

STEM CELL RESEARCH

HEARING
OF THE
COMMITTEE ON HEALTH, EDUCATION,
LABOR, AND PENSIONS
UNITED STATES SENATE
ONE HUNDRED SEVENTH CONGRESS

FIRST SESSION

ON

EXAMINING THE SCIENTIFIC AND ETHICAL IMPLICATIONS OF STEM
CELL RESEARCH AND ITS POTENTIAL TO IMPROVE HUMAN HEALTH

SEPTEMBER 5, 2001

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STEM CELL RESEARCH

WEDNESDAY, SEPTEMBER 5, 2001

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The committee met, pursuant to notice, at 9:40 a.m., in room SD-106, Dirksen Senate Office Building, Senator Kennedy (chairman of the committee) presiding.

Present: Senators Kennedy, Dodd, Harkin, Mikulski, Jeffords, Wellstone, Murray, Reed, Edwards, Clinton, Gregg, Frist, Hutchinson, Warner, and Collins.

OPENING STATEMENT OF SENATOR KENNEDY

The CHAIRMAN. Good morning. I would ask if our guests would kindly be seated so that we can move along with the hearing. We have an enormously important hearing today and some really extraordinary witnesses, and we are here to listen and to learn, and we are grateful to all those who have come to share their experience and their knowledge with us in this hearing this morning.

It is a privilege to convene this hearing on the important issue of stem cell research. One of our greatest fears as human beings is that 1 day, we will learn that we or a loved one have cancer, Alzheimer's, diabetes, Parkinson's, heart disease, or any number of dread and deadly illnesses. But every day, thousands of Americans are stunned by such bad news. The phone rings, the doctor is on the line, and lives are changed forever by the awful news.

Stem cell research holds the greatest promise of hope for millions of Americans who face these diseases. Research on these tiny cells may mean that the next time a doctor gives the bad news of a horrible disease, the doctor can also say that these diseases are now curable.

So there is probably no more important work before this Congress than to support stem cell research, to provide life and hope to millions of Americans who would otherwise face lives of struggle, disability, and even death.

President Bush has opened the door to Government funding for this important area of health research, and we look forward to hearing from Secretary Thompson about his plans and those of the administration in moving forward on stem cell research.

The question before the Congress is whether the door is open wide enough; whether the stem cell lines identified by the administration are adequate and available for the research that is needed now to save lives.

Today our committee will hear from an outstanding group of leaders in national policy, in science and ethics, and in the law. Their testimony will be a useful guide to the committee and to Congress as we consider action in this important area.

We must make certain that stem cell research can fulfill its vast potential to improve the health and relieve the suffering of millions of Americans. President Bush has recognized the great value of this research with his recent decision allowing Federal funds for the work. But many in the scientific community are concerned that the President's decision establishes restrictive conditions on this critical research and will delay development of cures for dread diseases for many years, at the cost of countless lives and immeasurable suffering.

Failure to seize this unprecedented medical opportunity would be a tragic betrayal of the hopes and dreams of millions of patients who expect us to do all we can to develop these new cures.

The President has said that his policy, which limits federally-funded research to cell lines in existence before August 9, will make more than 60 cell lines available to researchers and that these cells will be adequate to conduct all needed research. But this conclusion is hardly clear.

Scientists question whether many of these stem cell lines will actually be usable and available. The President's limitation gives monopoly power to only 10 organizations that will now control the supply of stem cells. Most of the existing stem cell lines would not meet Federal guidelines for safety if they were to be used in actual clinical work with human patients. These lines may deteriorate and become unusable in just a few years.

New and more effective techniques for deriving stem cells may be developed but could not be used in federally-funded research under the President's guidelines.

The questions about the President's policy are serious questions, and they deserve serious answers because the lives and health of millions of patients and their families are at stake. It would be unacceptable to offer these patients and families the promise of effective stem cell research but deny them the reality of it.

Our committee today begins its oversight of stem cell research as it evaluates the need for legislation to assure vigorous, ethical stem cell research. I hope that our hearing will contribute to the understanding of these important scientific and ethical issues, and I look forward to the testimony of our witnesses and the comments of our colleagues.

Senator Gregg?

[The prepared statement of Senator Kennedy follows:]

PREPARED STATEMENT OF SENATOR KENNEDY

It's a privilege to convene this hearing on the important issue of stem cell research. Today, our committee will hear from an outstanding group of leaders in national policy, in science, ethics and the law. Their testimony will be a useful guide to the committee and to Congress as we consider action in this important area.

In recent years, remarkable progress has taken place in medical science. Advances in basic understanding of biology and the application of that knowledge to clinical practice have saved the lives

and preserved the health of countless Americans. Many conditions that once caused disability or death can now be treated and even cured. Yet despite this continuing progress, the lives of far too many Americans are darkened by illness.

Parkinson's Disease robs thousands of senior citizens of the power to control their own movements. Alzheimer's Disease impairs the mental abilities of far too many older Americans. Diabetes condemns children to a lifetime of insulin injections and the ever-present risk of coma or death. Spinal cord injuries confine thousands of our fellow citizens to wheelchairs. Cancer and heart disease exact an extraordinary toll of premature death on millions of Americans and their loved ones.

But for each of these disorders—and for many other serious illnesses—there is the promise of help and hope from a revolutionary new medical development. Stem cells may 1 day liberate children with diabetes from their dependence on insulin injections—restore the damaged brains of patients with Parkinson's Disease or Alzheimer's Disease, allow the paralyzed to leave their wheelchairs, regenerate hearts damaged by heart attack or coronary artery disease, and provide new cancer treatments.

This week, we have seen yet another example of the remarkable power of stem cells. Scientists at the University of Wisconsin announced that they have been able to turn stem cells into blood cells.

We must make certain that stem cell research can fulfill its vast potential to improve the health and relieve the suffering of millions of Americans.

President Bush has recognized the great value of this research with his recent decision allowing Federal funding for this important work. But many in the scientific community are concerned that the President's decision establishes restrictive conditions on this critical research and will delay development of cures for dread diseases for many years—at the cost of countless lives and immeasurable suffering. Failing to seize this unprecedented medical opportunity would be a tragic betrayal of the hopes and dreams of the millions of patients who expect us to do all we can to develop these new cures.

The President has said that his policy, which limits federally funded research to cell lines in existence before August 9th, will make more than 60 cell lines available to researchers and that these cells will be adequate to conduct all needed research. But this conclusion is hardly clear.

- Far fewer than 60 stem cell lines may actually be available. The National Institutes of Health combed the globe to find stem cell lines in far-flung laboratories—but it now appears that many of these cell lines are untested, unproven and may have uncertain medical value. Even many of the researchers who developed these lines have said that many of them have not been proven to actually be stem cell lines.

- Of those that are truly stem cell lines, virtually none have undergone the rigorous safety testing needed to assure that they will be safe to transplant into patients. Most of the stem cell lines appear to have been mixed with cells from laboratory mice. Yet, just 2 weeks ago, the Department of HHS issued strict new safety

guidelines for clinical use of human cells that had been mixed with animal cells. There is little evidence that existing cell stocks would meet these stringent criteria.

- Even cell lines that are safe and usable may not be available, because patent claims and legal restrictions may impede access to them. I know that Secretary Thompson has been working to resolve these difficulties, but many legal experts are skeptical that researchers will have sufficient access to viable stem cell lines.

- Researchers are also concerned that stem cell lines usable today may deteriorate and become unusable for research in a year or two. Under the President's policy, that could mean no stem cell lines at all would be available in the future for federally funded research.

Stem cell research is in its earliest stages. We cannot know what remarkable breakthroughs will be made in the years to come. In particular, new ways of establishing cell lines may be developed that can unlock the medical potential of these cells far more effectively. Yet under the President's plan, NIH-funded doctors would have no access to cells established with breakthrough techniques discovered after August 9th. Who knows what price we may pay by freezing medical progress as of this particular date? Imagine if we had imposed a similar restriction on the use of fetal tissue in 1954—a year before Jonas Salk announced that he had used fetal tissue in developing the polio vaccine that saved countless lives.

These are serious questions, and they deserve serious answers, because the life and health of millions of patients and their families are at stake. It would be unacceptable to offer these patients and families the promise of effective stem cell research, but deny them the reality of it.

Our committee today begins its oversight of stem cell research as it evaluates the need for legislation to assure vigorous, ethical stem cell research. I hope our hearing will contribute to the understanding of these important scientific and ethical issues, and I look forward to the testimony of our witnesses and the comments of our colleagues.

OPENING STATEMENT OF SENATOR GREGG

Senator GREGG. Thank you, Senator Kennedy. I thank you for holding this important hearing, which goes to a subject which has captured the Nation's attention because the potential for it is so immense. The potential is to address diseases which have plagued many citizens of our Nation and the world for years, for generations, and which now have a potential source of relief.

Clearly, stem cell research creates the opportunity to provide treatments for thousands of Americans suffering from a variety of diseases including cancer, diabetes, Alzheimer's, Parkinson's, leukemia, spinal cord injuries, and various other areas of care.

The therapeutic advances that have already been made by nearly 50 years of research on adult stem cells is very encouraging and deserves our continued and enthusiastic support, also. These therapies, unlike the unproven and untested potential application of embryonic stem cell therapies, which are at a minimum 5 and potentially 10 years away from clinical application, are actually being

used today and are being used very successfully, and we should not forget that.

We will hear today from Dr. Chute, who will talk about some of the applications of adult stem cell research and the therapies which have derived from adult stem cells. So as we embark on the road of addressing the issue of embryonic stem cell use, we certainly should not ignore the use of adult stem cells and should make that a priority of the focus of this committee also.

Clearly, embryonic stem cells and the policies which the President have outlined, however, have become the issue which we are addressing as the priority in this hearing. I certainly congratulate the President for bringing forward this issue in the manner in which he has. He has presented a thoughtful and I think comprehensive approach to how we should proceed.

The questions before this committee which we are to address are: 1) how is the President's policy going to work, and how is it going to be applied; and 2) we need to examine how we as a Federal Government should support the further research in the area of stem cells.

Senator Kennedy has noted that the President has identified 64 lines of potential stem cells which have been derived from embryonic cells. The issue, of course, is whether or not that is an adequate number and whether that number correctly addresses the issues which are involved, the questions of principles of life.

This is not an easy issue for us to address as a political body, but it is clearly one which we must address. I believe the President has made a comprehensive and aggressive attempt to try to bring this issue forward in a way which will allow science to pursue the opportunities that are there. It is my belief that we should not act precipitously to expand or to set out on another course, but rather, see and determine what the effects of the President's initial proposal are. We do not yet really know whether the 64 lines which have been identified are going to be adequate and whether the science which will be developed from those lines will effectively address the needs of people who are suffering from diseases which may be relieved as a result of the use of those stem cells. We do not even know whether those stem cells are going to be available for application to humans because of the manner in which they have been derived and been maintained.

These substantive questions have to be addressed as a threshold issue, I believe, before we start second-guessing the issue of whether the 64 lines is the appropriate number.

So there is a lot for us to talk about, a lot for us to look at. I believe this hearing is really an entry-level discussion of the topic, but hopefully, the results of the hearing will be that we will set ourselves on a path of reaching conclusions which will move forward the great opportunities that lie with this new area of stem cell therapy.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you very much.

Senator Harkin, we welcome your comments.

OPENING STATEMENT OF SENATOR HARKIN

Senator HARKIN. Thank you, Mr. Chairman, and I thank Senator Dodd for yielding his time.

I will not take long, and I will ask that my statement be made a part of the record as well.

The CHAIRMAN. It will be made apart of the record. We know that you and Senator Specter have conducted extensive hearings in your committee, so we are looking forward to your comments and to working with you.

Senator HARKIN. Thank you, Mr. Chairman.

I applaud you for having this hearing; it is very timely. It is something that, as both you and Senator Gregg have said, has captured the public's attention and imagination all over this country.

I think we have to pay very strong attention to whether we are opening the door, as you said, far enough to really be able to move aggressively in this research area. Certainly we are all concerned about the ethical implications of this new science, but we have wrestled with this over the last few years. We had an Ethics Committee at the NIH that came up with I thought very strong ethical guidelines that are now in existence at this point in time, but if there are others who have other views on this, we certainly welcome those also.

I have become more and more convinced that we have to move forward on this basic research. Every week, new findings come out. Just yesterday, we saw the potential of using stem cells to make blood cells at the University of Wisconsin, and the potential that that alone holds for our country.

So I think the concern that we have is whether or not, within the strictures of ethical guidelines, we can conduct good, sound science and use the massive resources of what my colleague and friend, Senator Specter, has often called the crown jewel of our Federal Government, that is, the NIH; can we use the power and the structure of the NIH and all the money we provide to the NIH to involve researchers all over this country to move this science forward as rapidly as possible, as I said again within ethical guidelines.

That is really what I think we are about, and those are the questions that we have to answer. I think the essential question is whether there are 64 cell lines, whether they are viable, and whether they can actually lead to therapies in the future. I think these are the essential questions that we have to wrestle with.

I thank you, Mr. Chairman, for holding this hearing, and I thank Senator Dodd for yielding me the time.

[The prepared statement of Senator Harkin follows:]

PREPARED STATEMENT OF SENATOR HARKIN

Thank you, Mr. Chairman. As you know, I've spent a great deal of time over the past two-and-a-half years thinking about stem cells. On the Labor, HHS, and Education Appropriations Subcommittee, Senator Specter and I have held nine hearings on this matter since December 1998, and we'll hold two more later this month.

We've heard from scientists like Dr. James Thomson, the first researcher to isolate stem cells from early human embryos. We've heard from ethicists and religious leaders. We've heard from several of our Senate colleagues, who have offered their thoughtful perspectives on both sides of this issue. And we've heard from victims of the many devastating diseases that could be cured as a result of stem cell research—diseases like Parkinson's, diabetes, ALS, and Alzheimer's.

After each one of those hearings, I've become more and more convinced that we need to move forward on this research. Every week, it seems, brings new findings about the potential of stem cells—just yesterday, in fact, scientists at the University of Wisconsin reported that they have figured out how to coax these cells into making blood.

We need to power that research with Federal dollars, and we need to do it quickly, ethically, and without unnecessary red tape. That's why I welcomed President Bush's announcement last month in support of Federal funding for research on existing stem cell lines as a positive first step.

Since then, scientists have raised a number of concerns about the President's plan. They question how many of the 64 stem cell lines identified by the NIH will actually prove useful for research. And there's a possibility that all of these lines have been mixed with mouse cells—a situation that could make it dangerous to test them on humans.

I share these concerns, but that's why I'm here today, and that's why my Appropriations Subcommittee will hold two more hearings later this month—to get some answers.

Mr. Chairman, you've assembled an excellent panel of witnesses for us this morning, and I look forward to the testimony.

The CHAIRMAN. Thank you very much, Senator Harkin.
Senator Frist?

OPENING STATEMENT OF SENATOR FRIST

Senator FRIST. Thank you, Mr. Chairman and Senator Gregg, thank you for jumping right in with this hearing so that we can more closely and more clearly examine the important issues of embryonic stem cell research.

On July 18, a little over a month ago, I announced my strong support for Federal funding of both embryonic and adult stem cell research. And, as we all know and have heard again and again through the press and through the various hearings that have been held, embryonic stem cell research holds great potential for advancing treatments for a broad range of diseases, illnesses, injuries, and conditions.

Yet I think we need to be very, very careful at this juncture, early in our discussions—and yes indeed, it is early in the evolution of this relatively new science—not to oversell the promise of this research to the American people. We must recognize that the field of embryonic stem cell research is young, it is early, it is pioneering; it is not yet tested. The benefits of this research, although we all attach huge hope to this particular field, have not yet been realized, and they are just possibilities.

I think we also need to recognize that there are millions of Americans, including myself, who hold very deeply-felt moral and religious concerns about research using stem cells derived from embryos.

The whole topic is important for us to address in a straightforward way. It is important because we as a Government have not yet come to grips with what is the appropriate ethical and moral construct, how much oversight, what should the guidelines be, as we enter into a field, maybe for the first time—the one exception might be genetics—but for the first time enter into a field that will so profoundly affect the course of human life and disease by manipulation by human beings and altering those basic, fundamental building blocks of life, what makes life, what is living, and indeed what makes us human. We just have not had to address that in the past in much of science or medical science. This is the first time.

We have the possibility of producing powerful treatments—we talk about cures and treatments—as we address this in a stepwise fashion. However, there is also the possibility of unintended outcomes, of outcomes that are unanticipated—and yes, you could even throw harm or potential harm into those unintended outcomes.

We are just beginning to understand the capacities of this science, the potential for this science, and therefore it is critical that we as public servants respond in a way that treats this pioneering research with awe and moral respect and great care.

The one thing we have realized over the last several weeks is how little we know about the State of the art today. Although people can be critical of the way public policy is being developed, we know a lot more today than we did 4 weeks ago and than we did 8 weeks ago. The press has participated through the hearings that have been held previously and through this hearing today.

All of this has made clear to me the lack of knowledge that we have as we address this issue of stem cells. Therefore, I think that, for the welfare of mankind, there is a moral imperative that we proceed with embryonic stem cell research but that we do so with caution and that we do so with restraint, remembering that it is untested and untried.

I have argued in the past that we need to proceed within a fully transparent, carefully regulated framework that respects the potential of this science but, at the same time, respects the moral significance of the human embryo. Earlier this year, I set out 10 principles which I felt establish this larger ethical framework of oversight and regulation.

I am very excited about the hearing today, the hearings that are planned among the various committees of the U.S. Senate and the United States Congress as we address these issues. I am 100 percent in support of what the President has put forward. For the first time—for the first time under President Bush's carefully balanced policy, NIH and NIH-funded scientists will be able to access embryonic stem cell lines that do hold the potential that we all understand is there.

These issues are difficult because they involve life, human life, the intersection of science and religion that we simply have not had

to address to this degree in the past. I believe the President of the United States has put forward a balanced approach that will allow stem cell research to begin immediately, right now, quickly, but to do so in a very careful way.

We will also talk a little bit in the hearing about the stem cell registry, which I am delighted that the President has put forward, as well as the Bioethics Advisory Commission, which I think is critical as we go forward.

Mr. Chairman and Senator Gregg, thank you for calling this hearing as we address these important issues.

The CHAIRMAN. Thank you very much.

If other members wish to include a statement in the record, they will be so included.

[The prepared statement of Senator Jeffords follows:]

PREPARED STATEMENT OF SENATOR JEFFORDS

Mr. Chairman, thank you for holding this hearing on an extremely significant issue that will have a profound impact on all of us. I want to especially applaud the effort of our colleagues, Senator Specter and Senator Harkin for their leadership on this issue. The hearings they have held in the Appropriations Committee have been instrumental in focusing attention on the promise and hope of stem cell research.

I also want to thank all of our witnesses and especially Secretary Thompson who, based on his experience as Governor in Wisconsin, has been able to provide so much guidance to the Administration.

President Bush's proposal focuses on allowing Federal funding for research on a small subset of the stem cells derived from very early stage embryos. Although it is a good first step, we need to explore other options. We need to make sure that his proposal is strong enough to propel the research and not impede it.

It is crucial that we allow our scientists to move forward with stem cell research because it holds the promise of providing answers for a host of diseases from Alzheimer's to heart disease.

Because the possibilities to eradicate so many diseases and disabilities are endless, the promise has raised hope for so many Americans.

Christopher Reeves, has encouraged all of us with his grit and determination to overcome the disability he suffers because of neurological damage. He knows all too well what stem cell research can do for him and thousands of others living with disabilities.

Another brave American, with whom we are all familiar, is Michael J. Fox. By publicly facing his Parkinson's disease and becoming a spokesperson for stem cell research, he too has pointed to the profound promise of this research. These men and many other Americans have testified in front of Senator Specter and Harkin and in numerous other venues about the potential of stem cell research.

Science has brought us to a fork in the road and I have confidence that we will take the right fork. We can approach this road morally and ethically and still continue to walk down a path that will save lives and minimize suffering.

I want to thank our other witnesses as well. These are profound issues that require the best advice available so I'm looking forward

to their statements. Thank you again for holding this hearing Mr. Chairman.

The CHAIRMAN. We will hear now from two Members of Congress, first from Senator Specter, who with Senator Harkin has been conducting very extensive hearings in the Appropriations Committee on the NIH and has taken a very serious interest in this issue. We look forward to hearing from him, and after that, a good friend from my neighboring State of Rhode Island, Congressman Langevin, someone who has thought about this over a very considerable period of time and is one of the new very bright lights in the Congress of the United States who can help us all understand this issue better as well. We look forward to hearing from him after Senator Specter.

Before we begin, I have a statement from Senator Collins.

PREPARED STATEMENT OF SENATOR COLLINS

Mr. Chairman, thank you for calling this important hearing on the President's plan for providing federal funding for embryonic stem cell research. I am a strong supporter of stem cell research and want to commend President Bush and his Administration for not only allowing this potentially life-saving research to move forward, but also for moving so quickly and aggressively to implement the plan.

Stem cell research holds tremendous potential to treat and even cure a vast array of devastating diseases and conditions, ranging from Alzheimer's disease, to Parkinson's disease, to ALS, spinal cord injury and cancer. This research has tremendous promise for millions of American families, and I applaud the President for taking such a positive step forward.

As the founder and co-Chair of the Senate Diabetes Caucus, I am particularly excited about the promise that stem cell research holds for a cure for juvenile diabetes, which has had such a devastating impact on millions of American children and their families. Early research has shown that stem cells have the potential to develop into insulin-producing cells to replace those that have been destroyed in people with Type 1 diabetes. One of the major limitations to success in this research is the limited number of insulin-producing cells for transplantation—an obstacle which could be overcome through embryonic stem cell research.

I do have some question, however, about the restrictions that the President has imposed in limiting this research to those stem cell lines that are currently in existence. As we will hear this morning, some researchers have expressed concern that there will not be enough stem cells available to support the hundreds and possibly thousands of research teams that stand ready to investigate them, which could potentially delay progress in bringing stem cell therapies into medical practice. Others have questioned whether the 64 stem cell lines that have been identified are all viable and of good quality and whether they would all be available to researchers.

Mr. Chairman, stem cell research offers tremendous hope to those suffering or dying from devastating illnesses. This morning's hearing provides us with an excellent opportunity to examine these questions and issues further, and I look forward to the upcoming testimony.

The CHAIRMAN. Senator Specter?

STATEMENTS OF HON. ARLEN SPECTER, A U.S. SENATOR FROM PENNSYLVANIA AND HON. JAMES LANGEVIN, A REPRESENTATIVE IN CONGRESS FROM RHODE ISLAND

Senator SPECTER. Thank you very much, Mr. Chairman and members of this distinguished committee, for an opportunity to present some of the findings which the Appropriations Subcommittee on Labor, Health, Human Services, and Education has noted during the course of some nine hearings which began 2 weeks after stem cells were first broached on the American scene in November of 1998.

The President made a profound statement on August 9 and has made an important opening of the door; but there is a real question as to whether the door is open sufficiently, and there is a real question about the accuracy of the facts which were presented to the President by the Department of Health and Human Services.

A key statement by the President related to 60 stem cell lines now expanded to 64, but in the intervening several weeks, it has become apparent that many of the lines cited are not really viable or robust or usable. For example, Gothenburg University in Sweden was reputed to have 19 lines, and they have at most 3. In India, the researchers were supposed to have 7 lines; none is ready for research. The San Diego Consortium was reputed to have 9 lines; again, none is ripe for utilization.

It is up to the congressional hearings to make a detailed examination as to the accuracy of the representations by HHS of robust, viable, and diverse lines.

Then, there are the intricate questions of informed consent. And then, perhaps most fundamentally is the issue of therapy. It was not addressed in the President's statement, but it has come to light in the intervening weeks that all of the stem cell lines have had nutrients from mice and have had bovine serum. Under the FDA regulations, there cannot be a mixing of the species.

Now, it is a complex matter, and there have been some exceptions, but I think it is going to be up to Congress in these hearings to make the determination as to what the facts are.

I think it is very important to focus on the need for an independent review of all of these facts. The information given to the President has not been complete. HHS has insisted, for example, that there are 19 lines from Sweden when Dr. Lars Hamburger has said that he personally advised the Secretary to the contrary. So these are facts which we must determine for ourselves.

I agree totally with what Senator Gregg has said, that we should not be precipitous. The issue as to the hope has been documented in a detailed manner by responses to letters which Senator Harkin and I sent to all the directors of the 25 institutes of the National Institutes of Health, who wrote back on the enormous potential for stem cell research in so many lines. And I regret but think it is necessary to inform this committee that when those letters were transmitted to the subcommittee, we found that they had been censored, and that many of the very, very positive statements which had been made by the directors of the institutes, illustrative of which is Dr. James Bailey, omitted from the letters we got, that

“it would be unfortunate if the ban on the NIH support for human stem cell research results in a missed opportunity to restore hope and quality.” Similar statements were made by Dr. Klausner as to cancer and many of the other institute directors.

When the issue of research was omitted, that is something which I believe has to proceed apace at the present time. There is some conversation about let us do the basic research if the lines are sufficient. The hearings in our subcommittee suggested that you need 200 lines. And bear in mind that the Congress has been enormously generous with NIH. That appropriations process started again with our subcommittee, and so far, we have added more than \$8 billion, and by the end of this year, on our anticipated doubling, we will have added \$12 billion to NIH funding. So there is ample funding to proceed.

And let there be no mistake—we believe that there should be funding on adult stem cell lines, on cords, on placenta, on every line, so that science should have the full range of opportunity.

Before the President’s announcement, there was considerable sentiment in the Congress and a considerable head of steam that the existing prohibition on use of NIH funds on stem cells had to be changed. Some 64 Senators signed a variety of letters, saying they favored stem cell research, and more than a dozen others made commitments to stem cell research but did not want to put it in writing. It is up to the Congress to take a look at these hard facts, and I suggest with a sense of urgency.

Karl Rove has been quoted as saying, “The President equates the enormity, gravity, and magnitude of this decision to an issue of war and peace and whether to commit American troops.” That is obviously a pretty strong statement.

My own statement has been that I believe that this issue of stem cell research, with its potential to touch virtually every family in America, all of whom are afflicted with either Parkinson’s or Alzheimer’s or heart disease or cancer, that there is no more important issue facing Congress except the issue of weapons of mass destruction.

