommittee was recessed, to reconvene subject to the call of the Chair.]

STEM CELLS

WEDNESDAY, OCTOBER 31, 2001

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 9 a.m., in room SD–124, Dirksen Senate Office Building, Hon. Arlen Specter presiding.

Present: Senator Specter.

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Good morning, ladies and gentlemen. It is 9 a.m., and we will proceed with this hearing of the Appropriations Subcommittee for Labor, Health, Human Services, and Education.

This is the 11th hearing of the subcommittee on the issues relating to stem cells. Shortly after stem cells burst upon the scene in November of 1998, this subcommittee held a hearing to explore their potential in early December of 1998, and in the interim we have inquired into many of the facets of this remarkable procedure for combatting major diseases confronting medical science.

There has been a considerable amount of controversy by some who claim that by extracting stem cells from embryos, that there is the destruction of lives. The fact of the matter is that there are many embryos created for in vitro fertilization, and only a few are used, and the rest are discarded. If there were any possibility that these embryos could produce lives, I certainly would be opposed to the destruction of any embryo that produced the stem cells, but that is not the fact.

In the bill on Labor, Health, Human Services and Education, we have appropriated $1 million as a start for stem cell adoption. If there is any opportunity for these embryos to produce human life, and there are those who would be willing to adopt the embryos and take the next step forward, that is something which certainly ought to be encouraged. This subcommittee is very anxious to promote that.

However it is calculated, there are many of these embryos which will end up being discarded and it is my view, and the view that has been expressed based on subcommittee's findings, that these embryos which are to be discarded ought to be used to save lives.

The President made a decision that existing stem cell lines as of 9 p.m. on August 9 could be federally funded, and immediately thereafter the questions arose as to whether those stem cell lines

were sufficient to carry on the requisite scientific research, and we are proceeding today to make further inquiry into that subject.

The appropriations bill for Labor, Health, Human Services and Education is on the floor today. After this hearing was scheduled the majority leader scheduled the Labor-HHS bill for floor action, so we are going to have to proceed in a very strained time frame to conclude this hearing by 10:15, and so my opening statement will be similarly abbreviated.

STATEMENT OF DR. WENDY BALDWIN, DEPUTY DIRECTOR FOR EXTRAMURAL RESEARCH, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Senator SPECTER. At this time we are going to turn to Dr. Wendy Baldwin, the Deputy Director for Extramural Research at the National Institutes of Health, a graduate of Stetson University with her bachelor's, and a Ph.D from the University of Kentucky. Prior to obtaining her present position, Dr. Baldwin served as Deputy Director of the National Institute for Child Health and Human Development at NIH. We are going to ask all the witnesses to abide by the 5-minute limitation so that we can conclude the hearing, as I said, by 10:15.

Welcome, Dr. Baldwin. We look forward to your testimony.

Dr. BALDWIN. Thank you, Senator Specter. I am pleased to appear before you today to inform you about steps the NIH is taking to implement the President's decision to commit Federal funding for research on human embryonic stem cells. As you know, on August 9, President Bush opened the door for Federal research in this very important, exciting, and promising area of research, and since that day, we have been laying the groundwork so that Federal funding for such research can begin.

We have met with the investigators and the providers of stem cells, and we have been taking many different steps to get this process underway and to let the research community know how to interact with the NIH and how to avail themselves of this new opportunity in science.

One of our first actions was to address the issue of the licensing agreement with the holder of the U.S. patent on embryonic stem cell technologies. On September 1, the Public Health Service signed a memo of understanding with WiCell Research Institute. This is a very important step, and while that agreement was for the PHS researchers, in fact it sets the stage for how researchers all around the world will be able to access this technology and be able to do the research.

That MOU is available on our web site. This is not only a tremendous step forward for that particular set of cell lines, but we think it also sets the standard. We expect that is going to serve as a model agreement. That is very important step sence people have to be able to get access to these lines.

Our next task was the establishment of a web-based human embryonic stem cell registry, which would list all of those lines that were eligible under the President's policy announcement. This registry has to be something that not only reflects that policy statement but is also useful to the investigator community. Right now, we are working on getting that tuned up, getting information avail-

able, making sure that it is presented in a way that the research community will know who to talk to and how to get access.

Once that registry is in place, we are going to begin funding research in this area. While the beginning of this research activity had a very unusual beginning—with a presidential statement—it is my goal to mainstream our support for research on human embryonic stem cells as soon as possible.

We have had a number of things to do. As we talked with the derivers, it was clear that some needed infrastructure support. The cell lines have to be functionally available, and there may be infrastructure needs.

We have also heard about needs for technical assistance. Again, that will vary by different investigators, but it is something we must pay some attention to.

We are looking also for ways to minimize administrative burden. Getting access to these lines is much like getting access to other research resources. We feel that there are steps we can take to minimize some of the administrative burden, if only to provide easy access to the guidance that people might need. If they need to import cell lines, they need to consider FDA, USDA, and CDC regulations. We think we can be helpful there to them. We are going to add information like that to our web site.

We know that the cell lines can be challenging to work with. We can provide a variety of training opportunities, not just for the external community but also for our research administrators who will have new issues to deal with as grants seek funds to do research with these cell lines. So there is much to do. Over the last few months, this has moved the NIH from an area of policy development to implementation. That is really why I am here today, because it is in my office that we deal with the different hurdles we have to get over before we can actually make grant awards in this arena.

We are going to work within the framework of the President's statement. But within that framework and with our registry posted, investigators will be able to use the full range of funding mechanisms. They will be able to apply all their knowledge and skills of dealing with research resources and dealing with application procedures and review and funding issues, so we are very pleased that this is going to give us an opportunity to really mainstream this work.

PREPARED STATEMENT

We expect to make our first grant awards in 2002. Investigators who are already funded can use our options for administrative supplements or even rebudgeting to begin work quickly. We are eager to explore the enormous scientific opportunities here. There are many steps that have to be taken so that we can make this resource available in a way that is truly useful to the research community and provides enough guidance for them that they actually know what to do to interact with the NIH.

So there is a great deal of work to do, and we are poised to do it, and I would be happy answer any questions that you have.

[The statement follows:]

PREPARED STATEMENT OF DR. WENDY BALDWIN

Mr. Chairman, Senator Specter, and Members of the Committee, I am pleased to appear before you today to testify about NIH's progress toward the implementation of the President's decision to permit federal funding for research using human embryonic stem cell lines.

As you know, on August 9, President Bush opened the door for federal support of this exciting and promising area of research. Since that day, NIH has been laying the groundwork so that federally-funded research can begin. We have met with the investigators from all over the world who are responsible for development of the existing stem cell lines that are eligible for federal funding. They are cooperating with the NIH to create a framework for researchers to conduct much needed basic research on these cells.

One of our first actions was to address the issue of licensing agreements with the holder of the U.S. patent of human embryonic stem cell technologies. On September 4, the Public Health Service (PHS) signed a Memorandum of Understanding (MOU) with the WiCell Research Institute of Madison, Wisconsin, (a subsidiary of WARF) for use by PHS researchers of WiCell's five existing human embryonic stem cell lines. The MOU permits PHS scientists, such as those working in the NIH intramural program, to publish freely the results of their research and permits the PHS to retain ownership to any new intellectual property that might arise from the conduct of such research. In addition, the MOU provides a "Simple Letter of Agreement" to govern the transfer of cell lines to individual laboratories with minimal administrative burden. Furthermore, WiCell has agreed to make stem cells available to PHS grantees under the same terms and conditions as those provided to PHS scientists. This agreement represents an important first step in allowing investigators to obtain the cells for their laboratory work under terms that are consistent with NIH's policy of shared research resources. We expect the agreement with WiCell will serve as a model for additional agreements with other sources of stem cell lines.

Our next task was the establishment of a web-based Human Embryonic Stem Cell Registry to list all of the cells that meet the eligibility criteria. The registry will include information about all the cell lines that are currently available for research. In order to establish the on-line registry, we have been obtaining assurances that all of the President's criteria were met, and gathering necessary information about these sources so that researchers can contact them directly for information. Thus, investigators will be able to discuss obtaining cells for their research and those who apply for federal funding can refer to one of the eligible sources in their funding application. I am pleased to announce that this registry will soon be operational and will be available to the public through the Internet.

When the registry is in place, NIH will begin funding this research using a variety of mechanisms: grants, contracts, cooperative agreements, and supplements to existing grants. There are many exciting avenues of research to be explored, and there certainly are many investigators prepared to apply for funding. In addition, we are talking with the different providers of stem cells to determine what might be needed to establish a research infrastructure that ensures the successful handling and use of these embryonic stem cells in the laboratory. We may need to provide technical assistance and funds for the expansion of stem cell lines so that they are available to as many researchers as wish to use them. We will try to minimize the administrative burden, in regard to requests for the distribution of cells, both for scientists who have derived these cells and researchers who wish to use them. For example, when researchers import biological products many of these derivers are outside the United States they must follow USDA, FDA and CDC regulations. We will be adding information to our web site to facilitate this process. Because these cells are challenging to work with, we need to determine in what manner we will provide training opportunities to researchers on technical approaches to grow and maintain these cells in their own labs. NIH may hold workshops and conferences to encourage broad scientific dialogue about research ideas, and the identification and resolution of technical problems inherent to any new arena of research. There is considerable work to do.

Over the past six months the NIH effort regarding research on human embryonic stem cells has moved from policy development to program implementation. While this is an unusual initiative in that it is based on a Presidential announcement, now is the time to bring this research into the mainstream of NIH funding activities. Working within the framework of the President's statement, investigators will be able to use the full range of funding mechanisms and begin to apply their usual practices regarding the acquisition and use of a research resource, in this case the stem cells listed on the NIH Registry.

Mr. Chairman, NIH is now poised to begin funding this research. We expect that NIH will make the first grant awards in 2002. In some cases, investigators who are already receiving funding for projects in research areas that are closely related to embryonic stem cell biology may seek supplemental funds or permission from NIH to utilize existing funds in these closely related areas. We are eager to explore the enormous scientific promise of these unique cells. There is much basic research to do, and it is time to move forward.

I am happy to answer any questions you may have.

Senator SPECTER. Thank you very much, Dr. Baldwin.

The September 7 issue of the Wall Street Journal reported that the in vitro fertilization clinic from which Reliance Life Sciences obtained their embryos was, as the Journal put it, the most mysterious in Bombay. The article claims that the clinic opened at the earliest in March of this year, and at the latest in May, and the article goes on to say the clinic, quote, would have to work unusually fast to produce excess embryos that quickly in 6 months. The question is, how did they obtain spare embryos in 6 months, when you can not have spare embryos until the donors have at least one successful pregnancy, which takes 9 months.

Are you familiar with that article, Dr. Baldwin?

Dr. BALDWIN. Yes, sir.

Senator SPECTER. How do you explain it?

Dr. BALDWIN. Well, we have interacted with every one of the providers, including Reliance. Reliance is a very large entity. It is not a quickly or recently formed entity. We have an assurance from them that they have, in fact, met the President's criteria.

Senator SPECTER. You have an assurance from Reliance, but have you made an independent inquiry in light of the substantial questions raised in this article?

Dr. BALDWIN. We will be making a trip to India in the next month.

Senator SPECTER. The answer is, you have not yet made an inquiry?

Dr. BALDWIN. We have made an inquiry. We have been satisfied by that inquiry. If you ask whether we have been on site——

Senator SPECTER. What inquiry did you make?

Dr. BALDWIN. We have met with the Indian derivers through videoconferencing. We have discussed these issues with them, and have satisfactory responses from them.

Senator SPECTER. What responses have you had on these issues?

Dr. BALDWIN. I would have to provide the detail of that for the record. That discussion was at the policy stage, before that activity moved into my office. I would prefer to provide you a more detailed answer to that.

We did summarize after each of our meetings with the providers that every one of them had, in fact, satisfied the President's criteria. In fact, they were quite forthcoming about their procedures.

Senator SPECTER. I have heard your generalizations, but we want the specifics. If you are unable to provide them at this time, then you submit them to the committee.

Dr. BALDWIN. I would be happy to submit them.

Senator SPECTER. By the end of the week?

Dr. BALDWIN. By the end of the day.

Senator SPECTER. By the end of the day?

Dr. BALDWIN. Absolutely.