I have a friend and constituent in Pittsburgh named Jim Kordi who suffers from Parkinson’s. Whenever I see Jim Kordi, he carries an hourglass, to remind me that the sands of time are passing and that the days of his life are slipping away. That is a pretty emphatic message from the hourglass.

So it seems to me that this is the kind of sense of urgency which ought to motivate this very distinguished committee and what we will be doing on two hearings later this month in our Appropriations subcommittee.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you very much, Senator Specter. Congressman Langevin?

Mr. LANGEVIN. Thank you, Mr. Chairman, members of the committee. I would like to thank you, Chairman Kennedy, and Senator Gregg, and of course, my senior Senator from Rhode Island, Senator Reed, and the entire HELP Committee for convening today’s hearing on stem cell research.

I am honored to be joining Senator Specter and Secretary Thompson, who will be testifying later, as well as several eminent

cellular biologists, shedding light on the ramifications of President Bush's August 9 decision.

Ladies and gentlemen, the issue that we face today is not whether to move forward with embryonic stem cell research but how. How do we ensure that all unnecessary barriers to the research and development of life-saving cures are removed? How do we establish parameters that provide ethical oversight of this most delicate issue? And how do we help as many people as possible as expeditiously as possible?

Unfortunately, today these questions are being answered in the context of a policy that impedes the potential of this Nation's leading scientists.

As many of you know, on November 7 last year, I became the first quadriplegic elected to the United States Congress. While my physical condition does not define me, it does affect me on a daily basis, providing me with a unique perspective on stem cell research.

At the age of 16, I spent my summer vacation participating in the Warwick Police Cadet Explorer Program. I had dreamed of becoming a police officer or an FBI agent for most of my young life. But on August 22, 1980, my dream was shattered. I stood in a locker room with a fellow cadet, watching two members of the SWAT team examining a new weapon which they thought was unloaded. That weapon accidentally discharged, launching a bullet that ricocheted off a metal locker and entered my neck, severing my spinal cord and leaving me paralyzed for life—perhaps until now.

While embryonic stem cell research could give me the chance to walk again, please understand that I am here today not just for myself or others with spinal cord injuries but also to help alleviate the pain and suffering of millions of people whose lives could be saved, lengthened and dramatically improved by this research.

Nearly half of all Americans could benefit from embryonic stem cell research, including the one million children with juvenile diabetes, the 8.2 million people with cancer, the 60 million people who are struggling with heart disease, the 4 million Alzheimer's sufferers, the 10 million people fighting osteoporosis, the 43 million arthritis sufferers, the quarter of a million people with spinal cord injuries, and the 30,000 people suffering with Lou Gehrig's disease.

Every family in America, ladies and gentlemen, has been touched by these diseases and conditions, and now we have the opportunity to offer them real hope.

That is why I support using stem cells derived from excess frozen embryos that would otherwise be discarded, which would allow us to save, extend, and improve lives. Every year, hundreds of thousands of couples experience the joy of childbirth through in vitro fertilization, a process which unfortunately creates more embryos than can be used. To relegate these potentially life-saving cells to the trash heap after the arbitrary deadline of August 9 is simply wrong.

While I applaud the door President Bush has opened with the new embryonic stem cell policy, I am frustrated with the discovery of just how little room it leaves for medical advancement. Despite NIH's recent disclosure of the 64 cell lines that existed before August 9, we are now learning that they are not all "robust" as once

claimed, and some of these cells are still in development and cannot yet be classified as lines.

Questions about the safety of using the cells in human trials are also surfacing because many researchers have mixed human cells lines with mouse cells, which poses the risk of infecting people with animal viruses.

Finally, we must recognize that irrespective of the President's guidelines for the existing embryonic stem cell lines, the private sector in the United States as well as the public and private sectors abroad will continue to conduct research on stem cells that fall outside the parameters established by the Bush Administration.

I would like to conclude with this. What will we do when an embryonic stem cell derived from the in vitro fertilization process after August 9 leads to a cure for heart disease, the number one cause of death in this country? Will we deny 60 million Americans this life-saving cure? And worse, what if such a cure is found through the morally offensive procedure of creating embryos purely for harvesting stem cells?

We must fund research on other cell lines besides the 64 cell lines identified by NIH, and we must provide strong oversight of this research to ensure that it is conducted by ethical means that do not force us to wrestle with similar moral quandaries in the future.

The administration's policy impedes unprecedented life-saving research and raises critical ethical dilemmas that we must not ignore. Because embryonic stem cell research cannot deliver on its promise of therapeutic benefit for millions of people under this policy, I am forced and compelled to oppose it.

I understand the struggle very well to balance a pro-life position with embryonic stem cell research. This is perhaps one of the most difficult decisions that I have ever had to make. Having come so close to losing my own life, I am reminded every day of how precious the gift of life truly is. That is why I am pro-life.

However, nothing is more life-affirming than using what otherwise would be disposed of to save, extend, and improve countless lives. I urge my colleagues to open the door to research on all excess embryonic stem cells derived in the in vitro fertilization process and to do so with Government oversight that ensures ethical research procedures.

Mr. Chairman, I believe that as a determined Nation, we have an obligation to get behind this research and to see it move forward and offer the hope of easing so much pain and suffering for so many million Americans.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Congressman, for a very moving presentation and statement, one that obviously includes a great deal of thought and examination on this issue from a personal perspective.

And I thank Senator Specter, who has given important leadership on this issue.

I think that unless there is a different opinion, I will excuse our two guests, thank them for their excellent statements, and ask that any questions to them be submitted in writing.

Senator REED. Mr. Chairman, can I simply say how proud we are in Rhode Island of our Congressman and how distinguished and effective he is with his principled discussion of these issues.

The CHAIRMAN. You certainly may.

Senator REED. He was an extraordinary public leader in our State in terms of his management as the secretary of State before he came here. We are all very proud of Jim and thank him for his wonderful statement.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you.

Thank you both very, very much.

It is a pleasure to welcome Secretary Tommy Thompson to speak to our committee on stem cell research. His sense of timing is impeccable.

The Secretary has a longstanding interest in this important issue since much of the groundbreaking research in this area was done at the University of Wisconsin. We look forward to hearing from him on how the Department of Health and Human Services plans to implement the President's proposal for funding stem cell research.

I can say just personally that the Secretary spent a great deal of time thinking about this issue. I know that he has spoken with most of the members of our committee, and I know as well that he spent a good deal of time during the President's consideration attending many of the briefings and expressing his views on this matter.

We know you have given a great deal of thought to this, Mr. Secretary, as you do to other issues. We welcome you to the committee and look forward to your testimony.

STATEMENT OF HON. TOMMY G. THOMPSON, SECRETARY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, WASHINGTON, DC.

Secretary THOMPSON. Good morning, Mr. Chairman, Senator Kennedy, Senator Gregg, and all the other members.

Let me start by thanking you for holding the hearing, and thank you all for being so interested in a subject that is very, very important to the American citizens and to the world. I certainly appreciate this opportunity to appear before this committee to talk about a subject that I am very personally deeply involved in and have been ever since Jamie Thomson discovered the embryonic stem cell procedure at the University of Madison 3 years ago, in 1998.

I am accompanied by Lana Skirboll, director of the Office of Science Policy at the NIH; Mark Rohrbaugh, deputy director of the Office of Technology Transfer; Maria Ferrar, director of the Office of Technology Transfer—and this happens to be her last day as a Federal employee, and she is here to support this procedure; and also, Kathy Zoon, director of the Center for Biologics Evaluation and Research at the FDA.

Let me begin by thanking all of you for your tremendous support of the Department of Health and Human Services and more specifically NIH. I want to thank you, Chairman Kennedy and Senator Gregg, for your support of research, all of you who have worked so hard to assist us in getting the dollars necessary to do the medical

research at NIH, and for your support for the great potential of stem cell research, both adult and embryonic.

I have submitted my written testimony for the record, Mr. Chairman, but there are some additional points that I would like take the opportunity to make this morning.

All of us stand today at the precipice of a new era where science holds the promise of curing the most devastating diseases. And most important, President Bush is ushering America into this new era by opening the door to Federal funding of human embryonic stem cell research in an ethical and solemn manner.

The President came to a thoughtful and deliberate decision that the administration will support policies that preserve and promote the sanctity of life while allowing important medical research to proceed.

There is nothing easy about human embryonic stem cell research. It is a complex issue with great ethical and moral implications. It is an issue that speaks not only to our greatest hopes and passions as a society but also to who we are as a society. The moral considerations cannot and must not be lost in this debate.

President Bush sent us on a wise and deliberate course with his decision to allow Federal funding of research on existing embryonic stem cell lines. His decision balanced our Nation's deepest respect for life with our highest hopes for alleviating human suffering.

These existing stem cell lines no longer hold the potential for life, but they do hold the potential to save life. It is that potential to save life that we must tap and bring to fruition, Mr. Chairman and members.

Our challenge now is to move beyond the halls of debate into the laboratories of science where we can do the basic research that will 1 day lead us to the therapies and the treatments for the most horrible maladies that plague humanity. This is an emotional debate. It is a debate that spawns a great deal of speculation and feeds many misunderstandings. My hope is that we can clear up the misunderstandings and recognize that the only way that we are going to resolve the speculation is to do the research and to find the answers.

The first thing we must all understand is the underlying need to conduct the basic research into embryonic stem cells. I cannot stress this point enough. We need to create a fundamental base of knowledge about how these cells function and how they can be manipulated, as well as get the answers to many other scientific questions.

Some people want to make the grand leap from the onset of federally-funded research to the cures for Parkinson's, Alzheimer's, and other diseases. If only it were that easy. It is easy to make such a leap in the emotion of this debate, but it is also inaccurate and unfair to do so.

The cures for these diseases are not just around the corner—I wish they were. Before we can even get to the stage of credibly talking about therapies for diseases, we must complete the basic research. This will take years, possibly 3, 5, and maybe even 8. No one knows for sure. And Senator Frist probably knows more than any of us about the time it took for transplants in heart surgery and how long it took to perfect.

But we now have the ability to do the basic research with the stimulus of Federal dollars. The role of the Federal Government should be and will be to make sure that that basic research takes place. With the support of Congress, this is where our investments will be going. And as we are investing in the basic research of embryonic stem cells, we will continue to fund research into the other types of stem cells, including adult, cord blood, and placenta. There is great value in all the research, and we have so much yet to learn about how much each can contribute to treating these diseases.

The private sector is going to continue to pursue stem cell research as well. And the logic of the American free enterprise system suggests that President Bush's decision is going to provide the incentive for the private sector to get more involved. Once the basic research is completed, the private sector will likely have great incentive to step in and transform the basic research into therapies for disease.

It is in that context of basic research that we must then address the underlying question of whether we have enough embryonic stem cell lines to meet the eligibility criteria. We believe the answer is yes. Let me explain by first addressing how we arrived at this number and then why we believe the number is sufficient.

So far, the National Institutes of Health has identified 64 stem cell derivations that meet the President's eligibility criteria. The President never spoke about or drew any limits on these lines based on where they were in their development. Furthermore, we have consistently said that these lines are at various stages of development. I have spoken to that fact; the NIH has spoken to that fact, and the NIH white paper identifying these derivations makes that fact crystal clear.

But unfortunately, and I believe unfairly, some are choosing to engage in word games or hear only parts of the story. What is most unfair is that some are trying to create conflict between myself, the NIH, and the Swedish scientists from the University of Gothenburg over the number of lines they have that qualify for Federal funding. They have 19 lines that qualify for Federal funding. That is what we said; that is what they have.

Let me be perfectly clear that there is no misunderstanding and no conflict between us. We are on the same page. In fact, I talked to Dr. Hamburger yesterday at 5 o'clock in the afternoon.

I would like to point out to the committee that this is the blastocyst, and this is at 5 to 8 days. The intercell mass takes 3 days, depending upon what procedure you use to take from the blastocyst to develop the cells. They are there in the proliferation stage in the petri dish. This is the characterization, and this is what you have to do to characterize if you are going to have a viable embryonic stem cell line.

This is the cell line established. This period takes 6 to 8 months from here, after it is removed, until it is perfected and before they start freezing the cells and are able to use them in the vials for further research.

The scientists in Sweden have three cell lines at this stage that are completed. They have four lines in the characterization process right now, and they have 12 in the proliferation stage. That is 19. All 19 of those lines qualify under the President's remarks for

funding. That means that they have been taken from the blastocyst and are able, before August 9 at 9 p.m., to qualify for Federal funding. That is the 19, and all 64 meet those criteria. All 64 are at different stages of development.

The Gothenburg scientists have 19 derivations that meet the eligibility criteria, and we have always acknowledged that most of these are in the earliest stages of development. We agree with their scientists that they only have three fully-developed lines, but they also agree with us that they have 19 in various stages that meet the eligibility criteria for funding. In fact, the scientists from Gothenburg had inquired if 50 other blastocysts that they own would qualify for Federal funding as well; they did not, because the embryo had not yet been destroyed.

I spoke yesterday with Dr. Lars Hamburger to once again make sure we have the same understanding, and there is absolutely no disagreement or misunderstanding between us.

Now let me explain why we believe that the stem cell derivations that we have identified are adequate and ample for basic research even though some are at various stages of development.

First, we will not be taking applications for funding until after October 1. To go through the procedure at NIH will probably take 8 to 9 months to get the dollars out unless there is an amendment to an existing grant, which could be sooner. During that 8 to 9 months, a lot of those 12 lines from Gothenburg will have been fully characterized and fully developed, making those available but at different stages.

I began by putting into perspective how much work can be done with the use of a small number of lines—and keep in mind that embryonic stem cells reproduce, and to the best of our knowledge right now, they do so endlessly.

For the past two decades, there has been research done on embryonic stem cells from mice. Ninety percent—20 years of research on mice—90 percent of that research has taken place with just five mice lines.

But a more impressive example is the work being done at the University of Wisconsin in Madison. UW scientist James Thomson was the first to isolate human embryonic stem cells and I believe probably has more experience and knowledge working with them than any scientist in the world. He has done nearly all of his research using just two of his five stem cell lines.

The Wisconsin Alumni Research Foundation which owns the five stem cell lines and licenses them through WiCell says it has enough to supply every researcher with a Federal grant. Those are not my words; that is WiCell, that is WARF, and that is what Jamie Thomson has indicated to them. So that is one owner with just five lines who indicates that they can feed all the scientists in the world at the present time wishing to engage in this research with Federal funds. That is a powerful statement, yet one that many are choosing to ignore.

What cannot be ignored is the remarkable amount of work already being done on these few lines. As you know, the University of Wisconsin Medical School reported Monday that its researchers under the direction of Jamie Thomson have turned human embryonic stem cells into blood cells called hematopoietic blood cells.

They did so using the WARF line. This breakthrough is a profound contribution to the research and understanding of stem cells.

I asked Jamie last night “How soon could you put that into therapy?” He said, “If everything broke, it would probably be 4 years, more likely 5 years or 6 years.”

The hematopoietic blood cells means that they have differentiated after they have been frozen the embryonic stem cells into a blood cell line, which makes it different then, after it is differentiated from an embryonic stem cell line. And even while a handful of lines can supply scores of researchers, the good news is that we have far more than just the five lines from the University of Wisconsin. We have identified dozens of already-developed lines—64 lines that meet the President’s criteria for Federal funding—but dozens of lines that have already been fully characterized and are ready to be sent out to researchers.

We have identified dozens of developed lines with the potential for many more to become fully developed and useful. As I indicated, it takes 6 to 8 months to fully perfect and develop an embryonic stem cell line from derivation. These lines come from five different countries—India, Sweden, the United States, Australia, and Singapore.

Certainly we wish each of the derivations were fully developed; but we must appreciate and we must not underestimate the basic research value of those stem cells in developing stages. We can benefit from research into their development. So the 12 stem cell lines from Gothenburg University at this stage, at the proliferation stage or even at the characterization stage, can offer tremendous research on what stage they are in and how they may be further developed. So just because they have not been fully established as a cell line does not mean the research cannot go forward on different aspects of embryonic stem cells.

Certainly we wish that each of the derivations were fully developed; but we must appreciate and we must not underestimate the basic research value of those stem cells in developing stages. But we could even benefit from research in their development.

There are some who still wish and will argue that we do not have enough. Well, we disagree for the reasons outlined. The only way that you and I will be able to fully answer that question correctly is to do the research, get the scientists in and do the research. We need to move beyond the back-and-forth over the numbers and get to actual work and doing the basic research on the science.

The President has singled out the embryonic stem cells that are most immediately available for research, and he has done so in an ethically sound manner. We must seize the moment, Senators, and take advantage of the opportunities for research that these cells present.

Before I wrap up, let me just quickly touch on a few of the other hurdles we are clearing at NIH and the Department so that this research can go forward.

First, the NIH is in the process of developing a stem cell registry and making it available so that scientists know exactly what lines are eligible and who and how they can approach those lines for access. We are working to make the registry available on NIH’s

website very soon, and I would be able to tell you today that we will have that website up sometime within the next 10 days to 2 weeks.

Second, the FDA is making it clear that the use of mouse feeder lines or layers in the development of lines is not an insurmountable impediment to research including clinical trials.

I have a letter here, Senator Kennedy, and one for you, Senator Gregg, that outlines for the committee FDA's policy on xenotransplantation. I would like to point out that the FDA has assured me that the issue is not unique to embryonic stem cells. In fact, at the present time, we have 13 INDs dealing with xenotransplantation—currently—not embryonic stem cells—13 currently under development, new drugs using xenotransplantation.

They have several investigations for new drugs beyond that for xenotransplantation, products currently in clinical trial. So scientists should not let this issue deter them from research.

I am submitting this letter from the FDA for the record that outlines their stance on this issue.

Third, we are aggressively tackling many of the proprietary issues regarding the stem cell lines and their availability. We are encouraged that the owners of the lines want to make them available for basic research and are working very closely with all of them.

I would like to point out parenthetically that every one of the entities has been in to see NIH, and I have personally talked to them, and every one of them wants to cooperate and wants to contribute and wants this basic research to get started and continue.

In fact, I am very pleased today, Senator Kennedy, to announce that we have negotiated as of yesterday afternoon a memorandum of understanding that includes an MTA, Material Transfer Agreement, that will accelerate research on stem cells within the scientific community. The National Institutes of Health and WARF, the WiCell Research Institute, signed that MOU last night which will allow for the research use of its five existing stem cell lines that meet the eligibility criteria. The NIH scientists will have these lines available to them; they will not be limited in the amount of research they do and will not be limited to the publication.

This agreement allows scientists to access these cell lines for their own research, permits scientists to freely publish the results of that research, and allows the NIH to retain its ownership—its ownership—of any intellectual property that might arise from its research using those lines. Furthermore, the MOU provides for a simple letter of agreement to govern the transfer of cell lines with minimal administrative burden.

This is a groundbreaking agreement that we are happy to be able to report to this committee this morning, that hopefully will serve as the model for making the other lines available. But it also gives an indication of how serious the owners of these lines are about making their products available for basic research. We will continue to work with all stem cell owners to address proprietary issues.

Carl Gulbrandsen, of the Wisconsin Alumni Research Foundation is here today, and I would like to take this opportunity to publicly thank him, the folks at WiCell and the dedicated team from the

NIH Office of Technology Transfer, headed up with Maria Ferrar, for the hard work they put into reaching this agreement so quickly.

This agreement gives us even more momentum and incentive to get to work.

In closing, thank you again for giving me the time and the opportunity to outline some important and fundamental issues regarding the President's decision to allow embryonic stem cell research to go forward. Yes, I am passionate about this; I am excited and enthusiastic, as you are, about the President's decision. We all should be. There is great potential for good from stem cell research. But there is also much work to be done.

So let us come together and move forward. The only place where we are truly going to find the answers to all of our questions is in the laboratories of America and the world. President Bush has opened the laboratory door. Now let us get our best and our brightest scientists into the lab so that they can do the work.

Thank you, Mr. Chairman.

[The prepared statement and attachment of Secretary Thompson follow:]

PREPARED STATEMENT OF SECRETARY THOMPSON

Mr. Chairman, Senator Gregg, and Members of the Committee, I am pleased to appear before you today to testify about the President's decision to permit Federal funding for research using human embryonic stem cell lines. I am accompanied by Lana Skirboll, Director of the Office of Science Policy at the NIH, Mark Rohrbaugh, Deputy Director of the Office of Technology Transfer at the NIH, and Kathy Zoon, Director of the Center for Biologics Evaluation and Research at the FDA.

I am pleased to be here today because I believe that President Bush has made a wise decision, one that we can only guess at the import right now. This was not an easy decision, and as his words to the Nation made crystal clear, it was not a decision that was made lightly. President Bush is guided by a strong set of principles, and he, like all of us, strongly values human life. Importantly, no Federal funds will be used to support the destruction or creation of new embryos, and Federal funds will not be used to support research on stem cell lines that are derived from newly destroyed embryos. The principle that the Federal government should not encourage or sanction the destruction of embryos was a cornerstone of the President's decision.

This President, by exhibiting such strong leadership, has helped to create a research environment that we all hope will lead to cures for such diseases as diabetes, Parkinson's disease, spinal cord injury, stroke, Lou Gehrig's disease, and Alzheimer's disease—just to name a few. President Bush has given hope to us all; the scientific community, those suffering from these devastating illnesses, and anyone who has ever seen a loved one suffer from a debilitating disease.

Very early on in my tenure at the Department, I asked NIH to prepare a report on what was known about human embryonic stem cells: in short, to do a review of the science. What investigators found, and what the scientific community has been saying, is that today very little is known. The first human embryonic stem cell was isolated only a little over 3 years ago. Very few people in the world are working with this type of cell. Yet, in that short time, and combined with research that has been done on animal embryonic stem cells, we all have every right to feel hopeful about what scientists may be able to accomplish.

Human embryonic stem cells are unique. They are capable of continuous self-renewal and of the ability to give rise to all cell types that comprise the human body. But at this point, we know almost nothing about their potential to treat disease. And we don't know how they compare to adult stem cells.

On August 9, 2001, the President announced that Federal funds may be awarded for research involving the use of human embryonic stem cell lines that meet the following criteria:

- The derivation process was initiated prior to 9:00 p.m. EDT on August 9, 2001;
- The stem cells were derived from an embryo that was created for reproductive purposes and was no longer needed for such purposes; and

- An informed consent was obtained for the donation of the embryo, and that donation did not involve financial inducements.

When NIH first presented its report on the State of the science to me in June, it had documented at least 30 lines. In follow-up discussions, it was clear that NIH had heard about the possibility of others, even though scientists had not yet published their findings regarding some of these other lines, and many were in the early stages of development. So I asked NIH to go back, talk to these scientists and companies, and find out everything it could about the stem cell lines that currently exist. What investigators at NIH found was that more stem cell lines existed, in various stages of development, than anybody had realized.

Some were identified from publications and presentations at scientific meetings. Others were identified in the course of preparing the NIH report on stem cells through general discussions with the scientists who had worked in the field. In some cases, the organizations called NIH, and in others, information was provided to NIH during inquiries regarding compliance with the former NIH Guidelines.

To date, investigators from ten laboratories in the United States, Australia, India, Israel, and Sweden have reported to the NIH that they have derived stem cells from 64 individual, genetically diverse early embryos. These human embryonic stem cell lines are currently viable, exhibit characteristic stem cell morphology, and have undergone at least several population doublings. The majority of these cell lines are reported to express all of the markers known to be associated with human embryonic stem cells.

All 64 of these human embryonic stem cell lines, which are in various stages of development, meet the President's criteria and are therefore qualified for use in federally funded human embryonic stem cell research. The NIH has met or spoken extensively with each of the investigators responsible for the derivation of these cells. These scientists have expressed interest in working with the NIH and the research community to establish a research infrastructure that ensures the successful handling and use of these embryonic stem cells in the laboratory. How researchers will be able to use these stem cell lines, some of which are in the earliest stages of development, for laboratory research is a valid and important research question, and I encourage scientists to begin looking for an answer as soon as possible. Likewise, the question of how to determine the quality or usefulness of any cell line is an open question that also requires research, and we encourage investigators to apply for NIH grants to answer it.

By allowing, for the first time, the use of Federal funds for research on human embryonic stem cells, the President has opened the door to a promising field of scientific opportunity for some of the best and the brightest investigators who conduct their work with the financial support of the Federal government.

I am working with NIH to ensure that the scientific community will be able to use Federal funds to tap the extraordinary research potential of human embryonic stem cells. We are hoping to begin funding this research using a variety of mechanisms: grants, contracts, cooperative agreements, and supplements to existing grants. Today, our goal is to ensure that cells are available and ready for distribution and to help and encourage researchers who are working with these human embryonic stem lines, which are in various stages of development, to conduct the additional research that will make these lines available for research use. There are challenges ahead.

First, in order to facilitate the much-needed basic research using human embryonic stem cells, the NIH is creating a Human Embryonic Stem Cell Registry that will list the human embryonic stem cells that meet the eligibility criteria and provide basic information about the cells.

And there is more to do. We need to encourage the further characterization of those lines that are in the earliest stages of development. We need to provide technical assistance and funds for the large-scale expansion of stem cell lines so that they are available to as many researchers as wish to use them. We need to minimize the administrative burden, with regard to requests for the distribution of cells, both for scientists who have derived these cells and researchers who wish to use them. And because these cells are challenging to work with, we need to determine in what manner we will provide training to researchers on how to maintain, grow and handle 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. Finally, and most importantly, NIH needs to do what it does best: fund the most promising ideas, gain new knowledge from research, and use that knowledge to improve human health.

As with other types of research, recipients of NIH funding will be responsible for arranging access to particular cells that they determine are necessary for their re-

search. The NIH is interested both in accessing cells for use in its intramural research program, as well as in facilitating access for the broader research community. The goal is to encourage the transfer of cells from qualified providers under acceptable conditions and with as minimal an administrative burden as possible.

Recently, the NIH has met with investigators who have derived these cells to discuss these topics. At these meetings, the NIH has, on behalf of its intramural investigators, initiated negotiations with organizations that have derived human embryonic stem cells. Although the NIH does not have the authority to negotiate agreements on behalf of grantee institutions or third parties, it has been the NIH's experience in other cases that the agreement into which it enters may serve as a model for subsequent agreements negotiated by NIH-funded investigators, should their institutions choose to adopt it.

Some scientists have asked about the effect that patents filed or issued over the past few years will have on human embryonic stem cell research. The issuance of patents on new discoveries need not adversely affect continuing research, provided that the patent owners devise a licensing and sharing strategy to allow basic research to proceed. Experience has shown that conditions imposed by patent owners can be crafted both to ensure research uses and to provide appropriate incentives for commercial development. Although the specific terms and conditions of availability must be determined between providers of the cells and the recipients, we are pleased by the willingness of the researchers who have derived cells to make them available for use by federally funded researchers.

Although scientists will soon have the opportunity to explore the promise of human embryonic stem cells, I wish to make it very clear that this research must proceed responsibly and ethically. We have much to learn about these cells—much basic research that needs to be conducted. Clinical applications, which could possibly emerge only after considerable basic research, are years away. What is important now is that we begin the process of gaining a thorough and scientifically based understanding of the promise and potential of embryonic stem cell research.

The NIH is now implementing the President's policy. It is our hope that federally funded investigators will take full advantage of this new opportunity to conduct research on existing human embryonic stem cells and explore the enormous promise of these unique cells, including their potential to produce breakthrough therapies and cures. At the same time, NIH will continue vigorously to support research on animal stem cells and human adult stem cells, including those found in umbilical cord blood, so that in the not too distant future we will be in position to understand the relative benefits and limitations of all types of stem cells. With the help of the scientific community, this research will mark the beginning of a new era in modern medicine.

Mr. Chairman, it is time for federally funded scientists to begin the fundamental research that is needed to determine the true potential of stem cells. We will provide scientists with ample opportunities to fully investigate this potential. We urge the research community to begin these explorations with the profound hope that we stand at the threshold of a true breakthrough in our ability to treat disease and disability.

ATTACHMENT

DEPARTMENT OF HEALTH & HUMAN SERVICES,
ROCKVILLE, MD 20857,
September 5, 2001.

Hon. JUDD A. GREGG,
U.S. Senate,
Washington, DC. 20515-2101.

DEAR SENATOR GREGG: During the past few weeks, concerns have been raised about human embryonic pluripotent stem cells (HEPSC) and their eventual use in human clinical trials for a variety of therapies. The Food and Drug Administration would like to take this opportunity to clarify these issues. A similar letter is being sent to Senator Edward M. Kennedy.

While many questions are being raised, the science has not advanced far enough to answer them yet. HEPSCs were first isolated in 1998, and the scientific research about them is in its infancy. The FDA stands ready to work with the scientific community as they near the stage of human clinical trials. We encourage investigators to work closely with us to ensure that testing occurs in the most expedient and safest manner.

Most of the concerns raised to date are not unique to human embryonic stem cells. The use of irradiated mouse feeder layers in deriving HEPSC raises concerns that

also occur for other xenotransplantation products. FDA regulations do not prohibit using mouse feeder layers to make HEPSC products for human clinical trials. Of course, appropriate testing and precautions are necessary. FDA has a number of active Investigations for New Drugs (INDs) for xenotransplantation products currently in clinical trials.

Xenotransplantation products raise issues that several Public Health Service agencies address, including the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH) and Health Resource Services Administration (HRSA). In order to provide guidance to maximize the safe conduct of xenotransplantation trials, these agencies together with staff from the Office of the Assistant Secretary for Planning and Evaluation (OASPE) developed the PHS Guideline on Infectious Disease Issues in Xenotransplantation (1/18/01). The PHS Guideline on Infectious Disease Issues in Xenotransplantation and several FDA Guidance Documents (see below)¹ have defined xenotransplantation as “any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues or organs that have had ex vivo contact with nonhuman animal cells, tissues or organs.”

FDA regulates xenotransplantation products using the regulatory framework established for other biologics. Xenotransplantation products are, by their nature, also cellular therapies, and some are also gene therapies, and as biologics are subject to the provisions of the Food, Drug and Cosmetics Act and the Public Health Service Act and the appropriate regulations in 21 CFR. A number of clinical trials of FDA-regulated xenotransplantation protocols, including several in which the contact with the animal cells is ex vivo, are currently enrolling patients, after adequately addressing FDA’s concerns. Addressing FDA’s concerns have included use of precautions such as: (1) testing the xenotransplantation product for infectious agents by appropriate methods including co-culture assays to detect potentially unknown viruses, (2) educating patients regarding the potential infectious disease risks and monitoring and testing them for xenogeneic infections following treatment, (3) educating xenotransplantation product recipients to not donate blood or tissues for use in humans, (4) educating patient contacts, and in some cases monitoring them, (5) maintaining appropriate records of treatment with xenotransplantation products, (6) maintaining archived biologic samples from the patient, animal source, and product in the event that a public health investigation is needed, and (7) maintaining animal sources of xenotransplantation products in a manner appropriate to reducing the infectious disease risks of the product when used in humans. This latter precaution might not be necessary if a long-term established, well-characterized cell line with adequate documentation is used in xenotransplantation.

Thus, as intended and practiced, the FDA regulation of xenotransplantation products, while aimed first and foremost at safeguarding the public health, should not impose a substantial impediment to xenotransplantation product development, including HEPSC that are produced by culture in vitro with mouse cells. HEPSC, as with any other product, will be reviewed on a case-by-case basis to evaluate safety when an application for investigational use is submitted to FDA. In the meantime, sponsors planning the clinical use of HEPSC that have been developed by exposure to animal cells should visit the FDA Xenotransplantation Action Plan website (<<http://www.fda.gov/cber/xap/xap.htm>>) where links to all the published material and transcripts can be found. They are also encouraged to phone the agency (301 827–2000) with questions and concerns. Potential sponsors of any

¹ Guidance documents defining xenotransplantation:

- PHS Guideline on Infectious Disease Issues in Xenotransplantation, January 2001
- Draft Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning Use of Xenotransplantation Products in Humans, February 2001
- Draft Guidance for Industry: Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Xenotransplantation Product Recipients and Their Close Contacts, Through Whole Blood, Blood Components, Source Plasma, and Source Leukocytes, December 1999
- Guidance for Industry: Public Health Issues Posed by the Use of Nonhuman Primate Xenografts in Humans, April 6, 1999 (The actual wording of the definition of xenotransplantation in this document “the use of live cells, tissues, or organs from a nonhuman animal source transplanted or implanted into a human, or used for ex vivo contact with human body fluids, cells, tissues or organs that are subsequently given to a human recipient.”)

xenotransplantation products are often counseled directly by FDA personnel on how best to comply with FDA requirements on xenotransplantation.

Sincerely yours,

BERNARD A. SCHWETZ, D.V.M., PH.D.,
Acting Principal Deputy Commissioner.

The CHAIRMAN. Thank you very much, Mr. Secretary, for your presentation and for the obvious thought and commitment that you have reflected in the presentation and your knowledge about this issue. That will be of great help to all of us and to the country in terms of developing policy.

We will try to have 7-minute rounds; I think it will take at least that amount of time to ask a few questions.

First—and I want go through very quickly—you talked in the presentation this morning about 64 derivations on the stem cells. The President talks about as a result of the private research, more than 60 genetically diverse stem cells already in existence. Maybe it is semantics—I do not think it is—but there was a difference in terms of those two concepts.

Let me get to my first question. If the current stock of stem cells proves inadequate for effective research, or if there are no new breakthroughs in ways to extract stem cells, or if the existing cell colonies are unavailable due to patent restrictions, would you then consider revising the administration's policy to ensure that doctors will have access to the stem cells they need to develop the cures of the future?

Secretary THOMPSON. Senator, we feel very strongly that the cells are available. We feel that we have already knocked down the proprietary concerns with the first MOU, and we think there are many available.

There is also another procedure called "subclonal" that allows for the subcloning of these existing stem cell lines for further research being done. So we think it is adequate, and we do not believe that we would advise the President to change his policy.

The CHAIRMAN. Well, as you know, there are many scientists who disagree with you about the adequacy and the availability of the current stem cell lines, including some of the scientists who developed the lines in the first place.

As you pointed out, we only discovered human stem cells approximately 2½ to 3 years ago, and no one can know what new advances are just around the corner. We have seen repeated examples of the progress that scientists can make in a few short years—for example, it took 5 years after the start of the Human Genome Project just to determine the DNA sequence. Only 5 years after that, they sequenced the entire genetic code. Wouldn't it be a tragic mistake to freeze this field and its progress to August 9, when we do not know what improvements are going to come down the pike?

Secretary THOMPSON. Senator, the only real answer to that is that we have to do the research; we have to do the basic research. There has not even been the comparative research done between embryonic, adult, placenta, and cord blood stem cell lines. This research has got to be done.

I do not know if you or I or any scientist will be able to say at this point in time that the breakthroughs are going to be that

quick or whether these stem cell lines are going to be enough. I think that they are. I really believe that. And I think there is adequacy to do it. But the only way that we can get these answers is to get our researchers and our scientists into the laboratory to start doing that basic research.

The CHAIRMAN. I agree with you, and I think we all want them in the laboratory doing as well as they can, but as you well know, the stem cells receive their nutrients from mice tissue at the present time.

Secretary THOMPSON. Mice layers; right.

The CHAIRMAN. Yes. I will come back to this. There may be the development of a technology that could remove those once the determination is made about what those nutrients are. We would be denied under the August 9 restrictions, or the researchers would be, from taking advantage of breakthroughs in terms of new technologies in terms of the derivation of the stem cells, would we not?

Secretary THOMPSON. Some scientists are working on that particular question as we speak, Senator.

The CHAIRMAN. But they would be precluded from taking advantage of that new technology under the August 9 restriction, would they not?

Secretary THOMPSON. We do not believe so. We think that the——

The CHAIRMAN. Since all the current cells now derive their nutrition from mice cells—all of them now——

Secretary THOMPSON. That is correct.

The CHAIRMAN [continuing]. And I will get to the question about that issue.

Secretary THOMPSON. I am not sure——

The CHAIRMAN. Just let me finish.

Secretary THOMPSON. OK.

The CHAIRMAN. There may very well be the ability to derive those products as stem cells without using the mice; under the August 9th restriction, that would not be possible as I understand it.

Secretary THOMPSON. All I can say in answer to that is that one of the scientists did tell us that they think they have developed a system using pre-August 9 embryo derivations without mouse line. I am not at liberty and I do not know for sure. That was something that was said in passing in one of the discussions.

The CHAIRMAN. Well, it was an example of what might happen.

Now, here in this book are the CDC guidelines for transplanting animal tissues into human beings. “All cells,” it says in these guidelines—and this was published August 24—“All cells that come in contact with human cells designed to be transplanted should come from animals that are from a colony that is continually monitored for infectious diseases or from a colony that was not allowed to interbreed with animals outside the colony or routinely tested for infectious diseases or quarantined for 3 weeks prior to procurement of the cells.”

Now, virtually all of the stem cells approved under the President’s plan were grown in the presence of mouse cells. these mouse cells were almost certainly not procured from animals treated consistent with the guidelines described above.

Secretary THOMPSON. All I can tell you, Senator, is that these are questions that I raised with FDA, and they have indicated to me that they have many current clinical trials and INDs going on using xenotransplantation, and they have indicated to me—they are the experts—that they do not see this as really an impediment. They will be questioning it, they will be supervising it and doing the investigation, but as this letter points out that I am submitting for the record, Senator, it indicates that they do not believe this is a real impediment.

The CHAIRMAN. This is again an area where research takes strong exception with the nature of the research that is being done.

Let me come to another area, and this is the final area that I will have a chance to mention given the time. Under your policy, there are 10 organizations that are allowed to provide the stem cells to federally-funded researchers. People complain about OPEC being a monopoly, but even they have 11 members. I know that you are working hard to get adequate agreements, and I commend you for the agreements that you have announced here. You ought to be commented on that. The concern will be how many other agreements will be able to be signed, and that is basically what we want to do, because without signed agreements from the suppliers, it is hard for me to share the confidence that the problems will be satisfactorily resolved.

You have 10 organizations; you have been able to sign up one or two—one—whatever it is. You have these organizations that basically have control on these items. How can you give us the assurance given that kind of restriction that there will be availability and accessibility for researchers to do the job that is out there to be done?

Secretary THOMPSON. We have talked to all the entities, all 10 of them, and all have indicated that they would like to see the basic research go on. All of them have cooperated. WiCell is the one that has the patent in the United States at the present time. They are the one that has signed the MOU plus the Material Transfer Agreement letter as of yesterday, and they have also indicated, Senator, that they have five cell lines available right now, and they have also indicated that there will be no limitation on the scientists who want to apply to use those lines and that those liens will then be able to be used in research, and it will not be limited to the 10 entities. Any scientist—and they have already reached an agreement with the scientists at NIH to make them available for the NIH scientists as of today.

The CHAIRMAN. Senator Gregg?

Senator GREGG. Mr. Secretary, just as a threshold issue here, I want to clarify the situation of adult stem cell funding. Is it your intention and can you assure us that funds will not be diverted from adult stem cell funding research into fetal activity, fetal and embryo stem cell?

Secretary THOMPSON. Absolutely not. That is the beauty of the President's policy, Senator Gregg, that the basic research on the comparison of adult stem cells, embryonic stem cells, placenta flat and cord blood has never been done. The best thing we can do is to do that basic research and get it started in the laboratories. And no, there will be no reduction on adult stem cells. We used \$250

million last year on stem cell research, and I can assure you there is going to be more available for all forms of stem cells including and most important, adult stem cells and embryonic stem cells.

Senator GREGG. I think that that is very important. We have doubled, as was mentioned, the funding for NIH as a result of the efforts of Senator Harkin, Senator Specter, and a lot of it was really started by Senator Mack when he was serving in the Senate. There is certainly a lot of money at NIH these days, and it seems to me that with this exciting new area of therapy, we should be able to fully fund especially the adult area which is already producing results. We actually have physical therapies that benefit from adult stem cells right now today.

Secretary THOMPSON. We will not limit that at all. In fact, I talked with the NIH scientists as of last night and yesterday, and they have indicated they have enough money available for all good research projects. Also, because of this hearing and because of the President's decision and all of the publicity around embryonic stem cells, there is a tremendous amount of interest from scientists, researchers, and investigators around the country and the world who want to apply.

Senator GREGG. Let me go through a couple of elementary questions, because I think there are some initial policy issues that we have to get clear before we go into the substance of some of the issues that Senator Kennedy was talking about.

As I understand it, without Federal dollars, research on stem cells can proceed *carte blanche*; correct?

Secretary THOMPSON. That is correct.

Senator GREGG. So explain to us if you would why it is important to have Federal funds involved in this research.

Secretary THOMPSON. Because the private dollars will want to go as quickly as possible to a therapy. It is more important to do the basic research at the beginning, the kind of research that Jamie Thomson and other scientists who are the forerunners in this research field are doing. That comparison that I talked about in response to a previous question that you asked, Senator, needs to be done, and that kind of basic research comparison adult, embryonic and all the other stem cell lines will not be done just by the private sector. The Federal dollars allow that. That is point number one.

The second point is that Federal research dollars when they do this research encourages other scientists to get involved. And once the basic research is done, the privates come in and do more of the therapy research. So it is sort of a building block. That is why it is so important to get those Federal research dollars out quickly and into the laboratories as soon as possible.

Senator GREGG. That is an important point to make.

Second, what is the role of patents in this exercise? This company, Geron, which I am not familiar with, has the patents from the Wisconsin projects to the extent there is commercialization. What do you see as the role of patents in this exercise?

Secretary THOMPSON. First of all, Geron does not have a patent, Senator Gregg. WiCell is a subsidiary—

Senator GREGG. Or a license.

Secretary THOMPSON. They have the license. Geron has the license of three of the five lines, and they have already reached an

agreement with WiCell to make those lines available. That is part of the agreement, part of the MOU. Really, WARF and WiCell are directing this. They made the arrangements with NIH yesterday by signing the MOU and the Material Transfer Agreement letter to make these available to any scientist in the world who wants to apply through NIH.

Senator GREGG. I am talking more philosophically. What is the role of patents in this?

Secretary THOMPSON. Patents will come into play much more importantly when the therapies are developed and they go into commercial products; hopefully, as soon as possible.

Senator GREGG. So in the basic research area, you do not see that as being an issue.

Secretary THOMPSON. I do not see that as much of a restriction, no—based upon the agreement signed yesterday.

Senator GREGG. Can you explain why you picked the date August 9 at 9 p.m.?

Secretary THOMPSON. Because that is the time the President made his speech. And it was not my decision; it was the President's decision.

Senator GREGG. And what is the implication of that date, in your opinion?

Secretary THOMPSON. The implication is that there are embryonic stem cell lines available for basic research, there is money available for that basic research, and it allows us now to open the door to the laboratories, to get the money out, and to get the comparative and basic research done which is so important in this whole embryonic field of stem cells.

Senator GREGG. I believe the key to that decision was that you believe the embryonic stem cell lines that are out there can be used in a manner which, because they replicate themselves limitlessly, I think was the term you used—

Secretary THOMPSON. Endlessly.

Senator GREGG [continuing]. Endlessly—that because of that, there is no need to go past that date in order to find at this time adequate stem cells for the research that is going on. Is that correct?

Secretary THOMPSON. That is correct. They are pluripotent, which means they replicate, and as long as they do not differentiate, those cell lines are able to be used for basic research. And Jamie Thompson—we have five cell lines, and he is sort of the creator, the father, of the embryonic stem cell lines, and he personally uses about two of his stem cell lines for his research. As far as embryonic stem cell research, it has been done for 20 years on mice, and 90 percent of that research has been done on five cell lines.

Senator GREGG. And it is also, as I understand, the position of FDA as presented to us in this letter—and I have not read it yet, but you are characterizing it—that the xenotransplantation issues are not a problem when you move from basic research to therapy, and they are not going to be a problem for the FDA as to—

Secretary THOMPSON. FDA will certainly be looking at every facet of the procedures as we go along, but they also have currently 13 INDs going on with different aspects of xenotransplantation, and they have said that that should not act as the impediment or

reluctance to proceed on the research. But they will continue to supervise, they will continue to make sure that it meets all of the safety rules and regulations that CDC and FDA have put out.

Senator GREGG. Let me ask you another question which I think raises the issues that get to the issue of when—well, my time is up, so I am not going to get into that.

The CHAIRMAN. Senator Dodd?

Senator DODD. Thank you very much, Mr. Chairman.

Mr. Secretary, welcome.

Secretary THOMPSON. Thank you, Senator Dodd.

Senator DODD. It is good to have you with us today, and I appreciate your deep interest in this and your obvious knowledge of it. That is obviously helpful, and I am pleased as well that you have some wonderful folks from NIH with you here.

This is a tremendously important issue as you and others have pointed out. I have just a couple observations. I have asked unanimous consent that my opening statement be included in the record. Obviously, we are not going to resolve this issue specifically with a piece of legislation or even a speech on August 9. This is going to be an ongoing effort, and my hope would be that whatever policies are developed, and whatever finally comes out of this debate in the short term, that a decision will be made to revisit this issue periodically, almost sunset decisions, so that we will have the ability to come back and review decisions that have been made to determine whether in fact, since we are wandering or heading into uncharted areas, to put it mildly; I would hope that would be part of the consideration.

It causes me to comment and ask you to further comment yourself on Senator Kennedy's questions regarding these mouse feeder cells—and I hear you, and I know you are confident and hopeful that the research will be there to be able to extract these mouse feeder cells so as not to contaminate these stem cells in any way that would jeopardize human life.

Secretary THOMPSON. That is correct.

Senator DODD. But there is the possibility that that will not happen. Just as you hope that it will, we all understand that it may not work. So my question to you to conclude this line of questioning would be if in fact that is not the case, will the administration go back and revisit the August 9 deadline to determine whether we can develop some new lines.

Secretary THOMPSON. It is going to take such a long period of time to go from the laboratory to therapy to human clinical trials, Senator Dodd, that—everybody, including myself, has great anticipation and hope that we are going to be able to move directly to a cure for Parkinson's and so on and so forth, but it is going to take 5 to 8 years.

Yesterday, the hematopoietic blood cells were developed, and it is probably going to take 5 years—

Senator DODD. I understand that.

Secretary THOMPSON [continuing]. And during that period of time, I am sure that what I say today and the questions that you ask will be sort of arcane and will probably be ludicrous by the time we look at it 5 years from now, Senator.

Senator DODD. It is always dangerous when Congress—we all get worried about mad scientists—nothing is more frightening to me than Congress trying to be a scientist. So I appreciate what you are saying. The point I am trying to get at is sort of a mindset from the administration standpoint as to whether or not there is the flexibility to come back and revisit issues. I realize we cannot answer these questions, and it will take time, but I am trying to elicit from you as the spokesman for the administration your policy questions so that if in fact we are unable to extract the mouse feeder cells, thereby making these lines precarious at best, will the administration reconsider its August 9 deadline?

That is really my question. I understand all the scientific issues that we cannot answer today.

Secretary THOMPSON. The administration will not reconsider its deadline as far as the destruction of embryos.

Senator DODD. OK.

Secretary THOMPSON. It will reconsider all the policies and all the procedures and research going into embryonic stem cells on an ongoing basis as we find new things—

Senator DODD. I understand.

Secretary THOMPSON [continuing]. But the destruction of embryos for new embryos—no, it will not.

Senator DODD. OK. Let me if I can—I do not know if you heard Senator Specter or had a chance to read his statement, but he made some comments in there regarding the viability of the various lines that exist and raised questions about the Gothenburg University 19 lines, which you have addressed to some degree in your conversations apparently as late as yesterday with one of the scientists there. But I read a statement today that says that out of those 19—and I am quoting here from Hamburger, who I guess is the same fellow you talked to—

Secretary THOMPSON. Dr. Hamburger, right.

Senator DODD [continuing]. He says—and I am quoting him—“If we get three good lines out of them, we will be satisfied”—out of the 19.

How many lines do we need in order to—what is the minimum viable lines at the end of this process that we would need in order for there to be a viable level of research to be conducted?

Secretary THOMPSON. We believe that the five lines that currently exist will be able to get us a long way down the road doing the basic research, but there are many more. We feel right now that roughly, there are 25, 24 or 25, full cell lines established, and there are 64 in the various phases from the proliferation to the characterization to the cell line established, and out of those remaining ones, we think there will be a lot more that will be established that will be able to use the vials at the end where the cells are frozen and be able to send out to researchers around the world.

Senator DODD. In fact, you may want to—and I am just trying to understand what minimums are, and I agree with you, I am hopeful that is the case as well—but I want to get some sense of what is the bottom line that we are looking at here. If in fact we are only getting three, four, or five, would that be adequate, and your statement is that you believe it is. AT the end of all of this, at the end of all the 64 that are out there, the potential that are

out there, and you go through the steps which you have very clearly outlined here, if at the end, in that last step, there are five viable lines, your answer to my question is that that is more than adequate?

Secretary THOMPSON. We have 25, 24 or 25, adequate right now, so I am confident that that is enough, but I am also confident that there are going to be many more of the 64 that will be available.

Senator DODD. In the minute remaining, if I can—and again, for those of us up here who are trying to learn, this is pretty complicated stuff, and Bill Frist and others whom many of us listen to very carefully when they speak on these issues—and I have been fascinated from a personal standpoint with cord blood research and have been doing a lot of work in the last few days, and NIH has been very, very, helpful, and I have talked with them at length about the subject matter, and there is some great potential in cord blood research—maybe that is a subject for another discussion later on—but the position the administration has taken, that as of August 9, only those embryos that have already been moved in this process are the ones to be considered—I think all of us here would tell you that if there were any issue raised about whether somehow we were going to create a “hatchery,” producing embryos specifically for developing stem cells, I think we would vehemently oppose it, every one of us. I do not know of anyone who would take a different point of view. On the issue, however, of embryos being developed as a result of the wonderful advances in the science of in vitro fertilization, there are existing embryos out there, many of which will be destroyed. Does the administration take the position that we ought to pass legislation or that they are going to offer legislation that would ban the destruction of these embryos that are sitting there today that will be discarded?

Secretary THOMPSON. I do not think the administration has taken a position on that, Senator Dodd, but I would like to point out that those embryos right now—in order to establish a good line, it takes a lot of scientific ability to do that.

Senator DODD. I understand.

Secretary THOMPSON. And I have discussed that with Jamie Thomson, and he says a good line takes, with optimum conditions, 6 months, but it is usually closer to 8 months.

So that right now, we have these 64 in different stages, 24 that are almost fully developed. It would take another 8 months to be able under the best of circumstances to establish a brand, new line.

All I am saying is that we should get the research dollars out there for these basic lines. And it is going to take us some time, because the procedure at NIH to put out grant dollars as they tell me will be 8 to 9 months from now. So during this 8 to 9 months, several of those remaining from 24 to 64 are going to be fully developed, so there will be many more lines available for research and for development.

Senator DODD. I thank you, Mr. Secretary. My time is up, but just a brief, quick comment. My concern—and others will express their views—is with your answer to the question of whether you would revisit at all the August 9 deadline if in fact it turns out that we are not able to remove the mouse feeder cells. The rigidity of that concerns me, and also the decision—if we are going to draw

ethical lines here, if we are going to discard cells, there will be no effort to bad the discarding of those unused embryos, then we are blurring the lines further, it seems to me, and creating some great potential conflict here. So again, I appreciate your involvement, your determination, and your passion about the issue and look forward to an ongoing dialogue.

Secretary THOMPSON. Thank you, Senator Dodd.

The CHAIRMAN. Senator Frist?

Senator FRIST. Thank you, Mr. Chairman.

I briefly want to explore, since you have had so many conversations, the relationship between public and private funding. Right now, of the 64 cell lines, or the cell lines that are out there, all been developed with private funding, as of today—the research.

Secretary THOMPSON. No, I cannot answer that in the affirmative, because some of the universities in Sweden and some of the lines in India and Australia I am sure could have had public funding.

Senator FRIST. But in the United States, we have not been funding—

Secretary THOMPSON. In the United States, yes, that is correct.

Senator FRIST [continuing]. The creation of these cell lines.