Senator SPECTER. A question has been raised about the Swedish stem cells which make up almost half of the stem cell derivations, according to information provided to the subcommittee. There are barriers from the Gotebourg, Sweden group. The availability of the number of stem cell lines for U.S. researchers is restricted by the donors, since the original donation was for a period of 6 months, and the donors have a right to reclaim the donated cells. Is that correct?

Dr. BALDWIN. Yes, that is correct. But in Gotebourg they are going back to reconsent the donors so that they could meet our eligibility criteria. They would be doing that under any circumstances, and it is obviously essential for the NIH purposes. We have met with them. We do not feel there is going to be any problem in that regard.

Senator SPECTER. But they do not now have the donor's consent?

Dr. BALDWIN. Not for all of them. They had them at the time that they presented their material. The question in the consent form, where they said that they would only be used for 6 months, was an issue. That is a problem for them, as well as for any uses that might be made of them at the NIH. So they have told us that they are, in fact, going back to each one to reconsent.

Senator SPECTER. Is it true the donors have the right to reclaim the donated cells?

Dr. BALDWIN. I believe it is.

Senator SPECTER. So these are unanswered questions as to whether those cell lines are really available.

Dr. BALDWIN. Yes. We know that three of them are available.

Senator SPECTER. What's that?

Dr. BALDWIN. We know three of them are available now.

Senator SPECTER. Has the period of time expired for the donors to reclaim them?

Dr. BALDWIN. That is a level of detail—again, I would like to provide that for the record.

Senator SPECTER. Well, thank you very much, Dr. Baldwin. If you would stay with us, there may be some more questions which arise during the course of the hearing, when we hear from the other witnesses. If you could provide those materials to us by the end of the day, that would be very helpful.

Dr. BALDWIN. Thank you.

Senator SPECTER. I would now like to hear from Dr. Bert Vogelstein, president of the Biological and Biomedical Associations of the Stem Research Committee, National Academy of Science.

Dr. Vogelstein is professor of oncology at John Hopkins, where he holds a joint appointment in molecular biology and genetics, a bachelor's degree from the University of Pennsylvania—was that the College or the Wharton School?

Dr. VOGELSTEIN. College.

Senator SPECTER. Good for you, and an M.D. from John Hopkins University School of Medicine. Do you recall your class slogan from Penn, Dr. Vogelstein?

Dr. VOGELSTEIN. No, I do not—sorry.

Senator SPECTER. Thank you for joining us, Dr. Vogelstein. We look forward to your testimony.

STATEMENT OF BERT VOGELSTEIN, M.D., PROFESSOR OF ONCOLOGY AND PATHOLOGY, JOHN HOPKINS ONCOLOGY CENTER; CHAIRMAN, NATIONAL RESEARCH COUNCIL INSTITUTE OF MEDICINE COMMITTEE ON THE BIOLOGICAL AND MEDICAL APPLICATIONS OF STEM CELL RESEARCH

Dr. VOGELSTEIN. Thank you. I am here today as the chairman of the National Research Council Institute of Medicine Committee on the Biological and Medical Applications of Stem Cell Research.

We issued a report whose purpose was to look at how promising stem cell research really is, how far away we are from practical, therapeutic applications of this research, and what factors might either promote or hinder progress in the development of this research in the future.

We have made several recommendations, but in the interest of time I will just briefly mention two of the most important of them. First, while much can be learned from existing embryonic stem cell lines if they are made widely available for research, several concerns about these lines strongly suggested that we will need to develop new stem cell lines in the future.

Second, a substantial obstacle to the success of transplantation of these cells is the immune reaction of the patient's body to cells that it perceives as foreign. One of the most promising ways to overcome this obstacle is with a——

Senator SPECTER. Would you repeat the obstacle? I did not understand it.

Dr. VOGELSTEIN. Yes. Most people are excited about this research because of their potential medical implications, and particularly for transplantation for diseases like Parkinson's disease, diabetes, et cetera. These cells will have come in general from another person, and they will in general be rejected by the host, the person they are transplanted into. That will become eventually one of the most difficult obstacles to actually using this research to help people.

Now, how do we overcome that? There are several potential strategies, but perhaps the most promising of these is through the creation of stem cells using a technique known as somatic cell nuclear transfer. This technique is also called therapeutic cloning. It should not be confused with reproductive cloning. The purpose of somatic cell nuclear transfer, or SCMT, or therapeutic cloning, is to produce cells in culture, not to produce people.

Senator SPECTER. It should not be confused with what kind of cloning?

Dr. VOGELSTEIN. Reproductive cloning. Reproductive cloning purpose is to produce people. Therapeutic cloning purpose is to produce cells in a tissue culture dish.

Senator SPECTER. It is to produce cells?

Dr. VOGELSTEIN. Cells and tissues, heart cells, brain cells, pancreatic cells, and those cells then can be transplanted into people with a variety of diseases that would otherwise be lethal. Because these cells come from the person whom they are going to be transplanted into, they are genetically identical and should not be rejected. That is how they overcome the rejection problem.

PREPARED STATEMENT

Thank you for the opportunity to testify. I would like my statement to be put into the record, together with our report from the National Research Council, and I would be happy to try to answer any questions you might have.

[The statement follows:]

PREPARED STATEMENT OF DR. BERT VOGELSTEIN

Good morning, Mr. Chairman, and members of the Committee. My name is Bert Vogelstein and I am a Professor of Oncology and Pathology at the John Hopkins Oncology Center and a Howard Hughes Medical Institute Investigator. I am here today as the chairman of a National Research Council and Institute of Medicine Committee on the Biological and Biomedical Applications of Stem Cell Research which yesterday released the report: "Stem Cells and the Future of Regenerative Medicine."

Stem cell research gives hope to millions of Americans and people around the world who suffer from debilitating illnesses such as diabetes and Parkinson's disease-or who have suffered injuries to their spinal cords or other parts of the body-that new treatments and perhaps even a cure will someday make them well again.

Given that promise, as well as the ethical controversies it generates, the National Research Council and Institute of Medicine decided it would be a good idea to form a committee to take a look at how promising stem cell research really is; how far away we are from practical, therapeutic applications; and what factors might either promote or hinder progress in the development of stem cell therapies.

Our committee also took into consideration the fact that there are diverse views held in our society about the ethical controversies stem cell research raises. We included an expert in bioethics on our committee and invited philosophers, ethicists, religious leaders, and legal experts to a workshop we held on the scientific and ethical issues of stem cell research this past summer so we could listen to their views.

It is important to note that none of the members of our committee are conducting stem cell research ourselves, and none have financial interests in stem cell research. This was to assure that none of us had a vested self-interest in the outcome of this report.

Realizing the importance of stem cell research, The National Academies not only initiated but also funded most of this study itself, with additional support from the Ellison Foundation, to whom we are grateful.

It should be pointed out that we recognize that the role of the National Academies is to advise public policy, not set it. The purpose of our report was to tell policymakers what we know about the potential of stem cell research based on the best available science, but it is up to the government, and really all of society, to consider our advice and make decisions.

Let me give you a brief description of what stem cells are and what we know about their potential to be used as medical therapies, before I get to our findings and recommendations.

Stem cells are unspecialized cells that can renew themselves indefinitely, and under the right conditions, become, or differentiate into, cell types with specialized functions. They can be found in an embryo in the very early stages of development, in some fetal tissue, and in some adult organs.

Isolating adult stem cells is very difficult and there is only preliminary evidence that they can be turned into tissue characteristic of organs other than the ones from which they were taken. On the other hand, since 1998, we have been able to grow embryonic stem cells in the laboratory. In addition, embryonic stem cells are known to have the ability to differentiate into virtually all cell types. Researchers have had some success using transplanted embryonic stem cells from mice to restore some lost functions in diseased or injured animals. We found these studies to be promising, but not definitive, evidence that similar treatments can be successful in humans.

Let me now briefly summarize the committee's main recommendations:

First, although experiments in mice and other animals are necessary, they are not sufficient for realizing the full potential of stem cells to lead to tissue-replacement therapies for humans. Studies with human stem cells are absolutely necessary.

Second, although stem cell research is on the cutting edge of science today, it is still in its infancy. Current scientific data indicate that there are important biological differences between adult and embryonic stem cells and among adult stem cells found in different types of tissue. The therapeutic implications of these biological differences are not yet clear. Adult stem cells from bone marrow have so far pro-

vided most of the examples of successful therapies for replacement of diseased or destroyed cells. However, their potential for fully differentiating into multiple tissue types is still poorly understood and remains to be clarified. In contrast, embryonic stem cells studied in animals clearly are capable of developing into multiple tissue types and are capable of long-term self-renewal in culture. Because the application of stem cell research to therapy for human disease will require much more knowledge about the biological properties of all types of stem cells, research on both embryonic and adult human stem cells should be pursued.

Third, while much can be learned from existing embryonic stem cell lines if they are made widely available for research, concerns about the eventual accumulation of genetic mutations in these lines, and the fact that most have been cultured with animal cells and serum, means they need to be monitored very closely and that we will need to develop new stem cell lines in the future.

Fourth, human stem cell research that is publicly funded and conducted under the highest standards of open scientific exchange, peer-review, and public oversight offers the most efficient and responsible means to achieve medical breakthroughs. Stem cell science is still in the early stages where much more basic research is needed. Although research by private, for-profit companies will eventually play a critical role in translating the fruits of basic research into actual medical therapies, it is likely to take years to yield commercial products. Without public funding for basic research to get us to that point, progress is likely to be hindered.

Fifth, proposals for federal grants to work on human embryonic stem cells should be justified on the soundest scientific grounds and should be strictly scrutinized for compliance with existing and future federally-mandated ethical guidelines.

Sixth, we recommend that to assist in providing scientific and ethical oversight, a national advisory body composed of leading scientists, ethicists, and other stakeholders be established at the National Institutes of Health. This group could evaluate the technical merit of research proposals, monitor potential risks to research subjects, and ensure compliance with the law and ethical standards.

Our final recommendation is that in conjunction with research on stem cell biology and the development of stem cell therapies, research on the problem of transplant rejection should also be actively pursued. A substantial obstacle to the success of transplantation of any cells, including stem cells and their derivatives, is the immune reaction of a patient's body to cells that it perceives as foreign. Multiple approaches to reducing this problem should be explored, including ways to manipulate the genetic makeup of the stem cell tissue to make it less likely to provoke an immune reaction, and the creation of stem cells using a technique known as somatic cell nuclear transfer. This involves taking the DNA from a cell of a patient in need of a transplant, inserting it into an egg cell that has had its nucleus removed, and triggering cell division. The resulting stem cells and tissue that can be obtained from this procedure would be genetically identical to the patient's, and would in theory not be rejected by the patient's immune system when transplanted into him or her.

This procedure should not be confused with reproductive cloning which utilizes a similar technique for the purpose of implanting an embryo and creating a child. The issue of reproductive cloning is being looked at by another National Academies committee, which will issue its findings soon.

I would like to end by emphasizing again that stem cell research is in its infancy. Our committee is respectful of the wide array of social, political, legal, ethical, and economic issues that must be considered in policy-making in a democracy, and we have been impressed by the commitment of all parties in this debate to life and health, regardless of the different conclusions they draw. We hope our report, by clarifying what is known about stem cells and how best to realize their potential, will be a useful contribution to the discussion of this important issue.

Thank you for this opportunity to testify. I would like my statement to be put into the record, and I will be happy to answer any questions the Committee might have.

STEM CELLS AND THE FUTURE OF REGENERATIVE MEDICINE

EXECUTIVE SUMMARY

Stem cell research offers unprecedented opportunities for developing new medical therapies for debilitating diseases and a new way to explore fundamental questions of biology. Stem cells are unspecialized cells that can self-renew indefinitely and also differentiate into more mature cells with specialized functions. Research on human embryonic stem cells, however, is controversial, given the diverse views held in our society about the moral and legal status of the early embryo. The controversy

has encouraged provocative and conflicting claims both inside and outside the scientific community about the biology and biomedical potential of both adult and embryonic stem cells.

The National Research Council and Institute of Medicine formed the Committee on the Biological and Biomedical Applications of Stem Cell Research to address the potential of stem cell research. The committee organized a workshop that was held on June 22, 2001. At the workshop, the committee heard from many leading scientists who are engaged in stem cell research and from philosophers, ethicists, and legal scholars. (Audio files of the speakers' presentations are available at the workshop web site, www.nationalacademies.org/stemcells.)

The participants discussed the science of stem cells and a variety of ethical and other arguments relevant to public-policy as it applies to stem cells. The committee considered the information presented, explored the literature on its own, and contemplated the substance and importance of the preliminary data from recent stem cell experiments. The committee's deliberations on the issues led to the following conclusions and recommendations.

—Experiments in mice and other animals are necessary, but not sufficient, for realizing the potential of stem cells to develop tissue-replacement therapies that will restore lost function in damaged organs. Because of the substantial biological differences between animal and human development and between animal and human stem cells, studies with human stem cells are essential to make progress in the development of treatments for human disease, and this research should continue.

—There are important biological differences between adult and embryonic stem cells and among adult stem cells found in different types of tissue. The implications of these biological differences for therapeutic uses are not yet clear, and additional data are needed on all stem cell types. Adult stem cells from bone marrow have so far provided most of the examples of successful therapies for replacement of diseased or destroyed cells. Despite the enthusiasm generated by recent reports, the potential of adult stem cells to differentiate fully into other cell types (such as brain, nerve, pancreas cells) is still poorly understood and remains to be clarified. In contrast, studies of human embryonic stem cells have shown that they can develop into multiple tissue types and exhibit long-term self-renewal in culture, features that have not yet been demonstrated with many human adult stem cells. The application of stem cell research to therapies for human disease will require much more knowledge about the biological properties of all types of stem cells. Although stem cell research is on the cutting edge of biological science today, it is still in its infancy. Studies of both embryonic and adult human stem cells will be required to most efficiently advance the scientific and therapeutic potential of regenerative medicine. Moreover, research on embryonic stem cells will be important to inform research on adult stem cells, and vice versa. Research on both adult and embryonic human stem cells should be pursued.

—Over time, all cell lines in tissue culture change, typically accumulating harmful genetic mutations. There is no reason to expect stem cell lines to behave differently. In addition, most existing stem cell lines have been cultured in the presence of non-human cells or serum that could lead to potential human health risks. Consequently, while there is much that can be learned using existing stem cell lines if they are made widely available for research, such concerns necessitate continued monitoring of these cells as well as the development of new stem cell lines in the future.

—High quality, publicly funded research is the wellspring of medical breakthroughs. Although private, for-profit research plays a critical role of translating the fruits of basic research into medical advances that are broadly available to the public, stem cell research is far from the point of providing therapeutic products. Without public funding of basic research on stem cells, progress toward medical therapies is likely to be hindered. In addition, public funding offers greater opportunities for regulatory oversight and public scrutiny of stem cell research. Stem cell research that is publicly funded and conducted under established standards of open scientific exchange, peer review, and public oversight offers the most efficient and responsible means of fulfilling the promise of stem cells to meet the need for regenerative medical therapies.

—Conflicting ethical perspectives surround the use of embryonic stem cells in medical research, particularly where the moral and legal status of human embryos is concerned. The use of embryonic stem cells is not the first biomedical research activity to raise ethical and social issues among the public. Restrictions and guidelines for the conduct of controversial research have been developed to address such concerns in other instances. For example, when recom-

binant-DNA techniques raised questions and were subject to intense debate and public scrutiny, a national advisory body, the Recombinant DNA Advisory Committee, was established at the National Institutes of Health (NIH) to ensure that the research met the highest scientific and ethical standards. If the federal government chooses to fund research on human embryonic stem cells, a similar national advisory group composed of exceptional researchers, ethicists, and other stakeholders should be established at NIH to oversee it. Such a group should ensure that proposals to work on human embryonic stem cells are scientifically justified and should scrutinize such proposals for compliance with federally mandated ethical guidelines.

—Regenerative medicine is likely to involve the implantation of new tissue in patients with damaged or diseased organs. A substantial obstacle to the success of transplantation of any cells, including stem cells and their derivatives, is the immune-mediated rejection of foreign tissue by the recipient's body. In current stem cell transplantation procedures with bone marrow and blood, success can hinge on obtaining a close match between donor and recipient tissues and on the use of immunosuppressive drugs, which often have severe and life-threatening side effects. To ensure that stem cell-based therapies can be broadly applicable for many conditions and individuals, new means to overcome the problem of tissue rejection must be found. Although ethically controversial, somatic cell nuclear transfer, a technique that produces a lineage of stem cells that are genetically identical to the donor, promises such an advantage. Other options for this purpose include genetic manipulation of the stem cells and the development of a very large bank of embryonic stem cell lines. In conjunction with research on stem cell biology and the development of stem cell therapies, research on approaches that prevent immune rejection of stem cells and stem cell-derived tissues should be actively pursued.

The committee is aware of and respectful of the wide array of social, political, legal, ethical, and economic issues that must be considered in policy-making in a democracy. And it is impressed by the commitment of all parties in this debate to life and health, regardless of the different conclusions they draw. The committee hopes that this report, by clarifying what is known about the scientific potential of stem cells and how that potential can best be realized, will be a useful contribution to the debate and to the enhancement of treatments for disabling human diseases and injuries. On August 9, 2001, when President Bush announced a new federal policy permitting limited use of human embryonic stem cells for research, this report was already in review. Because this report presents the committee's interpretation of the state of the science of stem cells independent of any specific policy, only minor modifications to refer to the new policy have been made in the report.

RECOMMENDATIONS

1. Studies with human stem cells are essential to make progress in the development of treatments for human disease, and this research should continue.

2. Although stem cell research is on the cutting edge of biological science today, it is still in its infancy. Studies of both embryonic and adult human stem cells will be required to most efficiently advance the scientific and therapeutic potential of regenerative medicine. Research on both adult and embryonic human stem cells should be pursued.

3. While there is much that can be learned using existing stem cell lines if they are made widely available for research, concerns about changing genetic and biological properties of these stem cell lines necessitate continued monitoring as well as the development of new stem cell lines in the future.

4. Human stem cell research that is publicly funded and conducted under established standards of open scientific exchange, peer-review, and public oversight offers the most efficient and responsible means to fulfill the promise of stem cells to meet the need for regenerative medical therapies.

5. If the federal government chooses to fund human stem cell research, proposals to work on human embryonic stem cells should be required to justify the decision on scientific grounds and should be strictly scrutinized for compliance with existing and future federally-mandated ethical guidelines.

6. A national advisory group composed of exceptional researchers, ethicists, and other stakeholders should be established at NIH to oversee research on human embryonic stem cells. The group should include leading experts in the most current scientific knowledge relevant to stem cell research who can evaluate the technical merit of any proposed research on human embryonic stem cells. Other roles for the group could include evaluation of potential risks to research subjects and ensuring compliance with all legal requirements and ethical standards.

7. In conjunction with research on stem cell biology and the development of potential stem cell therapies, research on approaches that prevent immune rejection of stem cells and stem cell-derived tissues should be actively pursued. These scientific efforts include the use of a number of techniques to manipulate the genetic makeup of stem cells, including somatic cell nuclear transfer.

[CLERK'S NOTE.—The report from the National Research Council: "Stem Cell Research and the Future of Regenerative Medicine" can be found on the web at http://www.nap.edu/books/0309076307/html/.]

Senator SPECTER. Dr. Vogelstein, you start off saying that there is a need to develop new lines. Why?

Dr. VOGELSTEIN. There are several reasons for that. The currently existing lines, a relatively small number, are problematic because they accumulate mutations as they grow, and eventually they need to be used.

Senator SPECTER. Accumulate mutations? What do you mean by that?

Dr. VOGELSTEIN. Genetic defects. Every time a cell divides in tissue culture, it accumulates mutations. These mutations in aggregate may cause certain problems, especially when it is realized that they may not be suitable for patients for another 10 years or so.

Senator SPECTER. May not be suitable for patients for another 10 years or so?

Dr. VOGELSTEIN. Yes.

Senator SPECTER. Why is that?

Dr. VOGELSTEIN. This research is really in its infancy. By the time that enough research is done to allow transplantation with these cells, it is likely to be roughly 10 years.

Now, one cannot estimate that exactly, but that is consistent with Secretary Thompson's——

Senator SPECTER. So these mutations would be pronounced over a protracted period of time? They would not be usable?

Dr. VOGELSTEIN. That is one possibility, and it might be preferable to use fresh cells which have not accumulated as many mutations. That is one reason.

A second reason is that all of the existing lines have been cocultured with animal cells, or animal products, which present certain potential hazards.

There are other problems, too, but perhaps the main, or one of the most important points is that new technologies for generating these cells will undoubtedly continue to be developed over the coming years, and if one is forced to use only the stem cell lines that are now in existence, one precludes using new stem cell lines that may be better. As an example, it would be like forcing people to listen to vinyl records instead of using eight-tracks or CD's even when the technology becomes better, and when one realizes that this issue is much more important than sound quality, that may be quite limiting in the long term.

Senator SPECTER. Any more reasons why we need to develop the new stem cell lines?

Dr. VOGELSTEIN. I think those are the main ones.

Senator SPECTER. When you mentioned reason No. 2, that they are cocultured with animals, you are referring to the mouse feeder issue?

Dr. VOGELSTEIN. The mouse feeder cells as well as they have been cultured in serum generally derived from cows.

Senator SPECTER. And does that preclude their use in therapy?

Dr. VOGELSTEIN. It does not necessarily preclude their use, but it certainly, at least theoretically, provides a hazard, a zoonotic hazard if there are any viruses or other pathogens that were in the mice or the cows that could have been transmitted to these cells, and it is a potential danger. It obviously would be preferable if they had never been cultured with any animal produces.

Senator SPECTER. There is an amendment which is likely to be filed with our pending bill which I discussed yesterday with Senator Brownback. The thrust of it would be to ban therapeutic cloning, both public and private, and to impose a penalty of $1 million and a prison term. What effect do you think such an amendment, if enacted into law, would have on stem cell research?

Dr. VOGELSTEIN. Well, as our report noted, one of the most important ways to actually be able to use stem cells for medicine may involve embryonic stem cells created from therapeutic cloning techniques, and if one were to preclude that, the implication could mean that these regenerative medicine applications will never occur, and that the people with a variety of terrible diseases will never be able to benefit from this research. That is a possibility.

Senator SPECTER. Are you suggesting it might discourage such research?

Dr. VOGELSTEIN. I think that is an understatement.

Senator SPECTER. Well, I asked you a question about what the effect would be, and did not get very much of a direct answer. I expected a fair amount of outrage. What happened to your Pern class? Which class was it, by the way?

Dr. VOGELSTEIN. 1966.

Senator SPECTER. I was district attorney at that time, making the streets safe in West Philadelphia.

Dr. VOGELSTEIN. I remember that.

Senator SPECTER. Which was no easy job.

Dr. VOGELSTEIN. It would completely preclude such research, and the implications might well be that it would completely preclude the use of this whole technology, embryonic stem cells, for real medical applications. There is a great danger in that policy.

Senator SPECTER. Senator Brownback's amendment further bans any importation of any product derived from cloning. This undefined provision could keep Americans from benefiting from cures that may be developed from using therapeutic cloning outside of the United States. What impact would you see if it became law that you could not import any product derived from therapeutic cloning?

Dr. VOGELSTEIN. Again, it depends on what lines and reagents are developed outside the country, but since the current biomedical research is really an international effort, it is reasonably likely that the most useful lines and reagents will be developed outside of the United States and, if so, this policy would again inhibit or perhaps entirely preclude using the best technology to correct these diseases in people.

Senator SPECTER. Dr. Vogelstein, elaborate on the kinds of ailments which could be affected by therapeutic cloning. You mentioned pancreatic cells. What else?

Dr. VOGELSTEIN. Pancreatic cells for diabetes.

Senator SPECTER. Pancreatic cells for diabetes?

Dr. VOGELSTEIN. Yes. Nerve cells for Parkinson's disease.

Senator SPECTER. Would you repeat that?

Dr. VOGELSTEIN. Nerve cells for Parkinson's disease and Alzheimer's disease. Nerve cells for spinal cord injuries. Blood vessel cells for certain types of heart diseases, as well as heart cells, and I think one of the important things to note is that most of the diseases that I just mentioned, as well as many others which are catalogued in our report, there is no cure, and the only real hope for these people, at least according to current medical opinion, is through regenerative medicine.