Secretary THOMPSON. I do not know if they have or they have not internationally, Senator Frist. I cannot answer that.

Senator FRIST. As we look ahead, we know that this science is moving fast.

Secretary THOMPSON. Yes, it is.

Senator FRIST. It is hard even to project how long all these lines are going to be available, what the research is going to be like, what the breakthroughs are going to be, what the roadblocks are going to be. There is just no way to know, and we can debate it.

We are going to hear the argument again and again that we ought to have sort of a freestanding, let us use all the cells, and we need unlimited cell lines.

I think that what we have learned a lot recently is that you do not need unlimited cell lines, that there is a limited number, and now, unlike 4 weeks ago, we are saying is it 64 or 20. At Senator Specter and Senator Harkin's hearing about a month and a half ago, we initiated a lot of this discussion about how many cell lines do you need. It is different than transplantation, where you take the heart out of one person, you transplant it into another, and it helps them. These cells are self-perpetuating. So we have come a long way in the debate.

What is interesting as I listened broadly is that we have Federal funding, which is important; it legitimizes the field and gives you some control in terms of ethical oversight and prioritization. But at the same time, we have the private sector which, if this promise is real, is going to be heading off full-steam.

Secretary THOMPSON. Absolutely.

Senator FRIST. And by having some public funding, in fact we are going to accelerate that because it legitimizes the field.

What I want to make sure of, and what I have argued in the last several months, is that we have the ethical oversight. That will come through the hearing process here, but we need not just the ethical but the moral, ethical, and scientific oversight of what is

going on broadly, because the drive for science is powerful. It is to create, it is to discover, and that is good. On the other hand, as I said earlier in my opening statement, the potential for unintended consequences is there. And we are dealing with the creation of life, the manipulation of the basic building blocks of life, and what I am concerned about—and we have not talked about, and we do not have time to go into it in much detail now—is that larger ethical oversight.

The registry is a step in the right direction because that will give you at least a handle on the State of the art, private and public. The Bioethics Commission—at some point, I would like to hear more about that in terms of what the plans actually are in terms of oversight, what the focus will be, and the composition—you do not have to go into that right now, but again, I would think that they are going to look at the public sector as well as the private sector as we go forward.

Secretary THOMPSON. Yes.

Senator FRIST. And third, I am interested in scientific oversight and how we as a Nation—should we legislate it; do you do it through HHS—provide the appropriate scientific oversight. Right now, we are arguing—is 64 too many, or where is it in terms of the 64; is it 19, is it 5, is it 4—it is good because we are asking the questions, but we need ongoing oversight so that 3 months from now, when we find out that there are 200 cell lines, or there are 5, appropriate decisions can be made, or appropriate input is received.

And I guess what I would like to introduce as a question is what are we doing not just as far as Federal funding for the 60 cell lines, but in terms of getting the larger ethical, moral, and scientific construct both to oversee—not regulate, but oversee—and monitor the issues of both public and private sectors?

Secretary THOMPSON. That is a very good question, and let me respond this way, Senator. That is the reason why the President set up the Bioethics Committee, to look at those questions and to be able to make the recommendations to the administration on those particular questions that you have raised.

In regard to the Department of Health and Human Services and NIH, our responsibility is to implement the policy. We are doing several things to implement that policy. We are setting up the registry. We are talking to the scientists about whether or not we should have a repository of these cells at NIH. Some scientists would like that, other scientists are fearful of that. We have not been able to do that.

The third thing is to negotiate MOUs and Material Transfer Agreements, which we have already started.

So we are already a long way down the road in dealing with this implementation question. The ethical questions certainly will be considered as we go along, through the Department of Health and Human Services, but the overall review and direction and new policies on these will come out of this new commission set up by the President, headed by Dr. Kass.

Senator FRIST. Thank you.

Thank you, Mr. Chairman.

The CHAIRMAN. Senator Harkin?

Senator HARKIN. Thank you, Mr. Chairman.

Again, Secretary Thompson, I appreciated the conversation we had on the night the President made his decision. I have given my support to the President's decision. I think that he has moved us ahead in this area. Not being a scientist but having been involved with NIH for many, many years, I have been watching very carefully the development of this issue over the last couple of weeks.

There is a lot out there that we do not know and do not understand; a lot of controversy about these cell lines and how many Sweden has or India has. We do not really have all the answers yet, but I think it is incumbent on us to continue to delve into this to see if we can shed more light on it, to expand our knowledge of exactly what we are doing and what we are talking about.

Again, I am not saying that I do not doubt for a minute that the President did not give a lot of thought and a lot of time and consideration to this; it is obvious that he did. But a lot of us have been giving thought and time and consideration to this for years, and we still do not have all the answers.

So I am not going to take the position that what the President said on August 9 is the final end-all and be-all of everything, because even if he did give some consideration and time and thought to it, he could not have given—I mean, because of new things that are opening up and new things that are happening, we have to be able to adapt to this new science.

So my position is going to be one of basically just continuing to ask questions to try to find out whether or not under the ethical guidelines that we have established under the Bioethics Commission—by the way, most of which the President followed; the only difference was the timing, the 9 p.m. on August 9—but the other guidelines are all the same—informed consent, no monetary consideration, and only using the embryos for—

Secretary THOMPSON. The excess.

Senator HARKIN [continuing]. And not using any therapeutic type of embryo development. So, basically, it is all the same except for that time line; it is basically the same. And we may want to think about that time line, too, at some other point.

But I guess my concern is along the lines of what you said about the university in Sweden—and I have talked extensively with my colleague Senator Specter on this. Yes, there are three developed lines. I did understand that before I came to the hearing today. But the real open question is whether or not early on in the process, those cells that were extracted will lead to viable cell lines, and we do not know that yet.

Secretary THOMPSON. We do not know that.

Senator HARKIN. We just do not know that. I am glad to hear you—you agree with that, that we do not know that yet?

Secretary THOMPSON. We do not know that for sure.

Senator HARKIN. We can hope they do, obviously, but if they do not, and if we find out that in other cases in India and some of these other places, that the lines are not fully developed, then we might wind up with something quite less than 60 or 64; we might wind up with something quite a bit less than that. Is that correct?

Secretary THOMPSON. That is possible, Senator Harkin, but at the same—if I could answer in a little bit more detail, there are

dozens already in existence, and the time line—it takes 6 to 8 months to develop a good cell line. There are four in the characterization stage from Sweden and 12 over here that have just been derived. The four look very promising, and the 12—there are certainly some, I am sure, that will fail and some that will succeed. I cannot give you that number. But there are dozens that are available right now.

Even at this stage, there is some great research that can be done on those 12, and those are questions for the scientists to do, and we have not seen that kind of research done yet.

The President has allowed for the Federal dollars now to flow toward research in all of these areas, and hopefully soon to get to some therapies.

Senator HARKIN. And that is the second thing—it has to do with the therapies—and we will be delving into this more in our committee hearings in the future also. But you responded to I think it was either Senator Kennedy or Senator Gregg when they asked about the fact that the nutrient supply used for the development of these cells was evidently mouse cells. I did not know that before, but I guess this is true in almost—in every case.

The CHAIRMAN. All.

Senator HARKIN. All of them.

Secretary THOMPSON. Yes.

Senator HARKIN. So there is a contamination problem that I was not aware of before. I fully admit that I was not aware of this contamination problem.

And if we are looking at just what happened yesterday at the University of Wisconsin and the fact that they are able to at least initially take some of these embryonic stem cells and move them into blood lines, that is pretty astounding.

Secretary THOMPSON. It is exciting.

Senator HARKIN. That is astounding. In this short a period of time, we have done this. Mind you, they only derived these cells 3 years ago.

Secretary THOMPSON. Three years ago.

Senator HARKIN. And now we are making red and white blood platelets out of it.

Secretary THOMPSON. Platelets, right.

Senator HARKIN. That is pretty amazing.

But if there is a contamination problem, we could go down this line for, as you say, the next 5 years or so, but be working with things that, while they might prove out to be beneficial therapeutically, would not be able to be used because prior on, they were grown with a nutrient out of mouse cells.

It would seem, then, that we would have to go back and almost start all over again. Why waste all that time? My big concern is that I did not know and was not aware that all of these cell lines were grown in mouse cell nutrients as a basis, and that disturbs me. We need to ask the scientists more about what that means in terms of the therapies and how soon we can derive those therapies if in fact they are contaminated.

Secretary THOMPSON. Can I just answer in two ways? First, when we started on the 64 lines, nobody knew—you did not know, I did not know, nobody knew—how many lines were available. I

asked NIH to make a complete inventory of the lines—not at what place they were but whether or not the embryos had been derived as of August 9.

NIH did it once; they did it the second time after the President's speech; and the third time is coming in and talking to them. We found that there are 64, but they are in different stages; but there are dozens that have already been through the cell line established. That is number one.

At the bottom of the petri dish is where the mouse layers are placed. And it is sort of a traumatic experience for these cells as I understand it when they are taken away from the blastocyst and removed and put into the culture; they have to have something in order to grow and be able to replicate. That is probably the most difficult portion, and according to Dr. Thomson, that is where a lot of scientists failed. They need to be able to do that.

Then, FDA has established policies, and they have looked at this procedure. Kathy Zoon is here. She is in charge of this, and she has indicated that right now, we have 13 INDs, Initiatives for New Drugs, that have already been started using xenotransplantation. And she does not believe that this alone is going to prevent moving from here to therapy, and neither does Dr. Jamie Thomson.

Senator HARKIN. I appreciate that, but we need to delve into this further.

Secretary THOMPSON. Yes. And the blood cells, the hematopoietic blood cells—I talked to Dr. Thomson yesterday, and he said that it is going to take probably 3, 5, 6, 7 years.

Senator HARKIN. But those are still contaminated lines.

Secretary THOMPSON. I do not classify them as contaminated.

Senator HARKIN. Well——

Secretary THOMPSON. They have the cell——

Senator HARKIN. There is a cloud over them. There is a very dark cloud there.

Secretary THOMPSON. I do not want to argue with you because I am not a scientist, and I cannot know——

Senator HARKIN. Well, I am not, either, I am not either, but——

Secretary THOMPSON [continuing]. But I do not think they are contaminated, because I think they are going to be very useful and usable. I cannot say for sure. All I can tell you is what I talk to people and they tell me, Senator Harkin.

Senator HARKIN. We have got to follow up with the scientists on this. I do not know.

Secretary THOMPSON. Yes. The scientists have got to tell us that. That is why it is so important to get the scientists in the laboratory to start answering these questions, Senator.

The CHAIRMAN. As the Senator is winding up, as I understand it, mad cow resulted from a completely unanticipated transfer of infectious agent from beef to humans. No one anticipated that, no one knew about it. That is why these guidelines that you have issued in the CDC are so important, to make sure that we do not have unanticipated transfer and why those guidelines are so important. These stem cells that you have outlined here and the President, I do not believe meet those kinds of requirements, and looking through the letter that you sent here, I do not think that

should give us much satisfaction. But we will have another chance to come back to it.

Secretary THOMPSON. Senator, could I respond?

The CHAIRMAN. Yes, please.

Secretary THOMPSON. The truth of the matter is that the embryonic stem cells probably would not survive—would probably not survive—the removal from the blastocyst into the culture dish without the mouse layers that the cells rest upon and get the nutrients from. In order for us to do this research, we have to have this, and it is going to take 3 to 5 years to find out all of these answers.

The truth of the matter is we have got to get this basic research done, because the questions you ask are good ones, Senator Kennedy, and I cannot answer them, but I do know that the embryonic stem cells would not grow and replicate without the mouse layers, because they provide the security and the proteins.

The CHAIRMAN. But Mr. Secretary, they may very well have to use the mouse cells, but not these mouse cells—mouse cells that meet the kinds of requirements that CDC has outlined that might take 6 or 8 months. But the ones that are now being identified in these 64 lines do not meet the requirements of the protections that have been announced by your own agency and CDC; they just do not do that. We will spend more time on this, but the August 9 date arbitrarily says that we are only going to be able to use those that are already out there when, as you have said here, we could develop these in between 6 to 8 months, and we could do it with mice that meet the requirements of the CDC. But we are not going to be able to do that because we have the August 9 deadline, nor will we be able to even consider research that might be able to detect the kinds of nutrients that are so important in the mouse cells—that is what it is; it is these nutrients—and many of the researchers that I have talked to say we will be able to find out what those nutrients are, and we might not even need those mouse cells down the road, but we are going to be prohibited from using those cells in the future because of the August 9 deadline as well. These are some of the concerns.

Secretary THOMPSON. But Senator, the basic research can be done with the Federal dollars. On the private research dollars, there is no prohibition or inhibition whatsoever on private research coming in and using a new procedure and getting it ready for therapy, getting it ready for the development of a pill or a device.

The CHAIRMAN. Senator Warner?

Senator WARNER. Thank you, Mr. Chairman. I wish to commend you and our distinguished ranking member for initiating this hearing.

Those of us who have been privileged to attend this hearing I think will remember it in years to come, because this is an historic threshold for the Congress. This is the first full committee hearing on a subject that will place challenges to our Republic unlike any I have seen, literally, in the 23 years I have been privileged to serve in the Senate.

We are fortunate to have you at the helm at this particular time. You bring to your position vast experience in diverse subjects, and most importantly as Governor, caring for people. That is what the bottom line is in this.

And I commend the President, even though I and others stepped out somewhat ahead of the President in a letter—which I would ask unanimous consent be included as part of the record today—

The CHAIRMAN. It will be so included.

Senator WARNER [continuing]. Where 11 Republican Senators took a stance on this early on.

[Letter follows:]

U.S. SENATE,
WASHINGTON, DC 20510.

The President,
The White House,
Washington, DC 20510.

DEAR MR. PRESIDENT: We strongly urge you to continue the last Administration's policy of using Federal funds for research on human stem cells after these cells have been derived from embryos. In addition, we strongly urge you to support legislation which would remove the existing ban on the use of Federal funds to derive stem cells from embryos.

On the issue of stem cell research, we think our colleague, Senator Gordon Smith, went to the heart of the matter when he pointed out the difference between an embryo in a petri dish, which would not produce human life, as opposed to an embryo in the womb of a woman? where further development would produce life.

The essential consideration is that there are many excess embryos created for the purpose of vitro fertilization. The only issue is whether these embryos will be discarded or used for stem cell research to save lives. Stem cell research has demonstrated a remarkable capacity of these cells to transform into any type of cell in the human body. Stem cells could be transplanted to any part of the body to replace tissue that has been damaged by disease, injury or aging. If scientists are correct, stem cells could be used to treat and cure a multitude of maladies such as Parkinson's, Alzheimer's, diabetes, ALS, heart disease, spinal-cord injury, all types of cancers, burns, stroke, macular degeneration, multiple sclerosis, muscular dystrophy, autoimmune diseases, hepatitis and arthritis.

Current law prohibits Federal funding to create human embryos for research purposed through cloning, or through any other means. We do not object to these important prohibitions. However, creating embryos for research purposes is entirely different from using spare embryos left-over from infertility treatments. These spare embryos are now destined to be thrown away. Rather than discarding them, we support using these embryos in medical research to treat and cure disease.

Sincerely,

ARLEN SPECTER.
STROM THURMOND.
JOHN CHAFEE.
OLYMPIA SNOWE.
BEN NIGHTHORSE CAMPBELL.
GORDON SMITH.
SUSAN COLLINS.
TED STEVENS.
KAY BAILEY HUTCHISON.
ORIN HATCH.
DICK LUGAR.
JOHN MCCAIN.
JOHN WARNER.

Senator WARNER. So I look upon this as, not unlike our great pastime, a football field—at one goalpost, those standards of ethics, morality, and religion which have made this Nation the strong Nation and the envy of the world that we are today—and we have got to protect those in the future. At the other end of the field is the goalpost of alleviating human suffering and the need for this Nation to move ahead on the forefront of science.

My particular area in this Senate is national defense. Our country is a superpower, not because we desire to be, but because the

rest of the world has ceded to us that responsibility. We are working tonight on a military budget for the United States which is greater than cumulatively adding up all the other budgets of the world. It is astonishing. But we have taken that responsibility on.

The question before this President and successive Presidents, the question before this Congress and successive Congress is are we going to be a superpower in this exciting science, or are we going to put in a lot of arbitrary standards? If that is the case, what will happen is two things. If our Federal system—the President setting down the leadership, the Congress enacting the laws to support our President, and the courts trying to fairly arbitrate the differences of views—all three of our entities of Government will work together on this—but if we fail to convey to the American people and the rest of the world that we are fair and have objectivity and a realistic approach to this, the Federal Government will be left in a cloud of dust as the private sector marches off on this. We will also no longer be a nation of importers of brain power and scientists; our own scientists I am fearful will go abroad to where they can work on this. Then, we will lose as a nation that degree of oversight and control over our standards of ethics and morality if they all depart. Then, that science will come back into the United States, either legally or illegally, because you are just not going to stop the advancement. So this is a whale of a challenge.

Do you basically agree with that sort of philosophical approach that I have, and if so, what can we do to keep the private sector in a fair set of rules to do those things that perhaps our Federal Government will not do for the moment and to keep our scientists from leaving this country and going abroad?

Secretary THOMPSON. I think your comments were very thoughtful and very passionate, and I could not disagree with anything you said, Senator, and applaud you for saying it.

I would like to only clarify that prior to August 9, there were no Federal research dollars available. As of the President's speech there is money available. We made an inventory, and we have found that 64 embryonic stem cell lines exist that meet the President's criteria—that means for Federal funds.

They are in different degrees of development. Some are in the proliferation stage, some are in the characterization, some are in the cell line established. But they are all available for research.

The mouse research on embryonic stem cells has been going on for 20 years, and 90 percent of that work has been done on five lines. Dr. Jamie Thomson, who discovered the embryonic stem cells, has five lines, but he uses for his research purposes two lines, and he has lines available.

And WiCell, who has the patent, has indicated they have enough cell lines available for any researcher in America who wants to do the research.

I think it is a tremendous opportunity. This whole area of embryonic stem cells opens the door. Everybody who has some sort of malady or has a loved one or a dear friend who is suffering from dementia or cancer or so on is looking for this as the panacea. We have to be careful not to indicate that a cure is right around the corner. It is going to take several years. We need now to get the Federal research dollars and the basic research done, Senator, so

that private dollars can come in and develop the therapies once they are developed.

I believe that there is more interest because of this hearing, more interest because of the President's speech, more interest because of all the discussions around the country about embryonic stem cells, and that people know more about human biology and physiology than they ever have before, which is in and of itself a positive. And I think that scientists now calling NIH are excited about the potential.

I cannot answer all the questions, and none of the individuals up there can at this point in time. The important thing is to get the research started and make the comparisons so we know some of the answers, so we can come back here 2 years or 3 years from now and talk about this issue.

Senator WARNER. You are the President's principal advisor, and as I said, we are fortunate to have you. And I commend the President even though I personally feel somewhat that we should move a step further.

But the point is let us take one adjunct question, and that is human cloning. I am totally opposed. The President is totally opposed.

Secretary THOMPSON. So is the President, and so am I.

Senator WARNER. Should we effect here in the Congress rigid standards of law and indeed attach criminal penalties to that one area?

Secretary THOMPSON. I think we should prohibit human cloning, Senator.

Senator WARNER. And indeed go so far as to attach criminal penalties?

Secretary THOMPSON. That is a decision for the Senators.

Senator WARNER. I thank the chair. I thank the witness.

The CHAIRMAN. Senator Mikulski?

Senator MIKULSKI. Thank you very much, Mr. Chairman.

Mr. Chairman, I would like to ask unanimous consent that my opening statement be included in the record.

The CHAIRMAN. It will be so included.

[The prepared statement of Senator Mikulski follows:]

PREPARED STATEMENT OF SENATOR MIKULSKI

Thank you, Mr. Chairman, for holding this important hearing on stem cell research today. I am happy to have the opportunity to hear from Senator Specter, Congressman Langevin, Secretary Thompson, and from experts on this issue. The President had a difficult decision before him, and I appreciate the deliberative, responsible way he has approached it. I know that stem cell research is an extraordinarily complex scientific and ethical issue, and I am pleased that the President took such great care in making his decision.

One of the reasons I became a U.S. Senator was to save lives. Scientists tell us that stem cells may help lead to cures for diseases ranging from Alzheimer's to diabetes. Stem cell research could save lives. We owe it to every American suffering from these diseases to explore the scientific possibilities in front of us.

First, I share the President's opposition to human cloning. I also agree that we should use our resources to investigate the research possibilities of stem cells derived from adults and from umbilical stem cells.

Yet I disagree with the President's decision to allow Federal funding for embryonic stem cell research only in the most narrow way. I'm concerned that he has created an enormous loophole for researchers in private, profit making firms. Embryonic stem cell research will go forward with or without Federal funds. The President's decision leaves the majority of embryonic stem cell research to private firms in an unregulated atmosphere. My position is that there should be Federal support for embryonic stem cell research. With Federal funds comes Federal scrutiny, regulation, and transparency.

Stem cell research offers us a cornucopia of opportunity that may lead to treatments or even cures for diseases like Alzheimer's, diabetes, Parkinson's and more. Public funding—and the public oversight that goes with it—ensures that this research is conducted within a rigorous ethical framework. We can have both sound science and sound ethics.

Again, I thank the Chairman for calling this hearing on stem cell research. I look forward to working with my colleagues and the Administration on this important issue, and I look forward to hearing from our witnesses. Thank you.

Senator MIKULSKI. Mr. Secretary, I just want to really welcome you today and thank you, in your 6 months in office, for all the courtesy and collegiality and how responsive you have been to many issues that I have raised with you. I want to thank you for that.

I also want to thank you for inviting the women in the Senate to meet with you to talk about a women's health agenda.

I must say that I am impressed with the mastery that you have of the technical issues here. For a while there, I thought you were defending a Ph.D. in biology.

Secretary THOMPSON. I think I could almost write one right now, Senator.

Senator MIKULSKI. Yes, really. You can see that you have really put a lot of work into this personally and are very hands-on about it.

Let me go right to my question, which follows along the line of Dr. Frist. First, in terms of President Bush's position, we thank him for his deliberativeness. I too oppose human cloning, support the adult umbilical stem cells, and am glad that he took the next step in embryonic.

Let me tell you what my concern is. My concern is that the Bush framework creates a loophole, and the loophole is that embryonic research from discarded embryos will go on anyway, but that it will go on within the private sector environment, unscrutinized and unregulated, therefore lacking any type of transparency.

The fears that I have about that are twofold—number one, that big breakthroughs could come from those who hold the reins of profitmaking rather than being in a large public domain and therefore could not only profit but even profiteer by it.

No. 2, in an unregulated and nontransparent atmosphere, I am also worried about some of those grim things that President Bush is worried about. The biological revolution is stunning in terms of its opportunities, but it is also stunning in the way it can present to us a ghoulish, Huxley-like environment.

I wonder what you think about this loophole and the concerns that I have about this, and where do you see us heading in that, really, so much of the research could go on in this unregulated, untransparent, very profitmaking environment?

Secretary THOMPSON. Senator Mikulski, first off, thank you for your kind words. I appreciate it very much.

The President set up this Bioethics Commission headed by Dr. Kass to do just exactly what you are talking about—to develop the theories, encourage the adoption of laws, to make sure that the profiteering and other problems that you have indicated will not exist. Saying all that, before we get there, I do not believe that the privates are going to do the basic research; they never really have. The basic research is not what it is going to get them the money. The basic research is what NIH does; it is what Johns Hopkins does, it is what University of Massachusetts and University of Wisconsin and all the others do. They are the ones who are going to have to do the basic research. Once that basic research is developed, I believe that then, the private dollars are going to come in and try to take that basic research—but we will have intellectual property rights to that. Geron, WARF, NIH—the agreement we signed yesterday, the MOU that we signed with WARF, allows us to maintain our intellectual property rights on our discoveries at NIH, which is exciting, and the publications that are going to be going on in this area.

It is so important for us to get this research done. I cannot scientifically tell you that there will not be profiteering or a problem existing as you point out. I cannot say unequivocally that that is impossible. I can tell you that we are trying to contain any of those problems, and we are sure that they are in the future and not right now. What we need to do is get our best scientists to get the Federal dollars to do that basic research that is just crying for discovery, I believe.

Senator MIKULSKI. Thank you very much, Mr. Secretary. As I understand it, the thrust of your presentation is that essentially, this is a work in progress, the stem cell research, both from an administrative perspective as well as setting our bioethical standards. We have a benchmark. Actually, we have broad agreement on a certain bioethical framework. Much is made of the prickly distinctions, but by and large, I think we are all agreed that we do not want grim and ghoulish things to go on.

But as I understand it, while NIH begins its role, this Bioethics Commission will also commence its role and be looking at the issues of the greater in-depth of a bioethical framework as well as evaluating these breakthroughs. Am I correct in that?

Secretary THOMPSON. You are absolutely correct.

Senator MIKULSKI. And in other words, we are going to be continually reviewing it.

Secretary THOMPSON. Plus you cannot forget that Congress is also very much involved in holding hearings on this subjects as well, and making laws.

Senator MIKULSKI. But my point is that Congress will continue to hold hearings based on now what NIH is doing and also the work of this commission.

Secretary THOMPSON. Right.

Senator MIKULSKI. But essentially, this is the framework for embarking on this biological revolution.

Secretary THOMPSON. That is correct.

Senator MIKULSKI. Now a technical question—and I think that is good; I think we are going to have to hold periodic hearings on this—these stem lines that we have talked about, do they have a shelf life, and if they do, this could present great dilemmas for the Bush position.

I take the position of being allowed to do research on discarded embryos where there has been informed consent to do so and oppose creating embryos for therapeutic reasons. But what do we know about the shelf life, or should we save it for the “bio gurus” here?

Secretary THOMPSON. We know that for 3 years, the first embryonic stem cell line is still replicating. Dr. Thomson says that he believes they can continue to replicate indefinitely, and other scientists have said the same thing. I am not a scientist, and I have to take what they tell me as the gospel—but I believe that they will.