Senator SPECTER. Through what?

Dr. VOGELSTEIN. Through regenerative medicine.

Senator SPECTER. No cure for what?

Dr. VOGELSTEIN. For any of these diseases, Alzheimer's disease, Parkinson's disease, a variety of spinal cord injuries, certain types of diabetes, many others.

Senator SPECTER. So the only hope is through regenerative——

Dr. VOGELSTEIN. The only hope on the horizon is through transplantation of these stem cells, and the other important point to mention, which is again in our report, the details, but these are not rare diseases. We are talking about diseases which affect millions of people in the United States alone.

Senator SPECTER. You ticked them off. Diabetes, Parkinson's, Alzheimer's, spinal cord injuries, heart—are there others?

Dr. VOGELSTEIN. Yes. There is a whole list of them.

Senator SPECTER. We found it on page 6. Thank you very much. I want to have this in hand for the debate which we are going to have a little later today.

Dr. Vogelstein, what would be a more accurate and less inflammatory name than therapeutic cloning which would say about the same thing?

Dr. VOGELSTEIN. Well, in our report——

Senator SPECTER. You should have consulted with your public relations people before you put cloning in the title.

Dr. VOGELSTEIN. In our report I actually refer to it as somatic cell nuclear transfer, or SCNT.

Senator SPECTER. Repeat that again.

Dr. VOGELSTEIN. Somatic cell nuclear transfer. The acronym is SCNT, and we purposely used that term because of the great confusion between therapeutic and reproductive cloning, which is very unfortunate, because they are really quite different.

Senator SPECTER. Well, Dr. Vogelstein, thank you very much for your testimony, and thank you for the work of the National Academy of Sciences. We appreciate it.

If you would stay with us we may have some more questions as we hear from the other panelists.

Dr. VOGELSTEIN. Thank you very much.

Senator SPECTER. We would now like to hear from panel 3, Dr. Marti Pera, Dr. Joseph Itskovitz, Dr. James Thomson, Dr. Carl

Gulbrandsen. Dr. Pera is associate professor, senior research fellow at Monash University in Melbourne, Australia, and earned his master's from Oxford and his Ph.D. from George Washington University.

Thank you for joining us, Dr. Pera. May I first inquire if you are here for some conference, or here for some other purpose?

Dr. PERA. I am actually here on holiday, visiting my family.

Senator SPECTER. That is the best of all reasons. We are glad to have you available to testify today. Please proceed.

STATEMENT OF MARTIN F. PERA, Ph.D., MONASH UNIVERSITY, AUSTRALIA

Dr. PERA. Thank you, Mr. Chairman, for the opportunity to come and speak to you today. In my testimony I will respond directly to queries raised by your committee on our stem cell research and related matters.

The first question related to the current status of stem cell lines derived by our group in collaboration with Professor Bundus at the National University of Singapore. Our group has derived six independent stem cell lines. The lines were developed from embryos developed with informed consent by couples undergoing in vitro fertility treatment. They were surplus for clinical need. They had no financial inducement offered for their donation. All of these cell lines have been placed on the NIH registry of human embryonic stem cells.

Of the six cell lines, four have been sufficiently characterized to validate their identification in light of our present understanding of the biology of primate ES cells. These criteria include the demonstration that the cells express molecules on the surface of a particular set of genes characteristic of pluripotent stem cells, that they maintain normal genetic makeup as evidenced by normal chromosome number and morphology, that they are able to differentiate into a wide range of cells in vitro when grafted into experimental animals, and that they retain these properties for at least 150 population doublings, or generations, in vitro.

The remaining two cell lines have been successfully cultivated for 50 population doublings, and have been successfully cryopreserved. We are now completing the characterization of these remaining cells lines, which should be finished in the first half of next year.

The second question related to our definition of a successful derivation of an ES cell line. We consider that an attempt at derivation is successful in yielding a new line when the cell line has met the criteria I just outlined and has been successfully cryopreserved on at least three separate instances. Successful cryopreservation means the cell can be recovered in a viable form from frozen stock, and new cultures which also meet the criteria for ES cells may be initiated from the frozen stock.

A third question related to the adequacy of presently available cell lines to support basic research on stem cells. While at present we cannot be certain that all of the cell lines currently available for federally funded research will meet all of the above criteria listed for validation as ES cell lines, with the exception of those described in the literature by Dr. James Thompson and ourselves. However, if we make a reasonable assumption that there are at

least 20 cell lines available that will meet these criteria, that these cell lines will be widely and successfully distributed throughout the academic community, then such a panel of cell lines would probably be adequate to conduct much of the basic research into ES cell biology that is a prerequisite to any clinical application of these cells.

Senator SPECTER. Probably adequate to conduct much of the basic research?

Dr. PERA. Yes.

Senator SPECTER. That leaves two questions in your answer, probably adequate, and much of the research. Do you think the scientific community ought to rely on that kind of a judgment, probably, for much, and not with certainty for all?

Dr. PERA. In my opinion, the door should be left open to the derivation and the use of new cell lines for research.

Senator SPECTER. Thank you.

Dr. PERA. Regarding the use of existing cell lines in clinical therapies, it is possible that available cell lines will be useful in clinical therapies. However, to my knowledge the existing cell lines have been derived using mouse feeder cell support, and the Food and Drug Administration has indicated that any cell line produced for clinical use from such cells would be regarded for regulatory purposes as a xenotransplant.

Now, such a classification of this cell as a xenotransplant would not prohibit its use, but would place incumbrances on its use, and if actual hazards such as the transmission of pathogens from the animal cells were, in fact, documented, then it is likely that the use of the cell lines would be curtailed, so in my view it is almost certain that additional cell lines will have to be derived for clinical therapy in the future because of possible hazards associated with coculture of the stem cells with animal cells, and because cell lines representative of a greater degree of genetic diversity may well be required to circumvent problems of tissue rejection.

Senator SPECTER. When you say greater diversity, what do you have in mind there, Dr. Pera?

Dr. PERA. Greater genetic diversity. We all carry a particular set of antigens that causes rejection of those cells in a noncompatible individual, and that is caused by the essential genetic diversity of people, and we may need more cell lines more broadly representative of a wide range of genetic background.

Senator SPECTER. Are you thinking there about ethnic lines, about racial lines?

Dr. PERA. I am talking about genetic diversity in general, but racially as well.

Senator SPECTER. Well, what does genetic diversity mean beyond racial diversity, or ethnic diversity?

Dr. PERA. Well, within any racial or ethnic group there is a very wide range of what we call tissue histocompatibility antigens that are encoded by our DNA, so that while some races have a narrow range of these, in others there are many thousands of combinations in any given ethnic group.

Senator SPECTER. So that is even when you are dealing with no racial or ethnic diversity?

Dr. PERA. That is correct, yes.

Senator SPECTER. How many cell lines do you think would be required to solve this issue of genetic diversity?

Dr. PERA. That is a very difficult question to answer.

Senator SPECTER. That is why we have you here, Dr. Pera.

Dr. PERA. Unfortunately, I am not a transplantation immunologist, but the answer to that question depends in part on, I think, the clinical problem. In some clinical instances you may be transplanting the cells into a site where immunorejection is not such a great problem. It depends in part on how visible the stem cell derived cells are to the immune system, and it depends in part on how sanguine you are about our future prospects to manipulate the immune system.

Senator SPECTER. So with all those questions, would you say it is a fair conclusion that a great many lines may be necessary if scientists are to have a full range of opportunity for research?

Dr. PERA. In our present understanding, I think that would be a fair answer, yes.

The fifth question related to our plans to derive additional cell lines, and the answer is yes, we and our collaborators will certainly derive additional cell lines in the future to meet some of these clinical applications, as noted above.

A further reason for deriving additional cell lines is that since our knowledge of embryonic stem cells is constantly expanding, and our current techniques for derivation and maintenance of these cell lines are almost certainly suboptimal, it may be that our present methodology is somehow selecting for cells which are defective in some way that has not yet become manifest. Thus, in the future, guided by a better understanding of stem cell biology, we might wish to derive new cell lines with improved properties.

We were asked about obstacles to the distribution of cell lines, and to date the main obstacles we have faced in our efforts to distribute our cells have been limitations on our resources, which have really hampered our ability to produce cells for distribution and to train scientists in recipient laboratories.

These obstacles are likely to become less significant in the coming years, since we have received support from our Victorian State government to set up a small laboratory for stem cell production and training. Intellectual property issues have delayed completion in some instances of materials transfer agreements for the cell lines, but we have been pretty flexible in the approach to this matter, and it has not proven yet to be a major impediment.

The seventh question related to our interaction with the National Institutes of Health, and we did meet with officials from the NIH and Secretary Thompson in the summer of this year to discuss plans for listing of our cell lines on the registry.

The final question relates to recent progress in embryonic stem cell research, and looking globally, I think that within the past year several laboratories have reported the derivation of a wide range of cell types from spontaneously differentiated cultures, clearly, nerve cells, cardiac muscle cells, insulin-producing cells, and blood stem cells.

In particular, I think that substantial progress has been made in obtaining neural precursors from cultures of embryonic stem cells. We have obtained highly enriched populations of nerve cell precur-

sors, and we have been able to show that these can undergo normal differentiation and integration into the brain when grafted into the nervous system of experimental animals.

More recently, we have identified a key regulatory molecule that is active in controlling the early phases of stem cell differentiation, and shown that modulation of the signaling pathway can direct differentiation of stem cells toward the nerve cell lineage, so that in summary, in upcoming months I think we can expect to see more work which will enhance our ability to control the growth and differentiation of embryonic stem cells, and I think that this work will lead to a much more efficient production of specific, specialized cells required in research and regenerative medicine.

[The information follows:]

RESPONSE TO QUERIES FROM SENATORS SPECTER AND HARKIN

Current status of cell lines derived by our group.—In collaboration with Professor Ariff Bongso at the National University of Singapore, our group has derived six independent human embryonic stem (ES) cell lines from human blastocysts. These lines were developed from embryos donated with informed consent by couples undergoing in vitro fertility treatment. The embryos were surplus to clinical requirements, and no financial inducement was offered in return for their donation. All of these cell lines have been placed on the National Institutes of Health Human Embryonic Stem Cell Registry. Of the six cell lines, four have been sufficiently characterised to validate their identification as human ES cell lines in light of our present understanding of the biology of primate ES cells. The criteria for validation include the demonstration that the cells express certain specific marker molecules on their surface and a particular set of genes that are characteristic of pluripotent cells, that they maintain a normal genetic makeup as evidenced by normal chromosome number and morphology, that they are able to differentiate into a wide range of body cells in vitro and when grafted into experimental animals, and that they retain these properties for at least 150 population doublings in vitro. The remaining two cell lines have been successfully cultivated for 50 population doublings in vitro, and they have been successfully cryopreserved. Our laboratory is presently completing the characterisation of these remaining two cell lines, a task that should be finished in the first half of next year. There is at present no reason to believe these remaining two cell lines will not meet the criteria for validation listed above, but we must complete the necessary tests to ensure that they do.

Definition of successful derivation of an ES cell line.—We consider that an attempt at derivation is successful in yielding a new ES cell line when the cell line has met the above criteria and has been successfully cryopreserved on at least three separate instances. Successful cryopreservation means that the cells can be recovered in a viable form from frozen stock and new cultures which meet the criteria for ES cells may be initiated from the frozen cells.

Adequacy of presently available cell lines to support basic research on stem cells.—At present, we cannot be certain that all of the cell lines currently available for federally funded research will meet all the above listed criteria for validation as ES cell lines, with the exception of those described in the literature by Dr. James Thomson and ourselves. However, if we make a reasonable assumption that there are at least twenty cell lines available that will meet these criteria, and that these cell lines will be widely and successfully distributed throughout the academic community, then such a panel of cell lines will probably be adequate to conduct much of the basic research into ES cell biology that is a prerequisite to any clinical application of these cells.