Now, can I say conclusively that there is no shelf life? I cannot say that. I can tell you that they are usable as long as they are not differentiated. When the cell starts differentiating into a particular part of the body, then, like the hematopoietic blood cells—what has taken place at the end, after the embryonic stem cell line has been frozen, they have taken the cells out, and they have then differentiated those cell lines into blood cells, which is really exciting, creating blood, white corpuscles, red, and platelets. That to me is truly exciting, and it is a tremendous breakthrough, but whether or not it is going to be able to be used in therapy within 3 years, 5 years or 6 years, I do not think anybody can say at this point in time, Senator Mikulski.

Senator MIKULSKI. Yes. There are scientists, many of whom are involved in cellular research, at Hopkins who apprise me that they do believe that these cells do have a shelf life. But I think that you are saying that the science is so new, we are going to have to see this, and should it have a shelf life, confront those issues, because both the Commission and NIH will have had a chance to do their work.

By the way, how are we doing on getting new heads of NIH and FDA? You have great acting directors.

Secretary THOMPSON. I have made my views known to Senator Kennedy and to the White House, and I will hopefully hear good news from both of those people.

The CHAIRMAN. I hope to have good news, too.

Senator MIKULSKI. Well, like E.F. Hutton, I cannot wait until I hear the news since both of these flagship agencies are located in my State.

Secretary THOMPSON. I know. I am as anxious as you are, Senator Mikulski.

Senator MIKULSKI. Thank you, and let me know if I can help move the process along—again.

Secretary THOMPSON. I appreciate that.

Senator MIKULSKI. Ted, can we talk later?

The CHAIRMAN. We will talk. [Laughter.]

Senator Murray?

Senator MURRAY. Thank you very much, Mr. Chairman, and thank you for having this hearing.

Clearly, this is a very complex issue, and I appreciate all the knowledge that you have developed on this and the considerable amount of effort you have taken on a very difficult subject. Certainly the public is very, very interested in what we are doing and how we are moving forward from many different perspectives—obviously, from moral and religious, but also from a perspective that they do not want us limiting what we can do in the future in terms of life-saving processes that can be developed from what we set out here today.

I share the concern of Senator Mikulski in terms of private research. You have said very clearly that the administration has said that there will be no further destruction of embryos after the August 9 deadline, and I am worried about what kind of impact this will have on our research. I understand the commission that you have set out and that you see the Federal Government and NIH doing sort of basic research and then allowing private interests to move further. But you yourself know that private industry has a different motive than the Federal Government, which is why we have NIH and why we do research and why we put money into it. We can do the basic research with the best of intentions that the development will occur for diseases like multiple sclerosis or Parkinson's or other diseases, but private companies may well see that marketing and profit comes from male baldness and may set aside what we see as a public interest.

I am very concerned that a commission set up to look at bioethical standards is not going to—they cannot determine what profit means, but that is what private industry will do.

How do you reconcile this August 9 deadline with what private interests are going to want to do once we have done the basic research?

Secretary THOMPSON. I clearly can reconcile it because the private sector would not do the basic research that I think is so important. I do not think the private sector would spend its time or money making the comparison of embryonic stem cells versus adult stem cells versus placenta versus cord blood. I think that that kind of research needs to be done for you and for me to make the proper decisions, and I do not think the private sector will do that.

That is why, prior to August 9, the Federal research was not being done. The President—

Senator MURRAY. But you are limiting us to that basic research rather to what we can develop maybe in the future, 2, 5, 10 years from now, on specific diseases.

Secretary THOMPSON. No, I am not, Senator Murray, because the MOU that we signed yesterday with WiCell allows us to have the

five cell lines available right now for research and that the scientists at NIH will be able to keep their intellectual property rights and will be able to publish on what they discover. That may be a therapy on baldness, as you have indicated—I do not think that that is what we are that concerned with right now; we are more concerned with—

Senator MURRAY. But it may be the best marketing and the best profit for somebody.

Secretary THOMPSON. But that is for the private sector.

Senator MURRAY. Right, but we have to protect the public interest, and my concern is that having an August 9 deadline set, with no intention of ever going back and looking at it again, may very well preclude some of the important research we talk about at every hearing we have on this, that we tell our constituents that it may be available in the future for diseases that touch many, many families, that it will never be developed because we had a hands-off approach once the basic research is completed.

Secretary THOMPSON. I cannot answer that question except to say that we think there is ample supply of embryonic stem cell lines to do the basic research for the areas that you are concerned about for your citizens and that I am concerned about for all Americans and that the President is concerned with. He has just drawn a moral line, an ethical line, saying that there will be no further destruction of embryos that will get Federal funding of dollars. And that is probably something that you and I would never agree on.

Senator MURRAY. And I guess I am just stating a concern here.

Well, how do you see this affecting university research, which is often a collaboration of both private and Federal dollars?

Secretary THOMPSON. I think that that is going to have to be worked on, but I am confident that—

Senator MURRAY. How will it be worked on? Do we have a process in place to look at that?

Secretary THOMPSON. We do not as of yet, but we are working on it, Senator Murray. As you know, 75 to 80 percent of NIH dollars go back to universities for research dollars.

Senator MURRAY. Right, and it is often used in collaboration with private money. If private money uses stem cell lines that were developed after August 9, will we be precluded from doing collaborative research at universities on that?

Secretary THOMPSON. That question has not been raised, Senator, and a decision has not been made.

Senator MURRAY. I think it is an important one.

Secretary THOMPSON. I cannot answer that.

Senator MURRAY. Thank you, Mr. Secretary.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you very much, Senator Murray.

Senator Clinton?

Senator CLINTON. Thank you, Mr. Chairman, and thank you, Mr. Secretary.

I think, as probably all of us feel after these couple of hours together, there are a lot of unanswered questions which we will look forward to struggling through with you and those with whom you consult because clearly, as Senator Warner said, this is an issue

that has such great importance and resonance not only throughout our country but throughout the world.

I am still at the level of acquiring information and trying to get it straight, because there are just a lot of contradictory attitudes that are being expressed about what we have and what we do not have. I think it is important that we have a factual base.

You are not here, Mr. Secretary, for Senator Specter's testimony, but I am sure that your staff will fill you in and give you a copy of it. He certainly takes the position that is I think somewhat different from the one that you have expressed about what the viability and accessibility of the stem cell lines are.

We need to come to some basic agreement about what the evidence shows, and I hope that you will work with us on that, because certainly, Senator Specter and Senator Harkin have held a number of hearings on this issue going back now nearly 2 years, and Senator Specter has a different basis of information available to him than what you have presented. So I hope that we can work through that so we all know what we are talking about.

Second, the serious question that has been raised about the potential impact, if not contamination, from the mouse cells—and also, I believe blood serum from cattle is also used to nourish these cells in some of the settings—is one that we all have grave issues about. We are concerned that our Government's own standards about how to treat the introduction of animal elements into human material have not necessarily been followed in the various locations where we have identified these stem cells. So that clearly, we have a lot more work to do on that, because as you point out, the research is going to take a number of years, and I think many of us would be very disappointed if, at the end of all those years, the work could not be useful to the alleviation of human suffering because of the contamination that affected these cells.

One other question that I need some guidance about is in the President's speech, I believe he said he supported the House bill. As I understand the House bill, it not only bans reproductive and therapeutic cloning in the United States and certainly any Federal involvement in such efforts, but it goes a step further and says that if, in England or Germany or Japan, any therapy or treatment is created from therapeutic cloning, that treatment could not be imported into the United States.

Am I understanding that correctly in both the House bill and the President's position?

Secretary THOMPSON. Senator Clinton, I have not done any research on that subject, I am sorry to say, so I do not particular want to answer that question at this point in time. I would be more than happy to do the research and call you or write you with an answer on that.

But I would like to hopefully make a correction, and not to be confrontational. On the contamination, I do not believe that there is contamination. Just because these cells rest on a mouse layer of cells does not mean that they are contaminated.

I have talked to FDA, I have talked to NIH, and it is such a traumatic experience for these cells to be taken out of the embryo that they have to have this cushion—

Senator CLINTON. Mr. Secretary, I understand that, but the point that was made this morning—and I am just trying to get a base of information so that I can make the best possible decisions—but as I understood the chairman's point this morning, our Government has issued guidelines about how mouse nutrients are to be injected into any kind of human material. So that clearly, we know what happens—the xenotransplantation efforts that you referred to are ongoing. I read the letter that was distributed. Frankly, it still is a little concerning to me, because the long list of steps to be taken to guard against any kind of untoward consequences of xenotransplantation is a little bit daunting to me. But putting xenotransplantation to one side, as I understand what the chairman said, our Government has issued very strict guidelines about the introduction of mouse nutrients into the human material, and we have no guarantee that these stem cells in India or in Sweden or anywhere else have followed the American Government's guidelines, do we?

Secretary THOMPSON. We do not.

Senator CLINTON. We do not. So I do not think any of us wants to be confrontational. We are trying to understand what it is we are doing.

Secretary THOMPSON. I just—

Senator CLINTON. So if our Government has rules about how to avoid contamination that they have issued to researchers about how to use mouse nutrients, I think it is a fair conclusion to draw that in the absence of following those rules, some might conclude that contamination has or could occur. That is my only point.

So my only point is that as we go forward to try to understand what it is we are doing here, we need to be open. We cannot close our minds. This is not an inquisition. This is not trying to determine who is right and who is wrong. We are trying to figure out what we are doing. And there have been many questions raised since the President's speech that deserve an answer. The scientific community deserves an answer, the Congress deserves an answer, and certainly people who are out there wondering about this deserve an answer.

So on those several points, I would appreciate additional information.

Also, as we look at this, the question that was raised by Senator Mikulski, which I think is a very important one, is that we have chosen to adopt a different approach than Great Britain, for example. As I understand it, they have an Embryonic Research Advisory Board that attempts to govern both public and private sector investments in this research. We have adopted a different approach. We have adopted these restrictions on Federal funding and very few on private funding. And I take seriously your point and happen to agree with it that the basic research is likely to be done with the public sector dollars. That, though, raises some of the concerns that scientists have suggested to me, that is, that it is very difficult to do the kind of basic research without those public dollars. That really is the core of whatever therapeutic use can come from this research.

So that we are concerned, I think, about the potential shelf life of these stem cell lines, the specialization that can occur, rendering

them useless for the research, the numerous references to the mouse lines that have been developed—we do not know how many mouse lines it took to get those that are now replicable and usable. We are really out there in the dark, trying to figure it out. If we are going to make an analogy to the mouse lines, we ought to have as much information as we can to know if it was 1,000 mouse lines that eventually produced five viable mouse lines, or was it 64 mouse lines that produced five viable mouse lines. I do not have any idea.

So I think that every one of us is grateful for the hard work that you and the NIH and the professional staff have done, and we are grateful that the President had a deliberative process that led at least to the door being opened. But as we learn more about these 64 stem lines, as we try to figure out how to reconcile Senator Specter's very strong statement—it was a passionate statement this morning about what he believes to be the facts about these stem lines—with your very optimistic statement about the stem lines and the fact that if we go with the optimistic view, which is that this is all we need, and this is all we are going to get, how many years do we lose, what do we give up—the questions that Senator Warner raised.

So I think, Secretary Thompson, that many of us are still in the asking questions phase, and if I may, just one final question. You have said several times, and you said in response to Senator Murray that you envisioned private researchers taking up where the publicly-funded basic research leaves off. What thought has been given to how these private researchers will be able to overcome the proprietary rights issues as they engage in commercial development? With the kind of memorandum of understanding that you have reached between the Government and the research institutions—how will the private researchers be able to do that?

Secretary THOMPSON. Senator, first off, I did not mean to imply anything. I just did not want to leave this hearing saying that all of these lines are contaminated, and I do not think they are.

Second, you raised a lot of points. I do not know the answers. I can tell you that I have been involved in this thing since a month after Jamie Thomson discovered—first as a Governor; I have been an advocate and a passionate believer that this shows great promise, and I still believe that.

We have to do the research, and we have to do the basic research as you have indicated, to find out how can these cells be used. Adult stem cells may be more usable, more placid, than embryonic stem cells. That comparison has not been made; that has to be done.

In regard to the patent rights, I have talked to the people at NIH, and they tell me that this is no different, that the MOU and the statement of material transfer allow for this research to continue. The intellectual rights, the research writing of the scientists, will be able to continue and will be saved for NIH; but once they develop a product, like they do any other product, that does not use embryonic stem cell lines, the private sector and the patent laws and the commercial laws of America take over, and they will have to negotiate with WiCell or get a license to use that. But that is no different than any other product that has been developed by

NIH or by the private sector when there is an already-existing patent out there.

Senator CLINTON. Thank you.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you very much.

Senator Edwards?

Senator EDWARDS. Good morning, Mr. Secretary.

Secretary THOMPSON. Good morning, Senator Edwards. How are you?

Senator EDWARDS. I am fine. We appreciate your passion about this issue and the work you have done on it in the past. There were a number of us who had concerns when the President made his speech about the rigid guidelines that he established, understanding that there are serious scientific and ethical questions that have to be resolved, and how those guidelines would be applied in the context of a very new science. I think all of us recognize that this is a very new and rapidly developing science.

Secretary THOMPSON. And very exciting.

Senator EDWARDS. And very exciting, potentially very exciting.

I think our concern is that we want to make sure that that potential in fact is realized. At the time the President spoke and shortly thereafter when you talked about the subject, you talked about 60 some-odd stem cell lines being available and the nature of the research that you thought could be done based on those stem cell lines. Let me ask you first are you aware—have you actually been on site where these stem cell lines are located—and we have a list of where they are across the country and across the world. Have you actually been on site and examined the stem cell lines?

Secretary THOMPSON. No, I have not. I have been at the University of Wisconsin lab many times, but I have not been anywhere else, if that is your question.

Senator EDWARDS. The American Society for Cell Biology has established four criteria that they think should apply in this context in order to satisfy the research that needs to be done. The first is that the cell line be available to publicly-funded scientists both at the NIH and at universities around the country.

The second is that the owners of the stem cell lines not impose restrictions that would limit that research.

Third is that they have growth and handling characteristics that are compatible with quality research.

And fourth is that they retain the capacity to generate every adult cell type.

They are pretty simple, actually. One is to make sure it is available to the scientists who need to do the research; second, that there are not legal and other restrictions that would limit the ability to do the research; third, that the stem cell lines themselves are usable for the research that needs to be done; and fourth, that they have the capacity to generate the adult cell types that need to be generated.

Do you know as you sit here today how many of the stem cell lines that meet your test also meet those four simple tests?

Secretary THOMPSON. I know that 64 meet the President's guidelines in regard to Federal funding. There are 64 that we have inquired about and re-inquired about and have met with personally.

Senator EDWARDS. Can I interrupt you—do you think that those are reasonable tests, the tests that they lay out, those four simple tests?

Secretary THOMPSON. I think that those four are adequate, and I think that they will support—

Senator EDWARDS. You think they are reasonable.

Secretary THOMPSON. They are reasonable.

Senator EDWARDS. OK. Can you tell me as you sit here today—and you and the President have already established the limitations—can you tell me as you sit here today how many stem cell lines meet those four tests?

Secretary THOMPSON. Dozens.

Senator EDWARDS. What does that mean, “dozens”—25, 30? How many?

Secretary THOMPSON. I would say—dozens—I would say 20 to 25 at this point in time. But—you were not here—there are three stages that these embryonic stem cell lines go through. The first one is the proliferation, and there are several of those 64 lines that are in the proliferation line; there are several in the characterization line, which is over here; and several are in the “cell line established.” It takes 6 to 8 months to develop a good embryonic stem cell line, and there are some of these that have not met the full cell line establishment criteria yet—they will be by the time they apply for the money, and the money goes out at NIH. That is going to take somewhere between 8 or 9 months to get the money out.

To give you an example, in Sweden, Gothenburg University has 19 lines, Senator Edwards. Three of them are in the “cell line established,” which means they are ready right now for research and that further research could be done. Four of them are in characterization, and 12 are in proliferation.

Over the course of the next 6 to 8 months, several will move from proliferation to characterization to cell line established, and that is during the process that they will be applying for Federal research dollars.

To tell you exactly today how many, I cannot tell you. If I were pressed, I would say there would be 24 to 25 that would meet the “cell line established” criteria, Senator Edwards.

Senator EDWARDS. That leads me to my next question. When I originally asked you, you said “dozens,” and then, when I asked you a follow-up question about it, you said “24 or 25,” something in the—

Secretary THOMPSON. That is what—

Senator EDWARDS. How do you know that those 24 or 25 meet this reasonable, what you described as reasonable criteria that the cell biologists have established?

Secretary THOMPSON. Basically, because the MOUs that we have discussed with the 10 entities that have them have indicated they want to share with the scientists; two, that they can be used; three, that they replicate or are pluripotent, which is the scientific word for that. And I do not know what the fourth one was, but as I understand it, they meet those four qualifications.

Senator EDWARDS. Let me ask a follow-up question to that. How many genetically diverse stem cell lines, again as we sit here today—not the potential, but that we actually know about—have

the ability to regenerate themselves indefinitely? How many do you know about today?

Secretary THOMPSON. We think all 64.

Senator EDWARDS. OK. So it is some of the other tests that you are not certain whether they are—

Secretary THOMPSON. Yes. The other characterizations, the other things like the freeze-thaw testing, the cell marker assays, which are SSEA-3's and 4's and PTA-61's and 80's, and the chromosome analysis, and the testing for pluripotency—we are not sure about all of those things. But we do know that in order for this to be proliferating, they have already started proliferating right after they have been removed from the blastocyst and are in the cells in the culture dish. They are proliferating right then. So all 64 lines have proliferated; we do know that for a fact.

Senator EDWARDS. But you, HHS, NIH, have not physically been to the sites to actually examine the cells yourselves?

Secretary THOMPSON. No.

Senator EDWARDS. Do you plan to do that?

Secretary THOMPSON. I probably will not, but I know the scientists will be doing an exhaustive study, which they already are. We are in the process of setting up the registry. We have signed—you were not here—but we did sign an MOU and a Material Transfer Agreement yesterday with Wisconsin Alumni Research Foundation that allows for their five embryonic stem cell lines to be made available to the NIH scientists right now.

Senator EDWARDS. Are those five lines available to the nonNIH scientists around the country, publicly-funded scientists?

Secretary THOMPSON. Yes. Carl Gulbrandsen is here, and you can ask him that question, but he has indicated that, yes, any scientists who want those lines—

Senator EDWARDS. And what do we know about the availability of all the other stem cell lines?

Secretary THOMPSON. All we know—all I can tell you, Senator Edwards, is that the entities have been in to meet with Dr. Lana Skirboll and her staff, and I have personally met with them. I have not negotiated with them, but I have met with them, and they have all indicated to Dr. Lana Skirboll and to the staff at NIH that they want to make their cell lines available to scientists and for NIH to get the basic research done. They are excited.

Senator EDWARDS. But at this point, who controls that decision? Do they control it?

Secretary THOMPSON. The entities, the entities.

Senator EDWARDS. We as a nation have left to them control over what kind of research can be done on these cell lines?

Secretary THOMPSON. No, no. They own it; I mean, they have developed them, so they have control over them. And now what we are doing is—

Senator EDWARDS. So we have created through this decision by you and the President a monopoly in those people who have existing cell lines. If I understand you correctly, what you are saying is that they now have control over what research, if any, can be done by—it is all well and good that they are well-intentioned about it—I appreciate that—but suppose they decide that no, in fact, they are not going to permit the research to take place, or

they are only going to allow the NIH to do it, they are not going to allow the other scientists to do it?

Secretary THOMPSON. That is not what I have said, Senator. What I have said is that they have all indicated that they are in agreement and want to cooperate not only with NIH but with other scientists to do the basic research on their stem cell lines.

WARF has gone a step further. They have negotiated now with NIH an actual agreement which was signed yesterday with NIH to make their five cell lines that Jamie Thomson, the father of embryonic stem cells, has developed. He has licensed those to WARF; WARF in turn has licensed them or has given the permission to be used by NIH and other scientists through an MOU and a Material Transfer Agreement for any type of research that scientists want to do on those.

The second thing that we are doing is developing a registry at NIH, making all of these 64 lines hopefully available for scientists around the world to be able to pick the line that they want to use for their research projects when they apply for Federal research dollars.

Senator EDWARDS. The critical word there was "hopefully," and I know my time is up, but my obvious concern is—and I think it is a critical issue in this ongoing process—that by establishing the criteria that the President established, he limited the number of lines that are even potentially available and left in the hands of the people who presently have the proprietary control of those lines the decisionmaking about whether they are going to be publicly available. We cannot force them to make them available; they have a legal right to do whatever they choose to do. And I appreciate that they are well-intentioned, but it certainly has not been an unusual thing in the past to have people act out of their own personal financial best interest, and it would not be a shocking thing to see that happen in this case.

So I think the restrictions that have been imposed obviously create ongoing problems. I am hopeful with you that we will be able to get these folks to make these stem cell lines available, but I think it is a serious question as we sit here today.

I thank you, Mr. Secretary, for your answers.

Secretary THOMPSON. Thank you. All I can tell you in answer, Senator Edwards, is that we have five—the first one we have negotiated with, which is the one that has the patent in America, is the one we have reached an agreement with, and we feel very good about that, and we think the other ones will follow through.

I cannot promise you today that we are definitely going to have them all signed up next week, but we are working on them, and we are working as fast as we possibly can to reach an agreement with them.

Senator EDWARDS. Thank you, Mr. Secretary.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you.

Mr. Secretary, I will just make a very brief comments, and if others wish to ask a final question, obviously, they are welcome to.

No one could sit through the course of this hearing since 9:30 and not know of your own very strong commitment in terms of research in this area and your belief that this offers some enormous

opportunities and hope for families across this country in regard to these dreaded diseases that afflict every family in America—every family in America. That is very commendable. The President is fortunate to have the kind of advocate and advocacy that you have expressed here.

There are those who view this situation somewhat differently, and we are here trying to listen as we have carefully to your presentation, made in a very convincing way. Will there be the availability of stem cells for the research and the opportunities in an area that was really unthought of, or maybe thought of but not in reality until 2½ or 3 years ago, and with the best of the research that is done at NIH. Will there be sufficient product out there to permit opportunities for breakthroughs?

You make a very convincing and compelling case that there is, and I think there have been some legitimate issues and questions raised that cause us some concern. I think one of those issues that I raised very briefly, as others have, is the question of the conditions of safety and the issue of the use of nutrients from mice and the fact that in these various stem cell lines that you talk about here, you would be hardpressed to think that any of those followed the very strict guidelines that were issued on August 24th of this year on mice, from a colony that is continuously monitored for infectious disease. We know about mad cow disease; no one expected that that kind of infectious disease would be able to move from animals to human beings from a colony that was not allowed to interbreed with animals outside the colony and was routinely tested for infectious diseases and quarantined for 3 weeks prior to the procurement of cells.

Now we are told that we have to stay with these cells; even if we are able to take mice and create new stem cell lines further after August 9 that would meet all the requirements that the administration and CDC have put out, you are saying, “No, no, you cannot do it. August 9th is it.” And even if we are able to discover after 2½ years that we may be able to do it without nutrients from mice—maybe other kinds of nutrients would save us that kind of risk—we are told that we cannot do it because it is after August 9.

We commend you for the arrangements that you have made in being able to get one of the ten suppliers to make a strong commitment to make available their stem cell lines, and we are impressed by your own work in the past and saying that you have been in touch with all the others, and you believe that they will make them available. I think most of us would say that no one underestimates your ability to talk to someone and get an understanding and form an impression about whether that is for real or not, and I have a lot of respect for that. I think many would say we ought to get it in writing, because what we have seen as I understand it from similar situation is that there has not been the kind of readily available access when similar situations have been out there in terms of research at the NIH.

I think most of us have been around here long enough to see what OPEC was able to do to our economy and the impact that it has had on our society when they get together, 11 of them. And we

are talking not about 11 countries here, we are talking about some countries, but basically 10 entities, and that raises concerns.

So these are all important issues. We had comments about the patents, and you have commented about that, and I know you have worked on it. So these issues do raise some serious questions, but as far as I am concerned, I want to take what you have said here today and hear from our next panel their reactions, and then to work with you.

I do find at the end of the day that an August 9 deadline, sort of a drop-dead date, and the unwillingness, in spite of what follows in terms of breakthroughs in the areas of research, would serve as a barrier to important progress in terms of cancer or Alzheimer's, very troublesome.

But we have learned a good deal this morning, and I have been enormously impressed by your presentation. We will keep in close touch with you on this issue. We want no surprises—there could not be in any event. We want to work with the administration. We again thank the President for addressing it. It is just a desire to make sure that we are going to be able to get done what he has said he wanted done and what I think offers the greatest hope for the American people.

Senator Dodd?

Secretary THOMPSON. Can I just say thank you, Senator Kennedy, for your tremendous interest and passion on this subject. We may not totally agree on whether or not the August 9 deadline is correct or not, but I think we both agree that we need to get the research done and the questions answered—

The CHAIRMAN. Yes, yes.

Secretary THOMPSON [continuing]. And I thank you for your passion and your advocacy on this issue, and I want to publicly State that I support that and want to work with you as much as I possible can to accomplish that.

The CHAIRMAN. Thank you very much.

Senator DODD. Mr. Secretary, just to pick up on some of Senator Kennedy's comments—and Senator Clinton used the right word—this is not an “inquisition” at all. Obviously, there is deep interest in the subject matter not only here, obviously in the scientific community, and as you have heard, painfully, many cases from people at-large around the country who do not understand all of this. The news media may be in a sense hyping a bit what the potential is, but understandably, when you have a family member or a loved one who is suffering, and you hear about the potential to be able to deal with Alzheimer's or diabetes and other such illnesses, it is very, very exciting.

I for one want to thank you. You are in the box here, and we are raising the questions to you, but I think you deserve a great deal of credit for bringing this as far along as you have. There are some of us here who would have liked to see the administration go a bit further with this, in my view—not that I wanted to see it all; I strenuously oppose the idea of somehow creating what someone once used the word “hatcheries”; I would vehemently oppose that—but I also understand that with the ability to provide people with families through in vitro fertilization, and that there are excess embryos here—and I raised with issue you earlier as to whether or

not there is then going to be a position taken on banning the destruction of those excess embryos; and if there is, I suppose that would be consistent with the view that they cannot be used. If it is not, it raises the quandary—if you are not opposed to their destruction, how could you be opposed to using them, so that if in fact these other lines that hopefully are going to do exactly what you have described do not pan out, we have another source there to deal with.

But I think you have done a tremendous job, and you are right—we now have a position taken by this administration to publicly finance research, having drawn lines—and I have difficulty with the arbitrariness of August 9 and 9 p.m.—but nonetheless, this is breakthrough, this is good, and we ought not allow this hearing to end on a note that somehow, while there are still some disagreements over whether or not after August 9, there are some additional embryos to be used—this is very positive.

So I did not want the hearing to end without expressing my gratitude to you. I suspect you had an awful lot to do with this, the fact that there was that speech on August 9, and I suspect you had a lot to do with the fact that there was some breakthrough here, moving the line a bit further than I suspect some inside the White House wanted it to be moved. You do not have to answer that; I just have my own suspicions about it, and I am grateful to you, and a lot of other people are.

And I know that you have a first-rate team. I cannot tell you how excited I am about the work that is being done in adult stem cell research. I have had some wonderful conversations with my friend from Tennessee who has been enlightening me on cord blood stem cells and what that can mean. And at NIH, I have had wonderful conversations with the acting director out there about how realistic cord blood stem cells might be. Nonetheless the work that is being done is very exciting.

So I thank you for being here today and thank you for the work that you have done.

Obviously, some of the questions that have been raised, Senator Clinton's questions and Senator Kennedy's, we need to follow up on pretty quickly, because if it turns out that you are wrong, and we cannot extract these things, we will have to revisit this issue. I know you do not want to admit that this morning, but the only thing you said that worried me is that we will never reconsider the August 9th date, and I am not going to ask you to repeat that because I like to believe you might want to rethink it. So if we have to come back to that, we will have to come back to it, and we will talk to you when that occurs.

Thank you.

Secretary THOMPSON. Senator Dodd, thank you, and I thank all the members of the committee.

I will tell you this has been a great discussion. The beauty of it is that this holds so much promise for everybody out there who has a loved one suffering from breast cancer or dementia or anything else and is waiting for the possibility. We just cannot get the information out there that the cure is just around the corner; we have to get this basic research done.

Senator DODD. I agree.

Secretary THOMPSON. The President has allowed that to continue. I am excited about it, and I know that you are, Senator Dodd, and I thank you very much for all of your comments and all of your questions today.

The CHAIRMAN. Senator Frist?

Senator FRIST. Mr. Chairman, if I could have just 2 minutes. I again want to thank Secretary Thompson and the President for a lot of thought, a lot of consideration, a lot of individual meetings—and this issue deserves it because it is, again, as we look at science one of the few issues that we have had to face, that humanity has had to face, that has the opportunity for both promise, altering the basic building blocks of life, but also that could have unintended consequences. I want to thank you for that.

I do believe that we should expeditiously implement the policy put forth by the President, which is carefully crafted. As this moves forward, it will be important, again because science changes so rapidly, that we continuously reevaluate both the progress and the needs of this research.

If there is one thing that has come out from your comments and the comments in the last several weeks, it is that this is an uncharted area of scientific inquiry. This is clear whether we are talking about the number of necessary cell lines or about the mouse cells and xenotransplantation issue, which we have addressed in one context of transplanting whole organs but not quite as much in cells. It demands an ongoing public discussion among the policymakers, like those here today, the scientific community, whom we will hear from shortly, ethicists, the religious leaders, and the American people. It is absolutely critical to have that discussion on an ongoing basis—not just today, but on an ongoing basis—as science does change and progress.

We are going to have to wait several years before we know whether embryonic stem cell research is going to yield the promise that we all hope it will. In the meantime, I believe we should move forward expeditiously in implementing the President's policy and continue to examine the progress closely over the coming months and years.

Secretary THOMPSON. Thank you.

The CHAIRMAN. Thank you very much.

Senator Clinton?

Senator CLINTON. Secretary Thompson, I want to thank you as well. I would not want you to leave thinking that because I and others have raised some very tough issues, we do not totally respect what you are doing and have done.

I also want to thank our colleague, Senator Frist, because he also has had some things to say and do that have led us to this point, and we are very grateful for that.

But we need this kind of open, honest dialogue. This is a decision which, because of our living in a global media age, we are bringing in millions of people to be part of. It is not going to be made by scientists in a closed lab or by Senators behind closed doors. This is a society decision that has to be addressed in that way, and I know, given your background and what you have done with this particular issue and in general, that you understand that and will be working to lead public opinion as well.

Thank you very much.

Secretary THOMPSON. Thank you.

The CHAIRMAN. Thank you, Mr. Secretary.

Secretary THOMPSON. Thank you.

The CHAIRMAN. The hour is late, but we will try to get started with our panel, if we could. We will invite Dr. Douglas Melton, who is chairman of the Department of Molecular and Cellular Biology at Harvard University and a leading stem cell researcher and has made numerous important discoveries in diabetes research. Dr. Melton was honored for his outstanding accomplishments in medical research by being named to the National Academy of Sciences in 1995.

Ms. Karen Hersey is senior counsel for intellectual property at the Massachusetts Institute of Technology. She can speak from extensive professional experience on the complications that can arise in seeking access to essential medical research materials.

Dr. James Childress is the Edwin Kyle Professor of Religious Ethics at the University of Virginia. Dr. Childress served with distinction on the National Bioethics Advisory Commission whose report on stem cells is a thoughtful guide to the complex ethical issues raised by this research.

It is a special pleasure to welcome Dr. Childress, who was formerly the Joseph P. Kennedy Senior Professor of Christian Ethics at Georgetown University and has been a great leader in all areas of bioethics and is someone whom I have respected over a long period of time.

Dr. Kevin FitzGerald is the Doctor Lauler Professor for Catholic Health Care Ethics at Georgetown University and an associate professor of oncology. He has written extensively about the moral-ethical issues raised by new advances in medicine.

And Dr. John Chute conducts research on adult stem cells at the Bethesda Naval Medical Center. I believe that research on adult stem cells should proceed in parallel with a vigorous research program on embryonic stem cells. We welcome his testimony on this important topic.

It is a pleasure to have all of you, and we look forward to moving ahead.

I will ask Dr. Melton if he would be good enough to start.

STATEMENTS OF DOUGLAS MELTON, THOMAS DUDLEY CABOT PROFESSOR IN THE NATURAL SCIENCES, AND CHAIR, DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY, HARVARD UNIVERSITY; KAREN HERSEY, SENIOR COUNSEL FOR INTELLECTUAL PROPERTY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY; JAMES F. CHILDRESS, EDWIN B. KYLE PROFESSOR OF RELIGIOUS ETHICS, UNIVERSITY OF VIRGINIA; FATHER KEVIN FITZGERALD, DOCTOR LAULER PROFESSOR FOR CATHOLIC HEALTH CARE ETHICS AND ASSOCIATE PROFESSOR, DEPARTMENT OF ONCOLOGY, GEORGETOWN UNIVERSITY; AND DR. JOHN P. CHUTE, HEAD, HEMATOPOIETIC STEM CELL STUDIES SECTION, NIDDK, NAVY TRANSPLANTATION AND AUTOIMMUNITY BRANCH, NAVAL MEDICAL RESEARCH CENTER

Mr. MELTON. Good afternoon, Chairman Kennedy and Senator Frist. Thank you for inviting me to speak here today about human embryonic stem cells.

In the last 3 years, the potential of these cells has been widely debated in the public, and rightly so. The subject forces us all to revisit the question of when life begins, and we have to scrutinize the crossroads between scientific inquiry, our efforts to improve the human condition, and our moral and ethical responsibilities to preserve human dignity.

I am not here to testify on the moral, religious or political aspects of this research. I appear before you as a scientist and as the father of a young boy with Type 1 or juvenile diabetes. I will furthermore not speak to you about the human burden of a diabetes and will simply say that I work on human embryonic stem cells to try to treat or cure diabetes. My remarks today will therefore be confined to the scientific potential of these cells and the implementation of the President's plan about which we have already heard.

In my written testimony which I would like submitted for the record, I summarize the properties of embryonic stem cells and put that research in a larger context of recent biological activities and studies at the NIH.

Let me just say now that the ability of these cells to make any part of the body is what holds their promise for therapies. We have already heard about the numerous diseases that can be potentially treated—Parkinson's, Alzheimer's, osteoporosis, and the disease that has my full attention, juvenile diabetes. And I would simply like to say at this point that while adult stem cells have some similar properties, based on what we know today, adult stem cells do not have all the properties of embryonic stem cells.

To give an example, there is no credible evidence for the isolation or growth of an adult pancreatic stem cell, and that alone justifies, in my view, the work on embryonic stem cells.

I do not need to remind you all that the President made an important speech on August 9, and I would simply like to comment on that date as I feel it has important implications for the implementation of his plan.

That date was not chosen for scientific reasons, and its arbitrary selection will unquestionably have an effect on the progress of research. For example, as we have already heard, it will not be possible for federally-funded researchers to explore new ways to derive

human embryonic stem cells, stem cells that have a broader genetic diversity, or perhaps were grown in the absence of mouse tissue, for example, grown with human as opposed to mouse tissue.

Nevertheless, as Secretary Thompson has rightly pointed out, the door has been opened, and some research can now be done. I would like to address two issues and make a proposal for the implementation of the President's plan.

One of the things I feel the committee has struggled with is the lack of information about these 60-plus cell lines, and legitimate questions were asked about them. Let me simply say that scientists are by their nature inquisitive and skeptical, and we hold dear the practice of publishing results following an independent review by qualified experts.

Moreover, by publishing results, scientists generally agree that the reagents reported therein, including cells, are to be made available and shared with the research community. In this way, the results can be independently verified, and new directions and discoveries can be explored.

The problem with the present case is that only a handful of these 60-plus embryonic cell lines have been published, so it is not yet possible to give evaluation or comment on the quality of the lines. Nonetheless, legitimate questions can be asked about their growth, differentiation potential, age, and purity. These issues have already been raised this morning.

What I can say is that decades of experience with mouse embryonic stem cells show that they lose their differentiation potential, become contaminated, accumulate mutations, and tend toward spontaneous differentiation or uncontrolled differentiation after a certain period. This is related to the question that Senator Mikulski raised about shelf life.

Stated otherwise, there is incontrovertible evidence that old mouse embryonic stem cells do not have the same potential that young ones do. If I were to give an analogy with a human, it is true that these lines can grow forever and are in that sense immortal, but they lose their potential—a 150-year-old may still be alive but does not have the same potential as a 20-year-old.

I hasten to add that I am not criticizing the NIH nor the scientists who have reported the isolation of these 60 stem lines. Indeed, the scientists have not published their work, and they may well wish to further characterize the cells before doing so. It is therefore, in my opinion, too early to tell how many of the 60 lines are truly useful. Preliminary indications nevertheless suggest that the final number will be significantly less than 60. If the available lines have been extensively grown and have a high passage number, that will further reduce their value.

Let me now turn to the question of availability. A separate issue concerns whether these lines will be made available, and we have already heard that the entities that have derived the lines have proprietary and commercial interests. Experience shows that the negotiation of transfer from those who own the reagent to federally-funded scientists can be slow, expensive, and sometimes accompanied by onerous restrictions. It is obvious that the legitimate interests of companies may not coincide with scientists' research plans and our Nation's public health policy.

I was delighted to hear that Secretary Thompson has made progress with WARF in establishing one such relationship, but it is yet unclear whether he will be successful in doing so with the other entities.

To get to my final point, I would like to make a suggestion which I have made before to Secretary Thompson and the NIH, which is a plan to move forward that I think will be most effective given the limitations presented to the scientific community.

Specifically, I suggest that the NIH create a repository, not a registry, for the 60 embryonic cell lines. The NIH could collect the lines, determine their quality, and certify them for distribution to qualified researchers. Equally important, this plan would have the NIH negotiate favorable terms with all of the suppliers that could be set out in the Material Transfer Agreement.

At the moment, it is very difficult for scientists to individually negotiate such arrangements, and the Federal Government and the NIH are in an immeasurably stronger position than are individual investigators to obtain the human embryonic stem cell lines from suppliers. In that way, as I have said, they could verify their quality and arrange for their distribution.

I would like to know whether the NIH would be willing to consider doing that given that their resources far exceed those of individual investigators.

In conclusion, Mr. Chairman, I think the President and Secretary Thompson have proposed a plan that will allow federally-supported researchers to begin to explore work on human embryonic stem cells and work toward a cure. It is an important step. If my remarks today seem cautious, the reason is the uncertainty I have about the quality, availability, and longevity of the cell lines. Assuming that some of the 60 lines are made available, federally-supported scientists can work to understand how these cells can be directed to differentiate. This will lead to new insights into human biology and disease.

However, it seems to me perfectly clear that as these studies progress to the point where clinical applications can begin, I expect the plan will have to be revisited, principally because the viability or utility of the 60 cell lines will have been exhausted by that point.

In closing, I thank you and the committee once again for the privilege of speaking to you about this important area of biology.

The CHAIRMAN. Thank you very much.

[The prepared statement of Mr. Melton follows:]

PREPARED STATEMENT OF DOUGLAS MELTON

Good afternoon Chairman Kennedy, Senator Gregg and other distinguished members of the committee. It is my pleasure to appear before you today to speak about human embryonic stem cells.

Mr. Chairman, before I begin my remarks on stem cells, I want to take this opportunity to thank you and the other members of this subcommittee for your leading role in supporting the NIH. I thank you on behalf of the Nation's scientists who work to understand the basic principles of life and to cure human disease.

In the last 3 years, and increasingly so in the past few months, the potential of human embryonic stem cells has been widely debated in the public and rightly so. This subject forces us all to revisit the question of when life begins. We have to scrutinize the crossroads between scientific inquiry, our efforts to improve the human condition, and our moral and ethical responsibilities to preserve human dignity. Not surprisingly, a subject that combines the science of life's beginnings with politics

and religion has captured the Nation's attention. Indeed, this topic was recently the subject of President Bush's excellent speech on 9 August.

I am not here to testify on the moral, religious or political aspects of human embryonic stem cell research. I appear before you as a scientist and as the father of a young boy with Type I or juvenile diabetes. I will furthermore not speak to you about the human burden of this disease, but simply say that I work on human embryonic stem cells with the aim of providing a cure for diabetes. My remarks today will be confined to the scientific potential of human embryonic stem cells and the implementation of the President's plan.

While I'm certain the committee is well aware of the potential uses for human embryonic stem cells, allow me to briefly put this research in context. In the last century, biologists showed that genes are the units of development and heredity, discovered that genes are made of DNA, and recently completed sequencing the DNA that comprises the human genome, that is, sequencing the DNA of all human genes. This monumental achievement will stand as one of the most important scientific triumphs from the last century. Knowing the sequence of DNA allows scientists to uncover the basis for development, heredity and disease and challenges us to understand how the code of life is read or interpreted. At the same time, this enduring achievement should not cause us to forget that the unit of life is not DNA nor the gene, but rather the unit of life is the cell. Cells are alive and reproduce and among cells, stem cells are unique. Embryonic stem cells are special because they can reproduce to make more of themselves and they have the remarkable capacity to make any kind of cell in the body. One might think of them as the fire hydrant of all cells, having the capacity to renew or replenish lost cells and tissues. Understanding how these cells can duplicate themselves and how they specialize to make all types of cells will undoubtedly reveal important insights into human biology and disease.

The ability of stem cells to specialize or differentiate into any kind of cell is what holds their enormous therapeutic promise. Many of the diseases that currently plague our society are diseases of cellular deficiency, diseases in which one particular cell type is missing or defective. These diseases include Parkinson's, Alzheimer's, osteoporosis, some cancers and the one that has my full attention, juvenile diabetes. It has been estimated that as many as one hundred million Americans are affected by these diseases. Stem cells have the potential to replace the missing or deficient cells and it follows that the Nation's scientists and those suffering from diseases are anxious to aggressively pursue this research. I should like to note that while embryonic stem cells have a much broader potential for growth and differentiation than do adult stem cells, research on both adult and embryonic stem cells is warranted; it's too early to know which type of stem cell will be most useful. Whereas the last century of biology can be said to have focused on the gene and the sequence of DNA, I believe this century will see biologists come to understand and harness the unit of life, the cell, specifically stem cells.

PRESIDENT BUSH'S PLAN FOR SIXTY EMBRYONIC CELL LINES

President Bush has made clear his commitment to support research on human embryonic stem cells, highlighting the importance of this research. The President's plan provides the opportunity to advance embryonic stem cell research in the US, at least for a few years, and as such his plan marks an important commitment. The Honorable Tommy Thompson has worked diligently for this research and his continued leadership will be critical in moving forward with the President's plan.

For this field the date of the President's speech, 9 August 2001, is important because only stem cell lines in existence at that time, estimated to be about sixty, are eligible for Federal support. This date was not chosen for scientific reasons and its arbitrary selection will have an effect on the progress of research. For example, it will not be possible for federally funded researchers to explore new ways to derive human embryonic stem cells nor work with cells that have been isolated without possible contamination from mouse or other supporting cells. Nevertheless, it is now possible for the Nation's researchers to initiate studies on how embryonic stem (ES) cells differentiate and we can begin to explore their therapeutic potential.

Looking ahead to how the plan will work, I turn to two issues: the quality of the sixty cell lines and their access or availability.

QUALITY OF THE HUMAN EMBRYONIC STEM CELL LINES

Scientists are, by their nature, inquisitive and skeptical and we hold dear the practice of publishing results following an independent review by qualified experts. Moreover, by publishing results, scientists generally agree that the reagents reported, including cells, are available to be shared with the research community. In

this way results can be independently verified and new directions and discoveries can be explored. In the present case, only a handful of the sixty+ embryonic cell lines have been published so it is not yet possible to evaluate or comment on the quality of cells. Nonetheless, legitimate scientific questions about the growth, differentiation potential, age, and purity of the lines must be considered. Decades of experience with mouse embryonic stem cells have shown that ES cells can lose their differentiation potential, become contaminated, accumulate mutations, and tend toward spontaneous or uncontrolled differentiation. The fact that mouse ES cells lose their full potential with increasing age or passage number is only one reason to believe that the sixty+ cell lines will not be sufficient for the years of research required to investigate therapies with these cells. Looking ahead to clinical applications, including transplantation and the problem of immunological rejection, there will certainly be a need for broader genetic diversity of cell lines. There may also be a need for cell lines that have been isolated without the use of mouse feeder layers.

I hasten to add that I am not criticizing the NIH nor the scientists who have reported the isolation of the sixty human embryonic stem cell lines. Indeed, the scientists have not published their work and they may well wish to further characterize the cells before doing so. It is therefore too early to tell how many of the sixty+ lines are truly useful embryonic stem cell lines. Preliminary indications from press reports do suggest that the final number will be significantly less than sixty. If the available lines have been grown extensively and have a high passage number that will further reduce their value.

AVAILABILITY

A separate issue concerns whether the cell lines will be made available to federally funded researchers in a timely manner and without restrictions on their use for research. It is noteworthy that most of the entities that have isolated the sixty+ human embryonic stem cell lines are companies with proprietary and commercial interests. In addition, there are relevant patents on some of the cells that may further restrict their distribution and use. Experience shows that the negotiation of transfer from those who own a reagent to federally funded scientists can be slow, expensive, and sometimes accompanied by onerous restrictions on use. It is obvious that the legitimate interests of companies may not coincide with scientist's research plans or our Nation's public health policy.

I believe this problem of access is likely to be quite serious. The NIH plan to create a registry of cells will leave it to individual investigators to negotiate for transfer of the cells. This places a heavy burden on researchers and one can anticipate, at a minimum, significant delays. In some cases the terms of the transfer may be too restrictive to allow scientists access to the material. Finally, I note that some of the potential suppliers have already indicated that they lack the resources and incentive to prepare their cells for distribution.

CREATE A FEDERAL REPOSITORY FOR HUMAN STEM CELLS

I would like to suggest a plan that addresses both of these issues. Specifically, I suggest that the NIH create a repository, not a registry, for the sixty+ embryonic cell lines. The NIH could collect the cell lines, determine their quality, and certify them for distribution to qualified researchers. Equally important, this plan would have the NIH negotiate favorable terms with the suppliers, set out in a Material Transfer Agreement, so that scientists could use the cells for research purposes. The Federal government and the NIH are in an immeasurably stronger position than are individual investigators to obtain the human embryonic stem cell lines from suppliers, verify their quality, and arrange for their distribution.

SUMMARY

In conclusion, Mr. Chairman, I think that President Bush and Secretary Thompson have proposed a plan that will allow federally supported scientists to begin to explore the potential of human embryonic stem cells and work toward a cure for numerous diseases. This is a very important step forward. If my remarks today seem cautious, the reason is the uncertainty about the quality, availability and longevity of the cells. Assuming that some of the sixty cell lines are made available, federally supported scientists can work to understand how these cells can be directed to differentiate. As the studies progress to the point where clinical applications can begin, I expect the plan will have to be revisited because the viability or utility of the sixty+ cell lines will have been exhausted.

In closing, I thank you and the Committee once again for the privilege of speaking to you about this important area of biology.

The CHAIRMAN. Ms. Hersey?

Ms. HERSEY. Good afternoon, Mr. Chairman and distinguished members of the committee.

My name is Karen Hersey. I am senior counsel for intellectual property at the Massachusetts Institute of Technology. It is my understanding that I have been invited here today for the purpose of providing you with an introduction and an overview of the subject of Material Transfer Agreements, known as MTAs, about which you have already heard this morning, and the role that they traditionally play in the exchange of materials for scientific research.

As we already know from our colleagues at the University of Wisconsin, there is every expectation in the academic community that access to stem cells for research will involve the execution of a Material Transfer Agreement between the stem cell provider and the organization requesting them.

MIT does not have a medical school, and in terms of the numbers of materials that we request access to, it is small compared with those institutions that have larger faculties, larger student bodies, and medical schools. However, MIT's faculty, students, and staff are engaged in a substantial volume of research in biology, biotechnology, bioengineering, and so forth, where biological materials are used every day to investigate and teach areas of advanced science.

Like every research unit, whether academic or industrial, MIT investigators depend upon the availability of and the access to new materials developed by others to move their research forward. The materials are often proprietary to their owners and not commercially available, or they may be commercially available at a very steep price that the university generally does not have to pay only if it accepts materials under restrictive conditions. And in some cases, the materials will be made available to the academic and industrial communities under a common set of terms that we in academic find ourselves trying to work with in a contractual framework that is not suited to our environment.

Twenty years ago when I first joined MIT as a licensing attorney, the term "Material Transfer Agreement" was virtually unknown, or at least unknown to those of us in the administration. We can reconstruct from the lament we often hear recalling the "good old days" that materials were transferred from scientist to scientist and from organization to organization through a phone call or a verbal handshake. From time to time, one-page documents or releases arrived, generally containing warnings that the materials might be toxic, that they were not to be used for human subject research, and requiring the receiving party to release the sending party from all responsibility for use of the materials.

These one-page notifications were almost always signed by the investigator receiving the materials. A check of our database shows that MIT institutionally signed a total of eight MTAs in 1989.

That was yesterday. Today the story is far different. My office at MIT has overall responsibility for incoming material transfer activity at MIT. We have one attorney and one paralegal negotiating more than 75 Material Transfer Agreements a year. We have a database where all MTAs, their status as active or inactive, the lab where the materials are placed, and the responsible investigator

are logged, and where the restrictions on use of the materials are also logged. There are over 600 entries covering materials in active use, and we are a relatively small university. The larger State universities and medical schools are looking at exponential increases in these numbers.

So what has happened to change the simple handshake between scientists into a fullblown negotiation between organizations, often taking months? No doubt there will be any number of theories out there that might be supported, but as I consider events over the last decade and a half, it leads me to attribute the change to three factors.

The first is the explosion of the biotechnology industry and the recognition by both industry and the academic community during the 1980's and 1990's that certain combinations of the materials, certain methods of producing them or methods of using them, could in fact be patented.

From then on, the materials, especially those that were unique, took on an added value, and the transfer of them under terms that would protect intellectual property rights of the owner became singularly important.

The second was the companion recognition in the late 1980's that the sharing of materials might just translate into an advantageous business opportunity for the owner. If materials could be cast among academic scientists, industry bench scientists, and Government researchers, might there not be interesting knowhow, improvements, and new discoveries that could be reeled back in if the materials owner implanted hooks into its agreements?

Third, it is clear from the negotiations we conduct now that fear also played a role in the demise of the traditional transfer by handshake. That is, fear of deep-pockets liability if materials were misused and also fear that a potential business opportunity for the materials owner might be thrown away if materials were sent out with no hooks applied.

That background should provide a clearer understanding of why, in today's typical Material Transfer Agreement received by an academic institution, it is now common that some combination of limitations, restrictions, give-backs or reach-throughs will be found. Before the materials can be introduced into scientific research programs, the terms under which the owner is willing to make them available will need to be reconciled with the proposed scientific research program, the sources of funding for it, and the institutional policies having to do with freedom to publish, the importance of sharing research findings with colleagues, and technology transfer.

If I may, I would like to just take a very short time to take you through some of the very common but problematic terms that we are apt to see in the agreements that must be signed before the transfer of materials can be accomplished.

I would like to say that except as between nonprofits, it is totally unusual for us to see a one-page Material Transfer Agreement unless the type size is minute. Most often these agreements will run well beyond the two-page quick transaction limit. They will commonly define or identify the materials they cover and routinely expand that definition of materials to subsume any progeny that might be split off or replicated. While that is clearly understand-

able, unfortunately, all too often the definition of “the materials” is expanded by the owner to encompass “modifications and derivatives” of them. This is where the problems for the receiving scientists are likely to begin, for if the owner owns the materials under this expanded definition, the owner also ends up with ownership of the modifications and the derivatives made by the receiving scientist. The ownership problem is exacerbated if the materials provider also wants ownership rights to all improvements, inventions or discoveries developed as a result of using the materials.

If there is not an ownership issue, there is most likely a licensing issue. Materials owners may require an exclusive license, royalty-free, to “all inventions and research results” made through use of the materials; or they may require open-ended options or first refusal rights to license inventions relating to use of the materials.

The CHAIRMAN. We can give you another minute or two to wrap up.

Ms. HERSEY. Thank you, Senator.