Use of existing cell lines in clinical therapies.—It is possible that currently available cell lines will be useful in clinical therapy. However, to my knowledge the existing cell lines have been derived using mouse feeder cell support, and the Food and Drug Administration has indicate that any cell produced for clinical use from such lines would be regarded for regulatory purposes as a xenotransplant. Such classification of a cell line as a xenotransplant would not prohibit its use, but would place encumbrances on such use, and if actual hazards such as transmission of pathogens from the animal cells were in fact documented, then it seems likely the use of the cell lines would be curtailed. It is certain that additional cell lines will have to be derived for clinical therapy in future, because of possible hazards associated with co-culture of the existing stem cells with animal cells, and because cell lines rep-

resentative of a greater degree of genetic diversity may well be required to circumvent problems of tissue rejection.

Derivation of additional cell lines.—We and our collaborators will probably derive additional cell lines in the future, mainly to meet the requirements of clinical applications as noted in 4 above. A further reason for deriving additional cell lines is that since our knowledge of ES cells is constantly expanding, and our current techniques for derivation and maintenance are almost certainly suboptimal, it may be that our present methodology somehow is selecting for cells which are defective in some way that has not yet become manifest. Thus in future, guided by a better understanding of stem cell biology, we might wish to derive new cell lines which will have improved properties. Our main priority at present however, is to carry out the basic research which is an essential prerequisite to clinical use of ES cells or their derivatives, and we are doing this with our existing cell lines.

Obstacles to the distribution of cell lines.—To date, the main obstacles we have faced in our efforts to distribute our ES cells to workers wishing to conduct research in this area have been limitations on our resources, which have hampered our ability to produce cells for distribution and to train scientists in recipient laboratories. These obstacles will be less significant in the coming year, since we have received support from the Victorian state government to set up a small laboratory for stem cell production and training. Intellectual property issues have delayed completion of Materials Transfer Agreements for the cell lines in some cases, but we have been flexible in our approach to this matter and it has not proven to be a major impediment. ESI Pte., the company which controls intellectual property rights to our cell lines, continues to seek means to expedite distribution of these cells.

Interaction with the National Institutes of Health.—We met with officials from the National Institutes of Health and Secretary Thompson in August of this year to discuss plans for listing of our cell lines on the registry.

Recent progress in human ES cell research.—Within the past year, several laboratories have reported the derivation of a wide range of cell types from spontaneously differentiating cultures of human ES cells. These include nerve cells, cardiac muscle cells, insulin producing cells, and blood stem cells. In particular, substantial progress has been made in obtaining neural precursors from cultures of embryonic stem cells. We have obtained highly enriched populations of neural progenitors from human ES cell cultures, and have shown that these progenitors undergo normal differentiation and integration when grafted into the nervous system of experimental animals. More recently we have identified a key regulatory molecule active in the early phases of human ES cell differentiation, and we have shown that modulation of this signaling pathway can direct differentiation of ES cells towards the neuronal lineage. In upcoming months we can expect to see more work which will enhance our ability to control the growth and differentiation of ES cells; this work will lead to much more efficient production of specific specialised cells required in research and regenerative medicine.

Senator SPECTER. Dr. Pera, are there any laws in Australia, to your knowledge, which preclude extracting stem cells from embryos?

Dr. PERA. Yes, there are. It varies from State to State in Australia. In our own State of Victoria that sort of manipulation of an embryo is prohibited, and so we collaborated with groups from overseas to do that phase of the work.

In other States there are no restrictions. We have recently had a parliamentary committee of inquiry report on stem cells and related matters, and their report was, in fact, very favorable. It recommended stem cell research and endorsed derivation of new cell lines, and the idea is that with that recommendation the Federal Government will get uniform legislation.

Senator SPECTER. So you got the stem cell lines from overseas?

Dr. PERA. That is right. They came from Singapore.

Senator SPECTER. From Singapore?

Dr. PERA. That is correct.

Senator SPECTER. And do you receive any governmental funding?

Dr. PERA. We are just now receiving governmental funding. We have a program grant.

Senator SPECTER. From Australia?

Dr. PERA. It is actually funded by the Juvenile Diabetes Foundation, but through our National Health and Medical Research Council.

Senator SPECTER. Has NIH made our Federal funding available to you?

Dr. PERA. It is certainly open to us to apply for those funds, and we intend to do so.

Senator SPECTER. Well, thank you very much, Dr. Pera. We appreciate your being here.

You have six lines, four characterized and two uncharacterized?

Dr. PERA. That is correct.

Senator SPECTER. And what is your expectation as to the utility of the two uncharacterized lines?

Dr. PERA. From what we have been able to observe of them so far, they will be very similar in their properties to other cell lines, and we expect they will be validated as bona fide embryonic stem cell lines. We are doing that at the moment, and we hope to have the answer in the early part of next year.

Senator SPECTER. Thank you. I will turn now to Dr. Joseph Itskovitz, professor at Technion University, Haifa, Israel, and director of the Rambam Medical Center. Thank you for joining us, Dr. Itskovitz. Let me inquire preliminarily what brings you to the United States, something beyond this hearing? Are you here in the United States solely for this hearing?

Dr. ITSKOVITZ. We are also meeting with NIH people.

Senator SPECTER. Thank you for joining us. We look forward to your testimony. The floor is yours.

STATEMENT OF JOSEPH ITSKOVITZ, Ph.D., DIRECTOR, RAMBAM MEDICAL CENTER; PROFESSOR, TECHNION UNIVERSITY, HAIFA, ISRAEL

Dr. ITSKOVITZ. Thank you, Mr. Chairman. First of all, I am director for OB/GYN of the Rambam Medical Center.

Mr. Chairman, Senator Specter, members of the committee, I am pleased to appear before you today to testify on human embryonic stem cell research. I represent a group of 20 scientists and students currently involved in human embryonic stem cell research in Haifa for the last 3 years.

In September 1997, we established collaboration with Dr. James Thomson, leading to the derivation to the first five human ES cell lines, H1, H7, H9, H13, and H14 in Madison, and also the clonal derivation from a single derivation of H9.1 and H9.2 in human ES cell lines.

In July 2000, we derived three cell lines, I3, I4, I6, and then an additional line, J3 was established in January 2000 in Haifa from frozen cell embryos.

The lines met President Bush's criteria. Three cell lines, I6, I3, and J3 are well-characterized. They show characteristic morphology of ES. They have already been continued in the culture for at least 10 months. They express markers shown to be associated with human ES, and maintain normal clarity. The cells form antibodies in suspension in deficient mice which show formation of tissues from all three germ layers.

At least one single cell clone was derived from each of these cell lines. J3 is a unique cell line. It was derived from a culture in vitro for an additional week. There is a distinct morphology, and cells grow faster than other cell lines of the H or I series. It may represent a later stage of cell of the primitive ectoderm. The unique characteristics of specific pathways of differentiation is currently being examined.

In addition, we continue the culture H cell lines that originated from Madison. Altogether, we have in our laboratory in Haifa nine parental lines and many clonal lines, cultures continuously from the period between 10 months and 2 years. In August 2001, two studies conducted in Haifa were reported. The first study demonstrated that each ES cells can differentiate into myocytes with structural and functional properties of cardiomyocytes. This was reported by Kehat in the second paper by Assady. She demonstrated insulin production by human ES cells, reported, published in Diabetes.

These reports validate the H ES cell's model system as a potential basis for enrichment of human cardiomyocytes and islet cells, a possible future source for cell replacement therapy.

More recently, we have directed differentiation of human ES cells to insulin-secreting structures similar to pancreatic islets by using a modified method of Ron McKay's protocol. This was done by Segev. Furthermore, Assady unpublished, she has generated pluripotent undifferentiated cell lines transgenic for a reporter driven by the insulin promoter, an approach that can be used to monitor better cell differentiation and to isolate a rich population of insulin-producing cells for transplantation therapy.

In Israel, the Bioethics Advisory Committee of the Israel Academy of Sciences and Humanities has approved both the derivation of human ES cells and also research into therapeutic cloning. The Rambam Medical Center and the Technion School of Medicine view the embryonic stem cell project to be of major interest for basic and applied research.

PREPARED STATEMENT

Prior to September 11, we started a first round of discussions with our colleagues at various institutes and centers at the NIH. We are warmly accepted and intend to continue our discussion in order to generate collaborative research programs with NIH scientists and to obtain support for our internal research activity and the necessary supporting infrastructure.

[The statement follows:]

PREPARED STATEMENT OF DR. JOSEPH ITSKOVITZ

Mr. Chairman, Senator Specter, and Members of the Committee, I am pleased to appear before you today to testify on human embryonic stem cell research. I represent a group of 20 scientists currently involved in human embryonic stem (hES) cell research in Haifa for the last 3 years. In September 1997, we established a collaboration with Dr. James Thomson leading to the derivation of the first 5 hES cell lines in (H1, H7, H9, H13, H14) in Madison (Thomson et al., Science 282:1145, 1998) and also the clonal derivation from a single cell of H9.1 and H9.2 hES lines (Amit et al., Development 227:271, 2000).

In July 2000, we derived 3 cell lines 13, 14, 16, and an additional line (J3) was established in January 2000 all in Haifa. The lines met President Bush's criteria. Three cell lines (I3, I6, and J3) are well characterized. They show characteristic hES

morphology, have already been continuously cultured for at least 10 months, express markers known to be associated with hES and maintain normal karyotype. The cells form embryoid bodies in suspension and create teratomas in immune-deficient mice which show formation of tissues from all 3 germ layers. At least one single cell clone was derived from each of these cell lines. J3 is a unique cell line. It was derived from an embryo cultured in vitro for an additional week, has a distinct morphology, and the cells grow faster than the other hES cell lines of the H or I series. It may represent a later stage of cells of the primitive ectoderm. The unique characteristics for specific pathway of differentiation is currently being examined. In addition we continue to culture the H cell lines that originated from Madison. All together we have in our laboratory in Haifa 9 lines being cultured continuously from a period between 10 months and 2 years.

In August 2001, two studies conducted in Haifa were reported. The first study, demonstrated that hES cells can differentiate into myocytes with structural and functional properties of cardiomyocytes (Kehat et al., J Clin Inv 108:407:2001). In the second paper, Assady et al., demonstrated insulin production by hES cells (Diabetes 50:1691, 2001). These reports validate the hES cell model system as a potential basis for enrichment of human cardiomyocytes and islet cells, a possible future source for cell replacement therapy.

More recently we have directed differentiation of hES cells to insulin-secreting structures similar to pancreatic islets by using a modified method of Ron McKay's protocol (Segev et al., unpublished). Furthermore, Assady et al., (unpublished) have generated pluripotent undifferentiated hES cell clones, transgenic for a reporter driven by the insulin promoter, an approach that can be used to monitor (β-cell differentiation, and to isolate enriched populations of insulin-producing cells for transplantation therapy.

In Israel, the Bioethics Advisory Committee of the Israel Academy of Sciences and Humanities has approved both the derivation of hES cells and also research into therapeutic cloning.

Rambam Medical Center and the Technion's School of Medicine view the embryonic stem cell project to be of major interest for basic and applied research. Prior to September 11 we started the first round of discussions with our colleagues at various Institutes and Centers at the NIH. We are warmly accepted and intend to continue our discussions in order to generate collaborative research programs with NIH scientists and to obtain support for our internal research activity and the necessary supporting infrastructure.

Senator SPECTER. Thank you for that very fine statement, doctor. Your timing was the closest I have seen. You finished your 5 minutes with 1 second left.

In Israel, extraction of stem cells from embryos is lawful?

Dr. ITSKOVITZ. Yes.

Senator SPECTER. Have you received any funding from the Government of Israel?

Dr. ITSKOVITZ. Not for funding, not for derivation of the embryos. This was done, I would say, until now the money for my departmental budget, but currently further money is available for research on the human ES stem cell research.

Senator SPECTER. Are you discussing with NIH the possibility of funding from NIH?

Dr. ITSKOVITZ. Definitely.

Senator SPECTER. Which diseases will be available for stem cell treatment first, Dr. Itskovitz? What diseases do you look forward to working on from the stem cell derivation?

Dr. ITSKOVITZ. As I mentioned earlier, there is some preliminary data which is relevant mainly to insulin-producing cells for diabetes, Type II diabetes. The derivation of cardiac cells for the repair of cardiac damage in heart patients, and we are also doing some work now currently on blood vessel differentiation, actually in differentiation to construct blood vessels.

Senator SPECTER. Does your laboratory or any of your collaborators plan to work on therapeutic cloning?

Dr. ITSKOVITZ. Yes.