At a minimum, if the materials provider is a commercial company, a university may expect to grant that company a royalty-free, nonexclusive license.

I would just like to end by giving you a couple of observations that might help as you look at or contemplate the kinds of agreements that may come in with the materials that are going to be used by NIH research.

We do have at MIT a slightly more difficult time with material transfer agreements coming in from foreign organizations. There is a problem with control over use of the materials, intellectual property rights, and in fact, some of the materials are not owned by the foreign institutions at all but by the faculty, the scientists who develop them.

Finally, how do material transfer agreements really affect the scientific work of a university? They tend to be comprehensive legal agreements presenting unique and complex issues for a university. That means they are time-consuming to negotiate, as you have already heard, and hold up research efforts. They often contain ownership, licensing and reach-through terms and conditions that are inconsistent with Federal requirements attached to federally-funded research. They may prohibit or restrict publication of research in a way that is unacceptable for an academic institution. They may discourage innovation because in fact the materials provider will control commercialization rights.

Thank you very much.

The CHAIRMAN. Thank you very much, Ms. Hersey.

[The prepared statement of Ms. Hersey follows:]

PREPARED STATEMENT OF KAREN HERSEY

Mr. Chairman and distinguished members of the committee. My name is Karen Hersey. I am Senior Counsel for Intellectual Property at the Massachusetts Institute of Technology. I am pleased to have the opportunity today to provide you with an introduction to the subject of material transfer agreements and the role they traditionally play in the exchange of materials for scientific research. As we already know from our colleagues at the University of Wisconsin, there is every expectation in the academic community that access to stem cells for research will involve the execution of a material transfer agreement between the stem cell provider and the organization requesting them.

MIT is a small institution compared with most other U.S. research universities and we do not have a medical school. However, MIT's faculty, students and staff are engaged in a substantial volume of research in biology, biotechnology, bio-engineering, biochemistry and related disciplines where biological materials, including cell lines, plasmids, vectors, sequences, monoclonal antibodies and others are used every day to investigate and teach areas of advanced science. Like every research unit, whether academic or industrial, MIT investigators often depend upon the availability of, and access to, new materials developed by others to move their research forward. The materials are often proprietary to their owners and not commercially available; or they may be commercially available at a steep price that the university generally does not have to pay if it accepts the materials under restrictive conditions; and, in some cases, the materials will be made available to the academic and industrial communities under a common set of terms and we, in academia, find ourselves trying to work within a contractual framework not suited to the academic environment.

BACKGROUND

Twenty years ago, when I first joined MIT as a licensing attorney, the term "material transfer agreement" was virtually unknown, at least unknown to the administration. We can reconstruct, from the lament we often hear recalling the "good old days" that materials were transferred from scientist to scientist and from organization to organization through a phone call and a verbal handshake. From time to time, one page documents or releases arrived that generally contained warnings that the materials might be toxic, were not to be used on human subjects, and required the receiving party to release the materials owner of all responsibility for any use of the materials. These one-page notifications were almost always signed by the investigator receiving the materials. A check of our database shows that N41T institutionally signed a total of 8 MTAs in 1989.

That was yesterday. Today, the story is far different. My office at MIT has overall responsibility for the in-coming material transfer activity for MIT. We have one attorney and one paralegal negotiating more than 75 material transfer agreements each year. We have a database where all MTAs, their status as active or inactive, the lab where the materials are placed, and the responsible investigator are logged. There are over 600 entries covering materials in active use—and we are a very small university. The larger State universities and medical schools are looking at exponential increases in these numbers.

What has happened to change a simple handshake between scientists into a full-blown negotiation between organizations, often taking months? No doubt there will be any number of theories that might be supported, but as I consider events over the last decade and half, my experience leads me to attribute the change to three main factors.

The first is the explosion of the biotechnology industry and the recognition by both industry and the academic community during the 1980s and early 1990s that certain combinations of these materials, certain methods of producing them or methods of using them, in fact, could be patented. From then on, the materials, especially those that were unique, took on an added value and the transfer of them under terms that would protect intellectual property rights of the owner became singularly important. The second was the companion recognition by the late 1980s that the sharing of materials might just translate into an advantageous business opportunity. If materials could be cast among academic scientists, industry bench scientists, and government researchers might there not be interesting know how, improvements, and new discoveries that could be reeled back in if the materials owner implanted hooks into its agreements. Third, it is clear from the negotiations we conduct now that fear also played a role in the demise of the traditional "transfer by handshake". That is, fear of "deep pockets" liability if materials were misused and also fear that a potential business opportunity for the materials owner might be thrown away if materials were sent out with no hooks applied.

This background should provide a clearer understanding of why, in today's typical material transfer agreement received by an academic institution, it is now common that some combination of limitations, restrictions, give-backs or reach-throughs will be found. Before the materials can be introduced into scientific research programs, the terms under which the owner is willing to make them available will need to be reconciled with the proposed scientific research program, the source of funding for it, and institutional policies having to do with freedom to publish, the importance of sharing of research findings with colleagues, and technology transfer.

COMMON MTA TERMS, TODAY

First, let me say that, except as between nonprofits as I will explain later, it is very unusual for us to see a one-page material transfer agreement today, unless the type size is minute. Most often these agreements run well beyond the two-page quick transaction limit. They will commonly define or identify the materials they cover, and routinely expand the definition of the materials to subsume any “progeny” that might be replicated. Unfortunately, all too often the definition of what are “the materials” is expanded by the owner to encompass “modifications and derivatives” of them. This is where the problems for the receiving scientist are likely to begin; for, if the owner owns the materials, the owner also ends up with ownership of the modifications and derivatives made by the receiving scientist. The ownership problem is exacerbated if the materials provider also wants ownership rights to all improvements, inventions or discoveries developed as a result of using the materials.

If there is not an ownership issue, there most likely is a licensing issue. Materials owners may require an exclusive license, royalty-free, to “all inventions and research results” made through use of the materials. Or they may require open-ended options or first refusal rights to license inventions relating to use of the materials. At a minimum, if the materials provider is a commercial company, a university may expect to grant the company a royalty-free, nonexclusive license to inventions made as a result of using the materials. As a result, the promise of an MTA-encumbered invention as a viable business opportunity for the inventor and his or her institution is significantly diminished.

Where ownership and licensing issues can be successfully maneuvered around, other limitations, restrictions or encumbrances often result in additional obstacles. For instance, the materials provider may require the researcher to hold all results learned from using the materials in confidence, may require a right of review and approval for any publication dealing with the materials, may require a right of approval over any transfer to a third party of the materials, their progeny, derivatives, improvements and so forth, may tag on “reach-through” rights to second and third generation uses of the materials or derivatives of them in terms of royalty-sharing or first commercial rights to exploit. It should not be a surprise that the list of encumbrances generally grows with the perceived value of the materials as a business opportunity.

GENERAL OBSERVATIONS

I will finish up this short discussion of the role material transfer agreements play in current-day research efforts with a very few general comments.

- The transfer of materials from university to university or nonprofit to nonprofit is most often accomplished under a one-page document called a Uniform Biological Material Transfer Agreement, or UBMTA. This is a simplified method of transfer agreed upon among the U.S. research universities during the early 1990s with the help of NIH. The providing university does not attach strings to the use of the materials, but, in some cases does have an interest in where they may be transferred by the receiving university. An attempt was made at the same time to convince industry to join in a simplified transfer mechanism, but it was not successful.

- At MIT we have a slightly more difficult time with material transfer agreements from foreign organizations or companies. They seem to be concerned with maintaining control of their properties either by claiming ownership of derivatives and modifications or by prohibiting the receiving scientist from obtaining any independent intellectual property rights through uses of the materials. And, significantly, we find restrictions placed on uses, ownership and further transfer because foreign universities or institutes often do not own materials, or do not have the right to control the distribution of them. Unlike the situation with U.S. universities, in Europe and elsewhere materials are often the property of the scientist or professor who developed them.

- Where materials are patented there is an extra layer of complications that arises. The university community will very often be successful in getting a non-commercial research right or license to use a patent covering the materials, but this is as far as it goes. Any future commercial use requires a license from the patent holder or no license rights at all may be available, hence any commercial use that would infringe the patent is cut off all together.

- Finally, how do the material transfer agreements really effect the scientific work of a university? They tend to be comprehensive legal agreements often presenting unique and complex issues for a university. That means they are time consuming to negotiate and hold up research efforts. They often contain ownership, licensing or reach-through terms and conditions that are inconsistent with Federal

requirements attached to federally-funded research. They may prohibit or restrict publication of research in a way that is unacceptable for an academic institution. They may discourage innovation because the control of the research output rests with the materials provider or, at a minimum, establishes a preference for the provider to exploit new discoveries made using the materials. Last, and a subject we've not considered at all today, they may contain indemnification obligations that amount to strict liability and are either not within the statutory authority of a State institution to accept or present an unacceptable risk to the endowment of a private institution.

This concludes my brief remarks on a complex subject. I am most appreciative of the Committee's indulgence and will be pleased to answer any questions you may have.

The CHAIRMAN. Dr. Childress?

Mr. CHILDRESS. Good afternoon, Mr. Chairman and members of the committee.

I am James Childress. I teach religious ethics and biomedical ethics at the University of Virginia and also serve on the National Bioethics Advisory Commission.

I have been asked to present my own views on the ethical issues in human stem cell research. In doing so, I will sometimes draw on NBAC's report on this topic along with its recommendations, which I as a commissioner helped prepare and also endorsed.

I will briefly summarize several points from my longer written testimony and would respectfully request that that testimony be entered into the record.

The CHAIRMAN. All of the testimony will be included.

Mr. CHILDRESS. I thank you very much.

I appreciate the thought and consideration that went into President Bush's policy, but other more flexible policies are also ethically acceptable and even preferable.

President Bush's policy suggests that it is ethically acceptable to use Federal funds for research on stem cell lines that were derived prior to his announcement on August 9 if the derivation also met certain ethical requirements—specifically, that donors or embryos that were created solely for reproductive purposes must have given informed consent without any financial inducements.

If this policy is ethically acceptable and satisfies basic ethical standards—and I believe it does—it should also be ethically acceptable to do the same thing prospectively—that is, to provide Federal funds for research on stem cell lines derived in the future, after August 9 as well as before, within the same ethical guidelines. The prospective policy would offer greater and needed flexibility, especially in view of the scientific uncertainty about the value of the approved cell lines. And it would be ethically preferable because it would increase the possibilities for important research without violating ethical standards.

This prospective policy can be undertaken without sanctioning or encouraging further destruction of human embryos. Those were legitimate, major concerns in President Bush's statement. We can establish effective ethical safeguards to ensure that a couple's voluntary decision to destroy their embryos is voluntary and informed, or that their decision to donate them for research is voluntary, informed, and uncompensated. The research, then, would only determine how the destruction occurs, not whether it will occur.

In making these points, I want to stress that no consensus exists among religious and secular moral traditions in our society about

the moral status of the unimplanted human embryo. Public policy in our pluralistic society has to respect diverse fundamental beliefs, and yet it must not be held hostage to any single view of embryonic life.

Whichever policies are finally adopted to enable stem cell research to go forward within ethical limits, we will need a very strong public body to review protocols for deriving stem cells from embryos and to monitor these research. Perhaps the Council on Bioethics which President Bush has announced can fulfill these functions. If not, some other public body will be needed. For example, the UK has established a statute, the Human Fertilization and Embryology Authority, which would use all embryo research as well as licensing of reproductive technology and fertility clinics. It reviews all embryo research in public and private arenas. Congress might consider that model for our society as well.

In a recent editorial in *Science*, ethicist LeRoy Walters stressed that "Government's and their advisors should be humble and flexible, but also decisive and courageous." We must carefully scrutinize claims of scientific promise, but we must not unduly constrain research that may help alleviate human suffering and reduce the number of premature deaths.

Indeed, we have a collective moral duty to try to alleviate human suffering and reduce premature deaths just as we have a collective moral duty to respect important ethical limits in dealing with developing human life.

We must also provide clear and stringent ethical safeguards in stem cell research, along with strong review and oversight. And I think in the final analysis, we must avoid unduly rigid rules that appear to be arbitrary and inconsistent.

Thank you very much for your attention. I will be glad to answer any questions.

The CHAIRMAN. Thank you, Dr. Childress.

[The prepared statement of Mr. Childress follows:]

PREPARED STATEMENT OF JAMES F. CHILDRESS

Good morning, Mr. Chairman and members of the committee. I am James Childress. I teach in the Department of Religious Studies, the Medical School, and the Institute for Practical Ethics at the University of Virginia. I am also a member of the National Bioethics Advisory Commission (NBAC). I have been asked to present my own views on the ethical issues in the debate about public policies toward human stem cell research, especially embryonic stem cell research. Even though I am not testifying on NBAC's behalf, I will sometimes draw on NBAC's report and recommendations, which as a commissioner I helped to prepare and also endorsed.¹

AN ETHICALLY ACCEPTABLE POLICY

I very much appreciate the thought and consideration that went into President Bush's announced policy on the use of Federal funds in human embryonic stem cell research, but I would argue that other, more flexible policies are also ethically acceptable, and even preferable. Consider three possible options:

(1) Provide Federal funds for research on cell lines derived (using non-Federal funds) from embryos prior to August 9, 2001 within certain ethical guidelines (President Bush's announced policy).

¹ See National Bioethics Advisory Commission, *Ethical Issues in Human Stem Cell Research*, Vol. 1: Report and Recommendations (Rockville, MD, September 1999). In November 1999, I presented NBAC's views at the hearing on "Embryonic Stem Cell Research" before the Subcommittee on Labor, Health and Education of the Senate Appropriations Committee. I request that the Executive Summary of NBAC's report be entered into the public record of today's hearing.

Provide Federal funds for research on cell lines derived (using non-Federal funds) from embryos, earlier or in the future, within certain ethical guidelines (NIH's earlier proposed policy).

Provide Federal funds for both the derivation of, and research on, cell lines derived from embryos within certain ethical guidelines (NBAC's recommendation).

President Bush's announced policy (#1) suggests that it is ethically acceptable to use Federal funds for research on stem cell lines that were derived, using non-Federal funds, prior to his announcement on August 9, if the derivation also met certain ethical requirements, including the informed consent of donors of embryos created solely for reproductive purposes and the absence of financial inducements.² If policy #1 is ethically acceptable—as I believe it is—then it should also be ethically acceptable to do the same thing prospectively (policy option #2). That is, it should be ethically acceptable to provide Federal funds for research on stem cell lines derived in the future, after August 9 as well as before, with non-Federal funds and within the same ethical guidelines. This prospective policy would offer greater—and needed—flexibility for the short-term and long-term future. And it would be ethically preferable because it would increase the possibilities for important research, without violating relevant ethical standards.³

President Bush's statement noted that the first policy (#1), which includes about sixty stem cell lines (about which there is some scientific uncertainty and controversy),⁴ “allows us to explore the promise and potential of stem cell research without crossing a fundamental moral line by providing taxpayer funding that would sanction or encourage further destruction of human embryos that have at least the potential for life.” However, I believe that ethically we can provide Federal tax funds for research on stem cells derived after as well as before August 9, using non-Federal funds, and that this can be accomplished without sanctioning or encouraging further destruction of human embryos. To do so, we must establish effective ethical safeguards. Those safeguards should ensure to the greatest extent possible the couple's voluntary and informed decision to destroy their embryos—rather than use them or donate them to another couple—and their voluntary and informed decision to donate them for research. The research would then determine how the destruction occurs, not whether it will occur; as matters stand in most jurisdictions, couples may determine how to dispose of their embryos.

It is possible to go further than either of these first two policies and recommend, as NBAC did, a third option—the provision of Federal funds for both the derivation of stem cells from embryos and research on those cell lines, again in accord with ethical requirements. One argument for this option is that a strict separation between derivation and use would adversely affect the development of scientific knowledge. For instance, the methods for deriving embryonic stem cells may affect their properties, and scientists may increase their understanding of the nature of such cells in the process of deriving them.

In short, I see no ethical reason for limiting Federal funding to research with cell lines derived by some arbitrary date, as long as future derivation, with non-Federal funds (option #2) or Federal funds (option #3), also respects the same moral limits and we establish effective ethical safeguards. Indeed, our collective moral duty to alleviate human suffering and reduce the number of premature deaths provides a strong ethical reason to support this research, within moral limits.

RESPECT FOR THE EMBRYO

There is widespread agreement, as NBAC observed, that “human embryos deserve respect as a form of human life,” but, at the same time, sharp disagreements exist “regarding both what form such respect should take and what level of protection is required at different stages of embryonic development.”⁵ At the very least this “respect” implies

- that early embryos should not be used unless they are necessary for research,
- that embryos remaining after in vitro fertilization (IVF), as well as cadaveric fetal tissue, should not be bought or sold, and
- that alternative sources of stem cells should simultaneously be explored.

Indeed, given the promise of this research, and the uncertainty about which stem cells might be adequate and which might be superior for various purposes, research

²See President George W. Bush, “Stem Cell Science and the Preservation of Life,” *New York Times* August 12, 2001.

³This is similar to the policy NIH initially proposed in December 1999 and further refined in 2000.

⁴See “President Bush's Stem Cell Policy,” *A Statement of the American Association for the Advancement of Science*, August 17, 2001.

⁵See NBAC, *Ethical Issues in Human Stem Cell Research*.

on stem cells derived from different sources should be eligible for Federal funding. The goal of realizing the therapeutic promise of stem cell research is ethically significant. It is also ethically important to treat the different sources of stem cells with appropriate respect.

One interpretation of appropriate respect for early embryos would rule out their deliberate creation in order to use them in research. I supported NBAC's recommendation that, at this time, Federal agencies should not fund research involving the derivation or use of embryonic stem cells from embryos made solely for research purposes, whether they were made by IVF or by somatic cell nuclear transfer into oocytes. However, in this area, it is ethically dangerous to say "never." For now, it appears to be possible to develop enough cell lines without creating more embryos, and there appears to be no need for nuclear transfer unless and until therapy is possible, at which time matched tissue may be needed. As the science develops, it may be necessary to revisit the question about so-called "therapeutic cloning."⁶

DIVERSITY OF RELIGIOUS AND SECULAR POSITIONS

Views about appropriate respect for the embryo hinge on convictions about the embryo's moral status. As a scholar in religious ethics, I have been fascinated by the diverse religious views on human embryonic stem cell research, both across traditions and within traditions. On May 7, 1999 NBAC convened a meeting at Georgetown University to hear presentations on religious perspectives relating to human stem cell research. Altogether eleven scholars in Roman Catholic, Jewish, Eastern Orthodox, Islamic, and Protestant traditions presented formal testimony that day, and two others made statements in the public comment period. Their statements, as well as later statements of other traditions (e.g., the Mormon tradition), reveal significantly different perspectives on the ethical acceptability of research on unimplanted human embryos. Even when opposed to abortion, different religious positions may reach divergent moral conclusions about human embryonic stem cell research. Their different conclusions follow, in part, from different premises about the moral status of the early embryo existing outside a woman's womb.

No consensus exists among religious traditions or secular moral traditions—about the moral status of the extracorporeal embryo. This diversity sets the context for an ethical assessment of public policy toward human embryonic stem cell research. An ethical public policy in our pluralistic society has to respect diverse fundamental beliefs. And yet it must not be held hostage to any single view of embryonic life.

STEM CELL LINES DERIVED FROM ABORTED FETAL TISSUE

Another possible source of stem cells—human embryonic germ cells from aborted fetuses—has received scant attention recently.⁷ However, precedent exists in U.S. policies for providing Federal funds to support research on cell lines derived from aborted fetuses. This precedent appears in the framework developed for the use of cadaveric fetal tissue in transplantation research.⁸ This framework seeks to separate as much as possible a pregnant woman's decision to abort from her decision to donate fetal tissue for research. The rationale for this separation is to avoid any possibility, however slight, that the opportunity to donate fetal tissue in federally funded research could provide an additional motivation for a woman to have an abortion.

Several "ethical safeguards" were erected in order to prevent the use of fetal tissue in federally funded transplantation research from encouraging abortions. For example, these safeguards separate the consent process for abortion from the consent process for the donation of fetal tissue for research, and prohibit the donor of fetal tissue from designating the recipient of the transplant. These ethical guidelines, which appear to have been effective in human fetal tissue transplantation research, should now be extended to stem cell research as well, as NBAC has recommended and NIH has proposed.⁹

⁶NBAC's report on human stem cell research anticipated that privately-funded research would use deliberately created embryos, whether created through IVF or cloning, and that careful monitoring of this private sector research would enable the Federal government to determine when, if ever, the time has come to fund the creation of embryos for research.

⁷See Alta Charo, "Bush's Stem Cell Decision May Have Unexpected and Unintended—Consequences," *The Chronicle of Higher Education*, Tuesday, August 14, 2001.

⁸For the debate about human fetal tissue transplantation research, see the discussion in James F. Childress, *Practical Reasoning in Bioethics* (Bloomington, IN: Indiana University Press, 1997).

⁹See NBAC, *Ethical Issues in Human Stem Cell Research*, Vol. 1, pp. 68-69, Recommendation #1.

ANOTHER APPROACH TO PUBLIC POLICY—THE U.K. EXPERIENCE

The United Kingdom has responded quite differently than the U.S. to human embryonic stem cell research, including “therapeutic cloning.” Following the 1984 Warnock committee report, the British government implemented most of that committee’s recommendations in the 1990 Human Fertilisation and Embryology Act, which, among other things, established the Human Fertilisation and Embryology Authority (HFEA). Over the last decade, the HFEA, currently chaired by Ruth Deech, has had authority over in vitro fertilization, in policy and in practice. The Authority also licenses and monitors all human embryo research in the U.K., whatever the source of funding. In addition, it approves, in limited circumstances, the creation of embryos for research purposes. Over 53,000 embryos have been used in research, while 118 have been created specifically for research. In January, 2001, following vigorous public debate, the British Parliament approved regulations to enlarge the range of acceptable goals for human embryo research and also to permit the creation of embryos for research by nuclear transfer (“therapeutic cloning”).

In the U.K., then, years prior to the recent debate about stem cell research, several substantive and procedural standards were established for embryo research, including the creation of embryos for research. Furthermore, the public appears to have considerable confidence in that framework, based on a decade’s experience. As a result, the acceptance of “therapeutic cloning” required only an extension of the existing framework, rather than the invention of a new one.

The U.K.’s strict regulation of reproductive technologies and authorization, but also tight control over, embryo research appears to have created a context for a positive response to the possibilities of human stem cell research.¹⁰ By contrast, in the U.S., regulation of reproductive technologies and fertility clinics, which is under the control of the states, is, at best, limited and uneven, and the Federal government has not allowed the use of Federal funds for embryo research (though, of course, privately funded research proceeds). As a result, the task of formulating public policy toward human embryonic stem cell research is much more challenging in the U.S.

CONCLUSION

In conclusion, if President Bush’s announced policy is ethically acceptable, as I believe it is, there is, in my judgment, no cogent ethical reason for stopping where that policy stops with the use of stem cell lines that were derived from embryos by August 9, 2001. Indeed, that temporal restriction is difficult to defend from an ethical standpoint. It is possible to use non-Federal funds (or even, I would argue, Federal funds) to derive stem cell lines from embryos within certain ethical requirements, and to provide Federal funds for research on those lines without sanctioning or encouraging the destruction of embryos or the creation of so-called “extra” or “surplus” embryos in clinical IVF. I would support these other policy options (that is, derivation with non-Federal funds or with Federal funds) on the grounds that they will probably enable important research to proceed more rapidly, and will not breach crucial ethical boundaries. In addition, it is, in my judgment, ethically justifiable to provide Federal funds for deriving and conducting research on stem cell lines developed from aborted fetal tissue, in accord with the guidelines and regulations already established for human fetal tissue transplantation research.

Whichever policies are finally adopted to enable important and promising stem cell research to go forward within ethical limits, we will need a strong public body to review protocols for deriving stem cells from embryos (and from fetal tissue) and to monitor this research.¹¹ Perhaps the Council on Bioethics, which President Bush has announced, could fulfill these functions. If not, some other public body will be needed, as the U.K. experience suggests. In the UK, the Human Fertilisation and Embryology Authority is statutorily established, and that might be a model for Congress to consider. Indeed, Congress might consider whether we now need some oversight of human embryo research in the private arena.

It is safe to assume that no policy currently under discussion will be the final one. We will need to revisit this research again and again as the science develops and as its ethical implications become clearer, particularly through a public body’s review and oversight. Thus, no policy will end the national conversation about how to balance, over time, the relevant ethical considerations. Our public dialogue needs

¹⁰ For helpful discussions of policy in the U.K., see LeRoy Walters, “Human Embryo Research: Lessons from History,” *Science* 293 (August 24, 2001): 1401, and Nicholas Wade, “Clearer Guidelines Help Britain to Advance Stem Cell Work,” *New York Times*, August 14, 2001.

¹¹ See NBAC, *Ethical Issues in Human Stem Cell Research*, Vol. 1, pp. 74–77, Recommendation #8.

to continue, with the kind of reflective leadership that Congress, at its best, can provide. While this dialogue continues, we need a policy with greater flexibility than the one President Bush announced, but also with closer review and oversight than some would like.

In a recent editorial in *Science*, ethicist LeRoy Walters stressed that “Governments and their advisors will need to be humble and flexible, but also decisive and courageous.”¹² We must carefully scrutinize claims of scientific promise, being wary of unfounded optimism, but we must not neglect research that offers a significant prospect of major medical breakthroughs that may alleviate human suffering and reduce the number of premature deaths. As a society, we must provide clear and strong ethical guidelines, regulations, and safeguards in stem cell research, while avoiding unreasonably rigid rules that appear to be arbitrary and inconsistent.

Thank you—I will be glad to answer any questions.¹³

The CHAIRMAN. Father FitzGerald?

Father FITZGERALD. I would like to thank the chair, Senator Kennedy, and the members of this distinguished community for this opportunity to come before you today to discuss this issue.

I would like to bring to bear on this issue my background in molecular genetics, in bioethics and in religion to present a somewhat different perspective on this issue than I think we have heard yet today, and in doing so, I would like to offer a caveat. There is no way that I can do justice in the brief time allotted to me to the numerous serious, well-informed and thoughtful people who are deeply concerned about this research and the ethical and moral ramifications of pursuing it. These people, of course, include scientists who have no specific religious affiliation.