Senator SPECTER. What do you think the impact would be if we passed a law in the United States prohibiting therapeutic cloning and provided a jail sentence and a big fine, and prohibited the importation of any materials resulting from therapeutic cloning?

Dr. ITSKOVITZ. It is, I believe, now it is hard to predict, but I think that this technology should be left open for research. It is really difficult to appreciate now how this will bring us to the clinic to alleviate or overcome all of the problems of rejections that was mentioned before we can have a lot of information generated from animal studies regarding the therapeutic cloning, but definitely I think that this should be left open for further discussion with the public.

Senator SPECTER. Have you detected any differences between cell lines derived from frozen, as contrasted with fresh stem cell lines?

Dr. ITSKOVITZ. All of the cell lines were derived from frozen embryos.

Senator SPECTER. Do you think that limiting the research to the stem cell lines in existence as of 9:00 p.m. on August 9 is sufficient for the needs of the scientific community?

Dr. ITSKOVITZ. Currently I believe it is sufficient even for the near future, because an enormous amount of data can be generated from the current available cell lines, even if there are only 30, not 60, but in addition I believe that they should also leave the door open to generate new cell lines in the future.

I am not sure when and how soon, but the cell lines currently available will allow us to proceed very significantly with the basic research, and even with applied research, and maybe even bring us to the clinic, but definitely we should leave the door open in the future to generate a different type of cell line that I have already alluded to. One of them was established in my lab, and also in the case that we have cell lines that would not be compatible for therapeutic purposes after FDA reviewing and revision of the current cell lines that are available.

Senator SPECTER. Well, are the existing lines all adequate for therapy, considering the contamination, so to speak, from mouse feeders and bovine, et cetera?

Dr. ITSKOVITZ. There are no indications of contaminations. This should be checked, but basically, principally speaking this does not preclude the use of the cells as a transplant in humans. This was, at least by this being announced by the FDA——

Senator SPECTER. You say it does pose a problem?

Dr. ITSKOVITZ. Potentially it may cause a problem. If the FDA will not approve the current cell lines based on the definition that they are having for clinical purposes it is still enigmatic.

Senator SPECTER. Do you think FDA should approve their use for therapy?

Dr. ITSKOVITZ. The current?

Senator SPECTER. The stem cell lines that have been developed with mouse feeders or bovine.

Dr. ITSKOVITZ. If they are checked, and they would be disease-free, and other issues related to exposure would be settled, the FDA would be satisfied with it, it is okay.

Senator SPECTER. But you think even beyond that there is a need to have the availability of new cell lines in the future?

Dr. ITSKOVITZ. In the future, yes.

Senator SPECTER. Thank you very much, doctor.

We turn now to Dr. James Thomson, scientific director of WiCell Research Institute, chief of pathology at the Wisconsin Regional Primate Research Center, assistant professor of anatomy, University of Wisconsin Medical School, B.S. from Illinois, Ph.D. and DVM from University of Pennsylvania.

STATEMENT OF JAMES THOMSON, Ph.D., CHIEF SCIENTIFIC OFFICER, WiCELL RESEARCH INSTITUTE, INC.

Dr. THOMSON. Thank you, Mr. Chairman, for the opportunity to appear today to discuss human embryonic stem cell research. Today we are here because of your efforts, and we deeply appreciate your support.

The main issue today is whether the existing human ES cell lines that were derived prior to President Bush's policy announcement of August 9, 2001 are sufficient for human ES cell research to fulfill its promise. I believe that much of the recent debate about the actual number of existing cell lines has been misdirected. If there are only a couple of dozen such cell lines that are widely available to American investigators, it is likely that much of the basic research that must be done in order to develop new therapies can be accomplished. These cells can be expanded without apparent limit. Therefore, a reasonably small number of cell lines can supply the research needs of a large number of investigators.

The University of Wisconsin and the Wisconsin Alumni Research Foundation are both committed to seeing that the five human embryonic stem cell lines I have developed are shared widely with the research community, and we have already begun sharing these cell lines with investigators. I believe the existing human ES cell lines will support most of the basic research needs of U.S. investigators.

However, the existing human ES cell lines will not fulfill their promise unless NIH begins aggressively to fund this area of research. As of today, the NIH human embryonic stem cell registry is not yet up and running, and this is necessary to initiate funding. We and others have already provided NIH with the required documentation for the existing cell lines, and researchers are anxious to start submitting grant proposals in this area. Anything that this committee can do to facilitate this process will make a big impact.

There has recently been given a great deal of press attention given to the fact that human ES cell lines were derived in contact with cells from mice and with protein products from other species, including bovine serum. The intermingling of protein sources from multiple species raises legitimate safety concerns for future therapeutic products based on human ES cells because a possibility exists that pathogens could be transmitted between these species.

At the time that I was deriving our five human ES cell lines, I was consciously deriving them for research purposes, not for therapeutic purposes. I believe that future derivations can be done in a more controlled manner that would satisfy the FDA's safety concerns for therapeutic products.

Today, however, we do not yet know how to derive and grow human ES cells in the complete absence of these foreign cells or protein products.

Senator SPECTER. Let me interrupt you at that point, Dr. Thomson, to pinpoint the question as to whether the existing lines with a mouse feeder and the bovine aspects are adequate for therapy.

Dr. THOMSON. I think that is where the big difference is. I think for basic research the existing cell lines are probably adequate. For therapy, they are probably not. The existing cell lines may well be approved by FDA. There is historical precedence for them approving human health cell lines,not ES cell lines, with the same kinds of problems, but if I was a patient and I had the choice between cell lines derived on use already done and outside cell lines under more controlled conditions——

Senator SPECTER. And if you were a patient and told the only ones available were the ones——

Dr. THOMSON. If they are the only ones available, sure, but I would like to have that choice. It would be useful to derive more in the future.

Senator SPECTER. Because the risks involved with the mouse feeders and the bovine——

Dr. THOMSON. That is right. You can test them extensively for everything that is known, and if you miss something because it is unknown, it is still a potential problem, and FDA deals with those risks all the time, but it clearly would be preferable to derive them in complete absence of those problems.

Senator SPECTER. Thank you.

Dr. THOMSON. However, today we do not yet know how to derive stem cell lines that lack those problems. There is an active area of research in several lines, and I would guess over the next several years we will be able to derive new cell lines that do not have those problems. Because clinical trials based on human ES cells may be several years away, the several concerns about existing cell lines will not have any direct impact on initial basic research.

The President's decision does not affect the private sector's ability to derive new human ES cell lines, and I am confident that as improved human culture conditions are established the private sector will derive additional cell lines. However, I believe that the major innovative breakthroughs in stem cell research will continue to occur in academic research centers. New therapies are usually introduced into these clinics by major academic medical centers, but the ability of these medical centers to use new human ES cell lines derived by the private sector could be severely limited by the President's decision.

Academic medical centers receive Federal support, and the overhead from such Federal support could interfere with a physician's ability to use new human ES cell lines in clinical trials even if those clinical trials are privately funded. This is a serious concern that must be addressed if the President's policy remains in place once clinical trials are initiated.

Senator SPECTER. Would you repeat your last statement please, Dr. Thomson?

Dr. THOMSON. Academic centers receive NIH support for a variety of purposes. They get overhead for that that supports every-

thing from the lights to the heating system. The President's decision is interpreted very rigorously, that overhead intermixing with new cell lines could be a very big problem. It has been a very big problem up to now. We have had to separate our labs into separate places so they do not have the overhead problems, but you cannot separate the clinical trials from that overhead problem. It would be very difficult to do.

So as new cell lines are derived——

Senator SPECTER. You are saying the President's policy does not take into account overhead?

Dr. THOMSON. If new cell lines that are derived that are clinically more useful, even if they are privately funded in academic medical centers, it would be difficult for people to use them if the current policy continues.

Senator SPECTER. Why is that?

Dr. THOMSON. Because NIH money is intermingled into overhead, and that would be a potential support for clinical trials in an indirect way, so that is a problem that has to be addressed if this policy stays.

Finally, I believe the study of cells, both adult and embryonic, will revolutionize human medicine, but that this revolution will occur rapidly only if the proper infrastructure is provided to nurture it. The debate about whether adult or embryonic stem cells is better is a political debate not shared by mainstream stem cell biologists. For example, the knowledge gained from the study of embryonic stem cells will almost certainly advance the clinical utility of stem cells.

PREPARED STATEMENT

The development of clinical applications of stem cells requires novel collaborative interactions between scientists and physicians with diverse backgrounds. Multiple national stem cell research centers that support both embryonic and adult stem cells would significantly accelerate the field by providing a collaborative environment for the development of stem-cell-based therapies.

I look forward to your questions. Thank you.

[The statement follows:]

PREPARED STATEMENT OF DR. JAMES THOMSON

I want to thank both Senators Specter and Harkin for the opportunity to appear here today to address issues concerning human embryonic (ES) stem cell research. Additionally, I would not only like to thank these Senators, but Secretary Thompson as well, for their continuing support of human embryonic stem cell research. Today we are here because of your diligent efforts. I deeply appreciate your support.

The main issue to address today is whether the human ES cell lines that were derived prior to President Bush's policy announcement of August 9, 2001, are sufficient for human ES cell research to fulfill it's promise. I believe that much of the recent debate about the actual number of existing cell lines has been misdirected. If there are only a couple dozen cell lines that are widely available to American investigators, it is likely that much of the basic research that must be done in order to develop new therapies can be accomplished. These cells can be expanded without apparent limit. Therefore, a reasonably small number of cell lines can supply the research needs of a large number of investigators. The University of Wisconsin and the Wisconsin Alumni Research Foundation are both committed to seeing that the five human embryonic stem cell lines that I have derived are shared widely with the research community, and we have already begun sharing them with other inves-

tigators. I believe the existing human ES cell lines will support most of the basic research needs of U.S. investigators.

However, the existing human ES cell lines will not fulfill their promise unless NIH begins to aggressively fund this area of research. As of Monday, October 29, 2001, the NIH Human Embryonic Stem Cell registry, necessary to initiate funding, had not yet been posted. We, and others, have already provided NIH with the required documentation for existing cell lines, and researchers across the country are anxious to start submitting grant proposals in this area. Anything that this committee can do to facilitate that process would make a big impact.

There has recently been a great deal of press attention given to the fact that existing human embryonic stem cell lines were derived in contact with cells from mice and with protein products from other species, including bovine serum. The intermingling of protein sources from multiple species raises legitimate safety concerns for future therapeutic products based on human ES cells, because the possibility exists that pathogens could be transmitted between species. At the time that I was deriving our five human ES cell lines, I was consciously deriving them for research purposes, not for therapeutic purposes. I believe that future derivations can be done in a more controlled manner that would satisfy the FDA's safety concerns for therapeutic products. Today, however, we do not yet know how to derive and grow human ES cells in the complete absence of these foreign cells or protein products, and this is an area of active research in several labs. Thus, today we are not yet able to derive new human ES cell lines that lack these potential problems.

Because clinical trials based on human ES cells may be several years away, these safety concerns about existing cell lines will not have any direct impact on initial basic research. The President's decision does not affect the private sector's ability to derive new human ES cell lines, and I am confident that as improved culture conditions are established, the private sector will derive additional cell lines. However, I believe that the major innovative breakthroughs in stem cell research will continue to occur in academic research centers. New therapies are usually introduced into the clinics by major academic medical centers, but the ability of these medical centers to use new human ES cell lines derived by the private sector in clinical trials could be limited by the President's decision. Academic medical centers receive federal support and the over-head from such federal support could interfere with a physician's ability to use new human ES cell lines in clinical trials, even if those clinical trials are privately funded. This is a serious concern that must be addressed if the President's policy remains in place once clinical trials are initiated.

Finally, I believe that the study of stem cells, both adult and embryonic, will revolutionize human medicine, but that this revolution will only occur rapidly if the proper infrastructure is provided to nurture it. The debate about whether adult or embryonic stem cells are "better" is a political debate not shared by mainstream stem cell biologists. For example, the knowledge gained from the study of embryonic stem cells will almost certainly advance the clinical utility of adult stem cells. The development of clinical applications of stem cells will required novel collaborative interactions between scientists and physicians with diverse backgrounds. Multiple National Stem Cell Research Centers that support both embryonic and adult stem cell research would significantly accelerate the field by providing a collaborative environment for the development of stem cell-based therapies.

Senator SPECTER. Thank you, Dr. Thomson.

We now turn to Dr. Carl Gulbrandsen, managing director of the Wisconsin Alumni Research Foundation, and president of WiCell Research Institute. He received his bachelor's degree from St. Olaf, Ph.D. from the University of Wisconsin, and J.D. from the University of Wisconsin Law School.

Thank you for joining us, Dr. Gulbrandsen. The floor is yours.

STATEMENT OF CARL E. GULBRANDSEN, Ph.D., J.D., MANAGING DIRECTOR, WISCONSIN ALUMNI RESEARCH FOUNDATION, PRESIDENT, WiCELL RESEARCH INSTITUTE, INC.

Dr. GULBRANDSEN. Thank you, Mr. Chairman. Mr. Chairman, members of the subcommittee, I am pleased to appear before you again to discuss the role of the Wisconsin Alumni Research Foundation, and its not-for-profit subsidiary, WiCell Research Institute, supporting the important research necessary to move the science of embryonic stem cells forward. I would like to once again personally

thank Chairman Harkin and Senator Specter for their continued commitment to human embryonic stem cell research.

This testimony was prepared for the hearing originally scheduled for September 12, 2001. I would like to take a moment to offer our sympathies to the families of the victims at the World Trade Center, the Pentagon, and passengers of the flight that crashed in Pennsylvania. Those who have been exposed to anthrax and have died from anthrax infection also should have our deepest sympathies.

We at WiCell and the University of Wisconsin Madison involved in stem cell research are attempting to continue to move the program forward. While we are aware of the new landscape, we trust that the NIH and researchers all over the country will continue to pursue the promise of stem cell research.

Since August 1, 2001, when I was last before this body, a significant barrier to forward movement of the ES cell research has been removed. In that regard, Secretary Tommy Thompson deserves special thanks. His counsel to the President was clearly instrumental in guiding the President to decide on August 9 that embryonic stem cell research should receive Federal funding. After the August 9 presidential decision and before September 11 it was evident that the leadership of Tommy Thompson had made funding of embryonic stem cell research a high priority at NIH.

WARF and WiCell responded to that by negotiating and executing a memorandum of understanding with the United States Public Health Service that many commentators hailed as groundbreaking. I am here today to explain that agreement to you.

The agreement with the Public Health Service does two important things. First, under the agreement WiCell agrees to provide its human embryonic stem cells, which I will refer to as Wisconsin materials, to federally funded researchers at low cost and with few restrictions.

Second, it provides at no cost an automatic limited noncommercial license under WARF's embryonic stem cell patents to Public Health Service researchers using Wisconsin materials and to third parties who provide human embryonic stem cells to researchers under similar terms as the agreement we have with PHS as well as to those researchers receiving the third party materials.

Let me explain the agreement in more detail. The purpose of this agreement is to make the Wisconsin materials available to researchers at PHS and to federally funded researchers at universities and other research institutions as easily as possible. It is significant to note that the agreement with the Public Health Service does not require what is commonly referred to as reach-through rights. WARF and WiCell have a mission to serve the public good. In the interest of that mission we have provided research access to our patent rights and to the actual human embryonic stem cells cultured by Dr. Thomson.

These cells are the gold standard. They meet the four criteria outlined by the American Society for Cell Biology. It should also be noted that these cells were derived using only private funds and are the private property of WARF. Nevertheless, WARF and WiCell are making these cells available at low cost with few restrictions to assist scientists in moving the research forward as quickly as

possible. Scientists receiving Wisconsin materials under the agreement we have with PHS are free to publish and patent without consent whatever they discover using Wisconsin materials. The recipient institution will own such patents, and no commercial rights under those patents are owed back to WiCell.

What restrictions are in the agreement with PHS? The bioethical restrictions are those imposed by the University of Wisconsin Bioethics Committee and representations to donors of embryos used to derive the Wisconsin materials that some experiments would not be done with donated embryos. Under these restrictions, the researcher receiving Wisconsin material agrees not to mix the materials with an intact embryo and place the material in a uterus, or attempt to make an embryo with the material.

The agreement with the Public Health Service does not permit diagnostic or therapeutic use of the Wisconsin materials. There are two principal reasons for this restriction, safety and liability. The Wisconsin materials are research materials. While we hope that research using the Wisconsin materials will ultimately lead to lifesaving therapies, at the present time there is no certainty that the Wisconsin materials themselves are suitable for diagnostic or therapeutic use. They were not prepared under the conditions that the FDA ordinarily requires for commercial diagnostic or therapeutic products. It would be irresponsible for WiCell to allow such use with its materials at this time.

In fact, virtually all research material transfer agreements being used in the United States today have similar restrictions. In view of that, a failure by WiCell to require such a restriction would expose it to an unreasonably high risk of liability should an accident occur.

The Wisconsin materials may not be used under the agreement that we have with the PHS in a research program where a non-Federal research sponsor requires a grant back of commercial rights. Under such circumstances, the researcher or the sponsor will need a commercial license from WiCell. If such circumstances exist, under the agreement that we have with PHS WiCell has agreed to provide such a license under terms no less favorable than other similar commercial licenses to the extent that such rights are available.

The Wisconsin materials may not be transferred to a third party without WiCell's written consent. However, WiCell has agreed under the agreement with the PHS to make materials available to such third parties under the simple letter agreement for teaching or noncommercial research purposes. This prohibition against transfer is in large part due to WiCell's obligations to assure that the Wisconsin materials are not used in violation of the bioethical restrictions.

Beyond this, the researcher agrees to follow all applicable statutes, regulations, and guidelines related to handling use and disposal of the materials. The agreement does require an annual certification by the Public Health Service and the researcher that they are in compliance with those restrictions.

WARF, WiCell, and the University of Wisconsin Madison believe in and are excited about the future of medicine utilizing embryonic stem cell technology. By allowing Federal funding for this research,

the Government has taken an important first step. The next step is to provide sufficient funds to make a difference.

According to the testimony at the Kennedy hearing in early September, approximately $250 million of NIH funding is currently spent on adult stem cell research. I would hope that at least that amount and preferably more would be devoted to embryonic stem cell technology.

PREPARED STATEMENT

Our goal is to see this technology widely disseminated and developed, and we believe that our licensing practices and the recently signed agreement with PHS reflect that goal. We know that Federal funding will increase the number of researchers who work on embryonic stem cells, and that these resources will bring the tomorrow of medicine closer to today.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF DR. CARL E. GULBRANDSEN

Thank you, Mr. Chairman. Mr. Chairman and members of the subcommittee, I'm pleased to appear again before you to discuss the role of the Wisconsin Alumni Research Foundation and its not-for-profit subsidiary, WiCell Research Institute, in supporting the important research necessary to move the science of embryonic stem cells forward. I would like to once again personally thank Chairman Harkin and Senator Spector for their continued commitment to Human Embryonic Stem Cell (ES) research.

This testimony was prepared for the hearing originally scheduled for September 12, 2001. I would like to take a moment to offer our sympathies to the families of the victims, at the World Trade Center, the Pentagon, and the passengers on the flight that crashed in Pennsylvania. Those who have been exposed to anthrax and have died from the anthrax infection also have our deepest sympathies. We at WiCell and the University of Wisconsin-Madison that are involved in stem cell research are attempting to continue to move the program forward. While we are aware of the new landscape we trust that the NIH and researchers all over the country will continue to pursue the promise of stem cell research.

Since August 1, 2001, when I was last before this body, a significant barrier to forward movement of ES cell research has been removed. In that regard, Secretary Tommy Thompson deserves special thanks. His counsel to the President was clearly instrumental in guiding the President to decide on August 9, that embryonic stem cell research should receive federal funding. After the August 9th Presidential decision, and before the September 11 attack, it was evident that the leadership of Tommy Thompson had made funding of embryonic stem cell research a high priority at NIH.

WARF and WiCell responded to that priority by negotiating and executing a Memorandum of Understanding (MOU) with the U.S. Public Health Service (hereafter referred to as "MOU") that many commentators hailed as groundbreaking. I am here today to explain that agreement to you.

The MOU does two important things: first, under the agreement WiCell agrees to provide its human embryonic stem cells ("Wisconsin Materials") to federally funded researchers at low cost and with few restrictions; second, it provides at no cost, an automatic, limited, non-commercial license under WARF's embryonic stem cell patents to Public Health Service (PHS) researchers using Wisconsin Materials and to third parties who provide human embryonic stem cells to researchers under similar terms as the MOU as well as to those researchers receiving those third party cells.

Let me explain the agreement in more detail. The purpose of this agreement is to make the Wisconsin Materials available to researchers at the PHS and to federally funded researchers at universities and other research institutions as easily as possible. It is significant to note that the MOU does not require what are commonly referred to as reach-through rights. WARF and WiCell have a mission to serve the public good. In the interest of that public good we have provided research access to our patent rights and the actual Human Embryonic Stem Cells created by Dr.

Thomson. These cells are the gold standard. They meet the four criteria outlined by the American Society for Cell Biology. It should also be noted that these cells were derived using only private funds and are the private property of WARF. Nonetheless, WiCell is making these cells available at low cost with few restrictions to assist scientists in moving the research forward as quickly as possible. Scientists receiving Wisconsin Materials under the MOU are free to publish and patent, without consent, whatever they discover using Wisconsin Materials. The recipient institution will own such patents and no commercial rights under those patents will be owed to WiCell.

What restrictions are in the MOU? The bioethical restrictions are those imposed by the University of Wisconsin Bioethics Committee and representations to donors of embryos used to derive the Wisconsin Materials that some experiments would not be done with their donated embryos. Under these restrictions, the researcher receiving Wisconsin Materials agrees not to mix the Material with an intact embryo, implant the Material in a uterus or attempt to make an embryo with the material.

The MOU does not permit diagnostic or therapeutic use of the Wisconsin Materials. There are two principal reasons for this restriction—safety and liability. The Wisconsin Materials are research materials. While we hope that research using the Wisconsin Materials will ultimately lead to life saving therapies, at the present time there is no certainty the Wisconsin Materials themselves are suitable for diagnostic or therapeutic use. They were not prepared under the conditions that the FDA ordinarily requires for commercial, diagnostic or therapeutic products. It would be irresponsible for WiCell to allow such use with its materials at this time. In fact, virtually all research material transfer agreements being used in the United States today have similar restrictions. In view of that, a failure by WiCell to require such a restriction would expose it to an unreasonably high risk of liability should an accident occur using Wisconsin Materials.

The Wisconsin Materials may not be used under the MOU in a research program where a non-federal research sponsor requires a grant back of commercial rights. Under such circumstances, the researcher or sponsor will need a commercial license from WiCell. If such circumstance exists, under the MOU, WiCell has agreed to provide such a license under terms not less favorable than other similar commercial licenses to the extent such rights are available.

The Wisconsin Materials may not be transferred to a third party without WiCell's written consent; however, WiCell has agreed under the MOU, to make materials available to such third party under the MOU and Simple Letter Agreement for teaching or non-commercial research purposes. This prohibition against transfer is in large part due to WiCell's obligations to assure that the Wisconsin Materials are not used in violation of the bioethical restrictions.

Beyond this, the researcher agrees to follow all applicable statutes, regulations and guidelines relating to handling, use and disposal of such materials. The MOU does require an annual certification by PHS and the researcher that they are in compliance with these restrictions.

WARF, WiCell, and the University of Wisconsin-Madison believe in and are excited about the future of medicine utilizing ES cell technology. By allowing federal funding for this research the government has taken an important first step. The next step is to provide sufficient funds to make a difference. According to testimony at the Kennedy Hearing in early September, approximately $250 million of NIH funding is currently spent on adult stem cell research. I would hope that at least that amount and preferably more would be devoted to ES cell technology.

Our goal is to see this technology widely disseminated and developed. We believe that our licensing practices and recently signed MOU reflect that goal. We know that federal funding will increase the number of researchers who work with ES cells and that these researchers will bring the tomorrow of medicine closer to today.

Senator SPECTER. Thank you very much, Dr. Gulbrandsen.

Are you saying, in effect, that your companies have made available your patents in an unlimited way for basic research?

Dr. GULBRANDSEN. That is right.

Senator SPECTER. But not for the application to therapy?

Dr. GULBRANDSEN. For commercial purposes that need to use our patents they will need to have commercial license from us.

Senator SPECTER. They will have to have a commercial license from your company, but I hear the reasons you have given that you are concerned about civil liability.

Dr. GULBRANDSEN. I understand. Yes.

Senator SPECTER. Any other reason?

Dr. GULBRANDSEN. No. The restriction in the memorandum of agreement to use of these materials for diagnostic or therapeutic purposes is principally a liability issue.

Senator SPECTER. Well, it seems to me that if you make available patents and somebody else undertakes activity which results in damage, it would not be your responsibility, but I am not going to second-guess your lawyers. We really have not come to the application for therapy at this point. Would your company be willing to consider at some future time licensing for therapy as the matter progresses and therapy becomes more a current issue?

Dr. GULBRANDSEN. Absolutely, and the difference here is not just a patent license, it is actually providing the materials. If we were just licensing the patent, the liability issue is much less, but in this case we are providing materials.

Senator SPECTER. You are providing materials? What do you mean?

Dr. GULBRANDSEN. The embryonic stem cells themselves, and so under our strict liability laws in this country those materials are dangerous. We would be liable.

Senator SPECTER. Well, maybe so, and maybe not, but are you saying in effect that if the liability issue could be resolved so that there would not be liability for your companies, that you would be willing to issue licenses for therapy as well?

Dr. GULBRANDSEN. Absolutely.

Senator SPECTER. What is the current status of WiCell's negotiations with the Geron Corporation regarding exclusive commercial licensing of the several additional cell types?

Dr. GULBRANDSEN. We are presently in litigation with Geron. The issue of their option rights to add additional cell lines is one of the issues in the lawsuit.

Senator SPECTER. What is the essential dispute there, the essence of the dispute?

Dr. GULBRANDSEN. The essence of the dispute is that under the license agreement Geron had a license agreement that extended at the end of July, that expired at the end of July, to add additional types of cells to their exclusive fields of use and diagnostics and therapeutics. We unsuccessfully negotiated with them. The option in our mind expired. They are disputing that, and so we turned to the court to settle the issue.

Senator SPECTER. Where is that case pending?

Dr. GULBRANDSEN. That is in the Western District of Wisconsin.

Senator SPECTER. How many memoranda of understanding have been negotiated with academic research centers?

Dr. GULBRANDSEN. Since the signing of the memorandum of understanding with the Public Health Service we have sent out 44 memoranda, or I guess 46 memoranda to other institutions.

Senator SPECTER. How about with private companies?

Dr. GULBRANDSEN. Private companies, we are presently discussing with three of the cell type owners a license.

Senator SPECTER. What compensation do you get from that, any?

Dr. GULBRANDSEN. From which?

Senator SPECTER. From the memoranda, from letting others have your patents.

Dr. GULBRANDSEN. From academic researchers that are receiving Federal dollars the fee is a one-time up-front $5,000 fee to transmit the stem cells to them.

Senator SPECTER. You must have very considerable legal fees in connection with all of these memoranda of understanding, do you not?

Dr. GULBRANDSEN. This is a not-for-profit, truly a not-for-profit. We are losing money on this. Yes, the fees are extensive. I did not mean to be flippant. We have invested an enormous amount of money in human embryonic stem cell research.

Senator SPECTER. Dr. Thomson, let me come back to you for a question. We are expecting another amendment on the Labor-HHS bill which would make unlawful any attempt to combine a human gamete with an animal gamete, or to combine human genetic material with the egg of an animal. This sort of hybrid raises a lot of questions, and has an alarming sound. Are there any scientifically valuable experiments that would be affected by this kind of a ban?

Dr. THOMSON. Yes. There is a fertility assay that uses human sperm, and it is an assay to detect fertility of the sperm. That is an existing assay that has been used for years now. There is probably other assays like that, that would be affected by that wording.

Senator SPECTER. Are you saying that that kind of a prohibition would be a significant limitation on scientific research?

Dr. THOMSON. I think to the people conducting those experiments, yes.

Senator SPECTER. Can you elaborate your reasons so that I could repeat them on the floor of the Senate?

Dr. THOMSON. Sir, there is an existing assay——

Senator SPECTER. If I find them persuasive, that is.

I would like to understand what you are saying.

Dr. THOMSON. There is an existing assay to test the fertility of human sperm, and it is based on whether it will actually complete some of the process of fertilization with a hamster, and that product does not divide, it does not turn into an embryo, but what you just said would ban that, and it is an assay simply to look at fertility. I do not know how widely it is used. So that is one assay that has already been done in labs, and that would be banned by that wording.

The thing that is probably intended to ban is taking a somatic nucleus and transferring it to a rabbit oocyte——

Senator SPECTER. Start again and explain it once more.

Dr. THOMSON. Which one, the fertility assay?

Senator SPECTER. What the impact would be on the prohibition which I just read to you.

Dr. THOMSON. There is already an existing assay which is used in clinics.

Senator SPECTER. An existing——

Dr. THOMSON. An existing assay based on the combination of human sperm and hamster oocytes, a hamster egg, and it is simply to see if that sperm has the ability to fertilize something. Now, the product of that cannot divide.

Senator SPECTER. The human sperm and the egg of an animal?

Dr. THOMSON. That is right.

Senator SPECTER. And the purpose of that is to test the potency of the human sperm?

Dr. THOMSON. Right, and since I am not in that field I do not know how widely it is used, but it is an existing assay.

Senator SPECTER. It is not used to create a new entity?

Dr. THOMSON. No. The combination apparently does not divide, and does not turn into an embryo, but it is enough to tell whether the sperm can penetrate.

Senator SPECTER. That kind of a combination would not be successful in creating another entity?

Dr. THOMSON. Not a hybrid, no, but by the wording you said, that would be banned. More generally there is an interest in some groups to do nuclear transfer from human somatic cells to animal oocytes to do essentially therapeutic cloning, which was described before, to make ES cell-like lines from that product.

Senator SPECTER. Would you repeat that, please?

Dr. THOMSON. There is an interest in using human oocytes, taking a nucleus from a patient, putting it into that animal oocyte, and letting the product grow to an appropriate stage and make an embryonic stem cell line. That embryonic stem cell line, if you can do that, and nobody has shown you can do that yet, would be matched to that patient, and you would get around the rejection problem.

There are several groups that believe it might be possible. There is no convincing evidence that scientifically that works yet, but that ban would prohibit a potentially promising area of research.

Senator SPECTER. Dr. Thomson, your five stem cells lines are among the oldest. Have they shown any signs of aging so as to be less useful?

Dr. THOMSON. No, but we probably have not tested them in the detail that is useful. Dr. Vogelstein mentioned that as you culture things, mutations occur. Most of those mutations would be likely very subtle things. They would be very difficult to detect, but they may have an impact on clinical applications, and so the level of detail that we have studied the cells would not allow us to see those changes yet. We have not seen any changes.

Senator SPECTER. Dr. Baldwin, would you mind stepping forward again, please?

Dr. Baldwin, Dr. Thomson raises an issue about the NIH registry, which is not up and running yet, and said if the subcommittee could do something about that, it would be enormously helpful. Is that correct, Dr. Thompson?

Dr. THOMSON. Correct.

Senator SPECTER. Why isn't the NIH registry up and running?

Dr. BALDWIN. We have been spending a lot of time working on the structure of the registry, ensuring that the information that is in the registry is accurate and useful, and dealing with other policy issues. We had other guidelines in place. We have to rescind those guidelines. We have been trying to get all of those pieces in place. We are very close. I think what you have already heard today is how much work has gone on since August 9.

Some of this activity we thought was moving along very briskly at the beginning of September. Our agenda collided with the world's agenda, and I cannot tell you anything other than we are

just delayed. We are a little behind where I thought we would be. I think we are very close, and people are working very hard in putting all of the different pieces in place.

Senator SPECTER. Are you saying the other responsibility of HHS has impeded getting the national registry up and running?

Dr. BALDWIN. Everything at the NIH has been affected by changes in security efforts on bioterrorism, people being drawn off to work on other issues that we did not anticipate, none of us anticipated.

Senator SPECTER. When do you expect the national registry to be up and running?

Dr. BALDWIN. I think it will be up fairly shortly. We have solved all of the procedural and programmatic issues.

Senator SPECTER. Within a week?

Dr. BALDWIN. I think that is a reasonable expectation.

Senator SPECTER. What else would you like to see done, Dr. Thomson?

Dr. THOMSON. I think that is a big one. There is a lot of investigators that want to apply for funding, and they have to wait for that.

Senator SPECTER. That will satisfy you today?

Dr. THOMSON. I am not easily satisfied.

Senator SPECTER. Dr. Baldwin, what about the issue that Dr. Thomson raises about the overhead issue that—well, you understand it without my reformulating it. Just respond to the question which you understand.

Dr. BALDWIN. I think the question of how indirect costs——

Senator SPECTER. Just a minute. Dr. Thomson, will you state the issue again so we have it clearly identified on the record?

Dr. THOMSON. The issue is that when an institution receives NIH funding it gets overhead to pay for buildings and infrastructure, and if you have a project that the President says you cannot use Federal funding for this, the cell lines would be something you could not use that money for, there is no way to separate the lighting and the heating from indirectly supporting those cell lines.

Senator SPECTER. What is the answer to that, Dr. Baldwin?

Dr. BALDWIN. That is current policy, and we know that some entities have set up separate facilities, or spun off separate entities so they can do work that does not have any commingling with Federal funds.

Senator SPECTER. Is that not really impractical?

Dr. THOMSON. When it gets to clinical trials it is very impractical. It is impossible.

Senator SPECTER. It seems to me it is, Dr. Baldwin. If you have an institution, to require that it be totally separate, a new building, different people, different arrangements totally——

Dr. BALDWIN. Certainly, at the clinical application stage that would be a big challenge. I think what we have heard this morning is there is a great deal of basic research that needs to be done on the cells lines that will be available through the registry. We have really talked today, I think if you sketched out all the research recommendations, about a decade's worth of research. As you have heard from me, my interest right now is to get the registry up so

we can begin to fund research grants doing that basic research, primarily.

Senator SPECTER. Dr. Thomson, how soon do you think this will be a practical problem?

Dr. THOMSON. Well, I think within the next 3 years.

Senator SPECTER. The next 2 years?

Dr. THOMSON. The next 2 to 3 years, and the reason is, investigators all over the world are improving the culture conditions of these cells, and there have been improvements since I originally derived them, and they continue to improve. I would guess over the next 2 to 3 years we would have extremely well-defined conditions that do not have all these problems with protein sources.

The other thing that happens over the next 2 to 3 years there will be specific kinds of cells that will have already been derived in therapeutically useful amounts, and that does not mean they can go to clinics right away, but it means that people have to initiate the dialogue with FDA to get approval for their cell lines, and within 3 years it will be very useful to have new cell lines that do not have the current problems.

Senator SPECTER. Well, Dr. Baldwin, you are in luck. You do not have to produce an answer by the end of today, like those other questions, or in a week, like the registry. You have a period of time, but I would like you to take it back to NIH and to HHS and address the issue. We have to find a way of solving that without requiring the recipients to have totally separate facilities.

Well, I think this session has been very helpful. This is our eleventh hearing on the subject. It may be that if we have a sufficient number of hearings, that we will not have to ask you to repeat your answers several times, we will be able to start to understand them the first time around, but this is a matter of great complexity, and it is a matter of great, great importance.

We are preoccupied, beyond any question, with the terrorism threats and the anthrax, and we had to postpone the hearing before from September 12, obviously, but we wanted to move ahead today. Although this kind of a hearing is important, as important as it is, it is not going to get a whole lot of public attention because of the bioterrorism problems, but we are dealing with a great many lives that can be saved here, and I think it is important to get that registry up and running and to move ahead.

This subcommittee intends to pursue this matter with real diligence, and we will have the issue on the floor today and the information which you have given here is going to be helpful as we face up to these amendments.

I will have another private conversation with you, Dr. Thomson, on this issue, if you would stand by. That would conclude our hearing. Thank you.

CONCLUSION OF HEARINGS

Thank you all very much for being here, that concludes our hearings.

[Whereupon, at 10:30 a.m., Wednesday, October 31, the hearings were concluded and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

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