Since I have limited time, let me focus on an issue that was raised earlier by Senator Frist and then again by Senator Dodd. That is the issue of what do we do when we do not know. There is much in this area that we do not know. We do not know much of the science, and we do not know much of what the ethical, moral, and social ramifications will be. How are we going to respond to that lack of knowledge, because in that lack of knowledge, we truly run the risk of overselling the promise and underemphasizing the problems associated with human embryonic stem cell research.

As Senator Clinton stated, it is extremely important that we receive and create a factual base here on this issue, and that factual base will, of course, include more than just the scientific facts.

In addressing this controversial issue, many groups and committees, such as the National Bioethics Advisory Committee as well as the proposed committee to be directed by Dr. Leon Kass, have been gathered together, bringing experts from various fields of inquiry and interest to propose how our pluralistic society should respond to this controversial area of biological research in pursuing progress while protecting justice.

For instance, as Dr. Childress has mentioned, in trying to balance the concerns of many people in our Nation, the National Bioethics Advisory Commission came to the understanding that human embryos are not just tissue; they do have some moral status and some value to society. In deciding that, the National Bioethics Advisory Commission as well as others who have come to similar conclusions set the bar higher for us to pursue human em-

¹² Walters, “Human Embryo Research: Lessons from History.”

¹³ I am grateful to Alta Charo and LeRoy Walters for their thoughtful and helpful comments on an earlier draft of this testimony; they are absolved of any responsibility for its content.

bryonic stem cell research than it might be set for other avenues of research. So in order to clear that bar and justifiably pursue this research, one would have to meet a higher standard.

Addressing a comment made earlier by Senator Specter—he said it is important that science may have the full range of opportunity—I think it is also important to recognize and remember that we already limit what science can do, especially in terms of human research.

The two areas that are most often raised as important to address in meeting that higher standard for human embryonic stem cell research are need and the number of people who will benefit from this research. Let me first address the issue of need. Do we need human embryonic stem cell research?

Granted, human embryonic stem cell research is scientifically quite interesting, fascinating, and of great interest to the people who do that research to pursue. However, oftentimes we talk about pursuing this in connection with the number of therapies and cures that will be discovered. In fact, I believe the phrases of countless numbers of people, and as Senator Specter said, it will touch virtually every family in America.

I would argue that we could make the same claims for other avenues of research, certainly research being pursued in genetic therapies, research in proteomics, research in drug development, and of course, research in adult stem cells. All these other areas of research do not need to set the bar as high in being pursued. Embryos, human life, is not destroyed.

Yet at the same time, scientists involved in those avenues of research could make similar claims as to the potential of their research and the number of diseases they are addressing.

Second, when we talk about the number of people who will be treated and/or cured by any of these medical areas of research, we must be careful. We must again be careful not to oversell the promise, and remember that in fact there are many, even in our own Nation, who do not have access to these new technologies and cutting-edge medical products.

Actually, Senator Murray brought up a very interesting example. She asked the question would we have to keep human embryonic stem cell products hostage to such things as male baldness. And the interesting parallel there is that in the early 1990's, a drug was developed with FDA approval to treat a disease that afflicts hundreds of thousands of people a year. It is called sleeping sickness. It happens in Africa. The drug was the most effective drug known against that disease. That drug was developed because it might be a cancer research tool or a cancer therapy. When it proved not to be so, the company that was producing the drug decided not to produce it anymore, even though it could cure or at least treat hundreds of thousands of people. However, the drug is back. It is back because it has a side effect—it causes hair loss. So they have turned it into a cream that women can use to treat excessive facial hair.

When we say that we are going to promise people these wonderful potential therapies and cures, are we indeed giving them the accurate assessment of how our systems work? My issue is not necessarily specifically with the pharmaceutical industry but in prom-

ising the people of this country and perhaps the world a solution and a promise that we cannot fulfill.

I very much appreciate the work of this committee, and I appreciate the reflection that has gone into the many proposals here and the many presentations, and I certainly hope that we continue in our reflection on this very serious issue.

Thank you very much.

The CHAIRMAN. Father, that drug that you are talking about is methyltrexate. My son, who had osteosarcoma, took that drug when he was in an NIH trial, and he survived. Now, there is about an 85 to 90 percent survival rate in children with that disease. So you would have a tough time convincing me on that particular one—I just picked that up.

Father FITZGERALD. Actually, the drug is not methyltrexate; it is F-fluorothene.

The CHAIRMAN. OK. I stand to be corrected.

[The prepared statement of Father FitzGerald follows:]

PREPARED STATEMENT OF FATHER KEVIN FITZGERALD, SJ

Advances in medical research are happening at such a rapid rate that it seems new breakthroughs are announced every week in the media. These advances present the possibility for treatments and cures unheard of only a generation ago. However, advances in research can also create ethical problems seemingly so complex and convoluted that we wonder whether or not the research is worthwhile. In our society, which claims to value both progress and justice, we must find a balance between the Utopian hopes and Frankensteinian fears generated by these advances in medical research.

One area of recent advance in medical research has raised new hopes for treating serious illnesses that result from the death or deterioration of cells and tissues we require for good health. These illnesses include terrible neurological disorders such as Parkinson's and Alzheimer's, as well as tragic injuries such as paralysis caused by damage to a person's brain or nervous tissue. The basis for these new hopes is a new understanding of human stem cells and their function.

What do these stem cells do? The normal function of stem cells is to produce new cells and to replace cells we lose through the natural processes of cellular aging and death. From the time a human being begins as a fertilized egg, that human being grows and develops by cells continually dividing to make more cells. Early on in our development, when we are embryos, the primary function of most of the cells is to divide and rapidly make more cells. "Embryonic" stem cells have not yet become any particular type of cell, such as muscle or nerve, and so embryonic stem cells are thought to be capable of becoming any type of cell in the human body.

As a human being continues to develop as a fetus, infant, child, and adult, the number of cells in the body increases. During these later stages, most of the cells stop dividing and take on specific duties and become brain cells, or liver cells, or skin cells, etc. However, some cells keep their ability to divide and replace other cells that have been lost due to damage or normal aging. These stem cells are generally called "adult" stem cells. Until just the past few years, adult stem cells were considered to be only in certain tissues, like blood and skin, and to have only the capacity to replace the cells of the particular tissue within which they were situated. Recent research has now indicated that adult stem cells are present in many, if not almost all, of the tissues of the body, including the brain. In addition, adult stem cells are not limited to replacing cells from only the type of tissue wherein they are found.

New breakthroughs in stem cell research have involved both embryonic and adult stem cells. Researchers have discovered ways to isolate and grow embryonic stem cells such that they can be directed to become different types of cells that are found in the body. Since during embryonic development embryonic stem cells do become all the different types of cells in the body, researchers speculate that it should be possible, eventually, to direct embryonic stem cells to produce whichever kind of cell is needed.

Though this research sounds very promising, there are both scientific and ethical troubles with embryonic stem cell research. One scientific obstacle is the problem of controlling the development of the embryonic stem cells into the type of tissue

one might need to treat a disease or injury. Since these cells have such a great ability to make more cells of any kind, it is important that researchers know that there are no uncontrolled embryonic stem cells being implanted into a person. An embryonic stem cell that does not convert into the type of tissue desired could cause significant harm to a patient by making the wrong kind of cells in the treated tissue, or by just growing out of control and creating a tumor. Much research on embryonic stem cells would still be required in order to insure the safety of these proposed treatments. This research, in itself, raises a key moral issue.

The key moral obstacle to embryonic stem cell research is that currently the only way embryonic stem cells are obtained is by destroying an embryo. Unlike tissue or organ transplantation, where the organs are removed after the death of a person, embryonic stem cells are not harvested after the embryo has died. The procedure for removing the embryonic stem cells from the embryo destroys the embryo.

Much of our health care tradition is based on the idea that healing is a benefit to be made available to all. Consequently, it is not acceptable that for some to be healed others must be sacrificed—no matter their State in life. In response to this perspective, some argue that frozen “spare” embryos, left over from in vitro fertilization treatments and not likely ever to be used to produce a pregnancy, might justifiably be destroyed in order to get embryonic stem cells. However, using a fundamental principle of health care which states that first of all one should not unnecessarily harm another, one can counter that no human life is “spare.” Who among us has the right to decide that another human life is a “spare” life, especially when that human life does not have the chance to contest the decision? We do not consider it appropriate to take organs from dying patients or prisoners on “death row” before they have died in order to increase someone else’s chances for healing or cure. Neither, then, should we consider any embryos “spare” so that we may destroy them for their stem cells.

This defense of human life does not mean that all stem cell research must be rejected. Research on adult stem cells should be encouraged, especially in light of the new results that indicate its amazing promise for treatment and cure. For example, blood stem cells may be able to replace lost brain cells or liver cells, and vice versa. In the not-to-distant future, the issue of rejecting transplants may no longer be a problem because our own stem cells will be used to repair and replace our damaged cells and tissue.

Even taking the promise of adult stem cells into consideration, some scientists argue that the most efficient way forward is to do research on all the various types of stem cells in order to see which will be best for treating the many different diseases we wish to cure. This approach of doing all the different types of experiment that can be done is often the best way for science to proceed. But is it always the best way for a society to proceed?

We Americans know from our own history with eugenics and research on minorities or the mentally disabled the tragedies that can occur when public policies concerning human experimentation are shaped primarily by the dictates of science. More broadly, the history of humankind abounds with examples of how biological characteristics such as race, gender, intelligence, and age, have been used as justification for discrimination against certain groups within a society so that the dominant groups in a given society might take advantage of the vulnerable and those on the margins of the society. In response to these wrongs, our society has chosen to limit what experiments can be performed on human beings, even though these limits may slow scientific progress. Are we not repeating this same tragic pattern by declaring embryos of significantly lesser value than other human beings because of their developmental status? And if human embryos do have some significant value in our society, as the National Bioethics Advisory Committee concluded, then considering all the basic research that still can be done using animal models, human tissue culture, and adult stem cells, why is there a continuing clamor for the destruction of human embryos to fuel stem cell research?

One reason often put forth as justification for the destruction of more and more human embryos is the need to bring healing and cures to the thousands, if not millions, who suffer from illnesses and diseases that may be amenable to treatment with embryonic stem cell therapies. Such an argument as this is of great significance for it connects to another fundamental principle of medicine: treat sickness and heal when you can. Yet, as the argument is stated, its significance rests in part on two assumptions: 1) that embryonic stem cells will be necessary, or superior to all other options, in the treatment of certain diseases, and 2) that the thousands and millions who need the treatments will have access to them.

Addressing the first assumption, we need to recognize that the diseases suggested as likely targets for human embryonic stem cell research are also the targets of researchers using other approaches, such as genetic therapies, drug development, and

adult stem cells. It may well be the case that for many patients the treatments for their illnesses may come more quickly from research avenues other than human embryonic stem cell research, and that these alternative treatments may even be better than any treatment derived from human embryonic stem cell research.

Regarding the second assumption, we need to acknowledge that even if treatments from human embryonic stem cell research prove to be the best available and are developed first, many people who need these treatments will not have access to them. For example, the World Health Organization statistics show that approximately 900,000 children die each year of measles. Human embryonic stem cell research is not needed to prevent measles infections and the cost of the measles vaccine is dramatically less than any human embryonic stem cell treatments will be for a very long time, if they are ever produced. Hence, just because many people in the world tragically share a devastating disease, the greater tragedy is that only a relative few get to enjoy the benefits of cutting edge medical technology. This tragic reality should not prevent our pursuit of medical advances, but it should also not be forgotten when we decide as a society which medical research is justified and which is not.

If the justification for proceeding with the destruction of human embryos for research rests even in part on these two assumptions of need and the number of those who will benefit, then this justification is flawed. Human embryos need not be destroyed in order that thousands or millions might be saved.

Indeed, without the continual destruction of human embryos the future of medical advance will still be one of great hope. There are many avenues of medical research that can be pursued with broad ethical and societal support. As a people who value progress and justice, we can decide to pursue every avenue of medical research that is respectful of human life in all its stages, and brings care and healing to all those in need.

The CHAIRMAN. Dr. Chute?

Dr. CHUTE. First, I want to thank you, Senator Kennedy, and the committee for inviting me to appear today.

I come to this issue as a clinician first, as a clinically trained hematologist and oncologist. For the past 5½ years, I have also been directing research in adult hematopoietic stem cell biology.

I also want to say that it has been with great interest that I have followed the work of Dr. Thomson and those who have done embryonic stem cell line research. I have been fascinated that they have been able to propagate these cells in vitro as long as they have shown they can in peer-reviewed journals and that they can get these cells to differentiate into neuronal epithelial muscle and hematopoietic cells.

It is very understandable that patients with very serious diseases are very excited and hopeful that there may be cures in the future for such things as diabetes, Parkinson's, and Alzheimer's derived from further research on these cells.

But as the national discourse on embryonic stem cell research has progressed, there has been, ironically, a diminishing appreciation of the exceptional progress that has been ongoing and occurring in adult stem cell research, and I appear today to highlight the critical importance of the ongoing research in adult stem cell biology. In the year 2000, there were 1.2 million new cases of cancer in the United States. Cancer is the second leading cause of death in the United States, and the incidence of cancer is increasing. Adult hematopoietic stem cells have been and are currently used successfully in the treatment and cure of patients with leukemia, lymphoma and other hematologic malignancies.

Also of great interest is that newly developed methods of transplanting adult hematopoietic stem cells have now been shown to effect major remissions in solid tumors. There is a group at NIH led by Dr. Barrett and Dr. Chiles that has recently shown that kidney

cancer can be put into remission with the donation of normal peripheral blood stem cells, which is a fascinating new development in the use of these cells to treat cancer.

Therefore, as this work moves forward, an even greater number of patients will benefit from adult stem cell transplantation. As further evidence, I submit to you that the two most important medications that we as oncologists give to patients in their cancer treatments are epagen and nupagen, which are both growth factors, both of which were developed and isolated through federally-funded adult stem cell research. These medications promote the recovery of red and white blood cells following chemotherapy and allow patients' quality of life to be significantly improved while also preventing life-threatening infections.

Adult hematopoietic stem cells are the ideal vehicle for gene therapy to treat such diseases as sickle cell anemia, hemophilia and immune deficiencies. More than 100,000 children in America are threatened with these life-threatening genetic diseases. For the first time in the past 2 years, two recent publications have shown the successful gene transfer into patients with disease. Both of these studies used adult hematopoietic stem cells.

At the end of the year 2000, there were 70,000 Americans awaiting organ donation for kidney, liver, heart, or lung disease. Recent animal studies indicate that the co-administration of hematopoietic stem cells along with organ transplantation may dramatically lessen the need for immunosuppression. If this work moves forward, thousands more patients will be able to be successfully transplanted with organs with much less morbidity.

In addition to these current applications, even broader clinical therapies will derive from adult stem cells in the near future. Published reports in the last 5 years have shown that transplants of bone marrow stem cells can differentiate in vivo into functional liver cells, skeletal muscle, brain cells, and even functioning cardiac myocytes. These data indicate that a rare subset of hematopoietic stem cells is in fact pluripotent and possess at least limited plasticity. Adult cord blood stem cells can be maintained now in culture for up to 12 weeks. Our laboratory has shown that bone marrow stem cells can be expanded 10-fold in just a week of culture under specialized conditions. Whether adult stem cells will match embryonic stem cells in the treatment of diseases like Parkinson's or Alzheimer's remains unknown, and in my opinion is probably unlikely. But given the dramatic progress in adult stem cell research in the last 5 years, I think continued funding is merited.

To close, I would like to just make two points about embryonic stem cell research that are scientific concerns. First, immune barriers for embryonic stem cells to work in transplantation for treatments like Alzheimer's and Parkinson's will require immune barriers to be crossed. Scientists who are experts in this field, specifically, Dr. Thomson at Wisconsin, have argued that cloning is the way to get beyond this. In fact, I think the scientific community recognizes that if these immune barriers cannot be crossed with some method such as nuclear transfer, the translation into actual therapies for patients will be extremely difficult.

Second, animal studies indicate that the transplantation of embryonic stem cells actually has a high incidence of teratoma, or tumor development, in small animal models. In vitro differentiation and genetic engineering of embryonic stem cells prior to transplant have been proposed as methods to circumvent this problem, but both of these approaches have further technical concerns. As Dr. Thomson himself has recently cited, the heterogeneous nature of embryonic stem cell development in culture has hampered the use of embryonic stem cell derivatives in transplantation.

I close with the very brief following statement. The limitations of embryonic stem cells as a source of transplantable tissue should be openly and honestly presented to the public, since treatments and cures using these cells are certainly not imminent.

In contrast, adult hematopoietic stem cells are successfully used in the treatment of patients with common diseases every day. Genetic engineering is not required for these cells to be safely applied. New treatments for diseases are imminent with adult stem cells and not hypothetical. While scientists continue to explore the basic biology of embryonic stem cell lines, the needs of thousands of patients who benefit from adult stem cell research should not be sacrificed.

Thank you.

[The prepared statement of Dr. Chute follows:]

PREPARED STATEMENT OF JOHN P. CHUTE, M.D.

I would like to first thank Senator Kennedy and the Senate Committee for inviting me to appear at this important hearing. As a clinician who does research, it is an honor to be here. My specialty training is in Internal Medicine, Hematology and Medical Oncology. Upon completion of my clinical training in 1996, I joined the Stem Cell Biology Laboratory at the Naval Medical Research Institute. Since June 1999, I have been the Head of the Hematopoietic Stem Cell Studies Section within the joint NIDDK/Navy Transplantation and Autoimmunity Branch. The focus of our lab has been the development of methods to cultivate and expand adult hematopoietic stem cells for medical therapies. Therefore, it has been with great interest that I have followed the remarkable progress which has been made in the development of human embryonic stem cell lines. I have admired the work of investigators like Dr. James Thomson at the University of Wisconsin in demonstrating that embryonic stem cell lines can be propagated in vitro through hundreds of cell divisions and that these cells can be induced to differentiate in vitro into neuronal, epithelial, muscle and hematopoietic cells, to name just a few (1,2). In contrast, the experience of investigators in attempting to propagate and induce the in vitro differentiation of adult hematopoietic stem cells into diverse tissues has been generally unsuccessful (3,4). Understandably, physicians, legislators, the media, and most importantly, patients, have become increasingly hopeful that the further development of human embryonic stem cell research might lead to treatments and even cures for diabetes mellitus, parkinson's disease, alzheimers, muscular dystrophy, and other degenerative diseases. Unfortunately, the optimistic pronouncements by members of scientific community about the "imminent" therapies which would be forthcoming from embryonic stem cell research has raised the innocent expectations of the most vulnerable members of our society (patients with debilitating diseases) to a level which medical researchers may never meet.

Last month, President Bush set forth a policy to provide Federal funding to support ongoing research on specified human embryonic stem cell lines. During his address, he noted that the Federal government, via NIH, currently spends approximately 250 million dollars annually on "stem cell research". The overwhelming majority of this money heretofore has been applied to basic and clinical research on adult-source stem cells. In order to jump-start the Federal funding of embryonic stem cell research, it has been discussed that 100 million of the Federal dollars which the NIH would have appropriated toward adult stem cell research will be taken to support the fledgling embryonic stem cell initiative. Sacrificing 40% of the current adult stem cell research funding for the purpose of initiating further embry-

onic stem cell research would be a mistake of historical proportions and would risk harming hundreds of thousands of patients in the United States who currently benefit from adult stem cell based therapies.

The American Cancer Society estimates that there were 1.2 million newly diagnosed patients with cancer in the U.S. in the year 2000 (5). Cancer is the second leading cause of death in the United States and it continues to gain on the leader, cardiovascular disease. Adult stem cells from bone marrow, cord blood, and peripheral blood have been and are currently used safely throughout the U.S. in the treatment and cure of tens of thousands of patients with leukemia, lymphoma, and certain types of solid cancers (6). Current research advanced by NIH researchers further indicates that, when given in a "nonmyeloablative" manner (less toxic), patients with solid tumors (e.g. kidney cancer) for the first time are achieving complete remissions simply due to the anti-cancer effect of the infused bone marrow cells (7). These results indicate that an even greater number of cancer patients will benefit in the near future from adult stem cell transplantation. But more research funding will be needed to meet these goals. The success of adult stem cell research can also be measured by examining the two most important medications given to all patients who undergo chemotherapy and radiation: these medications, erythropoietin (epogen) and neupogen are natural growth factors which act within human bone marrow to stimulate red blood cell recovery and white blood cell recovery following highly toxic chemo- and radiation therapy. Without these 2 medications, thousands of cancer patients would require longer hospitalizations, suffer significant life-threatening infections, and patient quality of life would be dramatically worsened. Both of these medications were discovered via research on adult hematopoietic stem and progenitor cells.

In our laboratory, we have utilized Federal research funds to search for the genes and proteins which induce the self-renewal of adult hematopoietic stem cells (8). We are currently participating in a cooperative research agreement with Large Scale Biology Corporation (Vacaville, CA and Rockville, MD) to apply high level protein identification techniques to achieve this end. We anticipate identification of specific human stem cell growth factors within the next 2 years. This research may lead to new therapeutic growth factors which could be administered to patients with cancer to allow earlier recovery from the adverse effects of chemotherapy and radiation. Yet, despite its potent effects in the elimination of disease, bone marrow transplantation is a morbid procedure for donors, requiring one liter of marrow to be harvested for each adult transplantation. Umbilical cord blood is an alternative and attractive source of hematopoietic stem cells for this purpose, and the ease of collection and banking of cord blood stem cells could allow for a universal bank of stem cells so that the majority, not the minority, of Americans might have an immunologically matched stem cell graft available for them should they need it. But more Federal funding, not less would be needed to develop such a national cord blood bank.

Adult stem cells from the bone marrow or peripheral blood are also the ideal vehicle for gene therapy to treat such common and debilitating diseases as sickle cell anemia, hemophilia, thalassemia, and immune deficiencies (9). More than 100,000 children are afflicted with life-threatening forms of these genetic diseases in the United States (10). For the first time, 2 recent reports have demonstrated successful gene transfer and gene expression of functional proteins in patients transplanted with adult stem cells. As adult stem cell researchers continue to provide new methods to successfully introduce normal genes into adult stem cells, major diseases such as sickle cell anemia and hemophilia will become treatable for the first time. In addition, with the advent of the human genome database, an increasing number of treatable genetic diseases will be identified. But more research funding will be required to reach these goals.

As of the end of the year 2000, there were 70,373 Americans awaiting organ donation for end stage kidney, liver, heart, or lung disease (11). Organ transplant recipients face major morbidities and life-threatening complications due to the immunosuppression which they require in order to prevent organ rejection. Recent research in animal models has indicated that concomitant infusion of donor bone marrow stem cells can induce an "immune tolerant" State in the recipient which may allow long-term acceptance of the donated organ without the requirement for prolonged immunosuppression (12). The standardized clinical transplantation of donor bone marrow coupled with organ transplantation could allow tens of thousands of more patients to be successfully cured of their end stage liver or kidney disease with much less morbidity and complications.

In addition to these current clinical applications, ongoing research indicates that even broader clinical therapies will derive from adult stem cells in the near future. Investigators have demonstrated in animal models that transplanted bone marrow

stem cells have the capacity to differentiate in vivo into liver cells, skeletal muscle cells, brain cells, and even functioning cardiac muscle cells (13–17). These data indicate that a rare subset of adult hematopoietic stem cells are pluripotent and possess at least limited plasticity. Scientists in the U.S. and Italy have recently demonstrated that cord blood stem cells could be maintained and expanded in number in culture for up to 12 weeks and our laboratory has recently shown that bone marrow stem cells can be increased 10-fold in 1 week of culture under specialized conditions (18–20). The capacity to expand the numbers of human adult stem cells in vitro is a critical first step toward harnessing these cells for future medical treatments. Whether adult stem cells will be useful in the future clinical treatment of diseases such as diabetes, parkinson's or alzheimer's remains unknown and perhaps unlikely. But given the dramatic discoveries of the past 5 years, along with the fact that adult stem cells are a proven safe and genetically stable source of tissue for transplantation, continued research on adult stem cells is merited.

Embryonic stem cells hold great promise as a potential source of tissues for the treatment of many debilitating and degenerative diseases. However, that potential faces several important scientific hurdles prior to the realization of patient application. First, immune-mediated rejection of transplanted embryonic stem cell grafts will occur in recipients unless the individuals are heavily immunosuppressed. This immunosuppression would result in major morbidities and life threatening complications for patients which might outweigh the potential benefits of the transplant (1). Alternatively, a patient's DNA could be introduced into an enucleated egg, for the purposes of generating blastocysts (embryos) which contain embryonic stem cells which would be immunologically identical to the patient. Even if this form of cloning was not controversial, it is highly inefficient and would likely require large resources of eggs for the purposes of developing genetically matched tissue grafts. Second, animal studies indicate that the transplantation of embryonic stem cells leads to a high incidence of teratoma (tumor) development. This risk is clearly incompatible with patient transplantation and requires that these cells would have to be induced to differentiate in vitro into desired tissue lineage or genetically engineered prior to transplantation (1). Such transplanted cells would likely have a limited in vivo life expectancy and might require additional transplantations over time. These limitations of embryonic stem cells as a source of tissue for human transplantation should be openly and honestly presented to the public, since treatments and cures from these cells are not imminent. Most importantly, the requisite studies in small animals and primates to prove efficacy and safety are far from completed. In contrast, adult stem cells are successfully used in the treatment and cure of many diseases every day and genetic engineering is not required for these cells to be safely applied. More importantly, new treatments are imminent, not hypothetical. While scientists continue to explore the basic biology of embryonic stem cell lines, the needs of thousands of patients who benefit from adult stem cell research should not be sacrificed.

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The CHAIRMAN. Thank you very much.

I thank all the members of the panel. We are going to recess, and I would like to come back with some questions at 2:15. I know this causes some concern, perhaps, for your schedules, but if you can come back—if you cannot, I can understand, and we will submit some written questions. I do not think it will take long; hopefully, we will have you out by 3 o'clock. So if we could do that, we would very much appreciate it. We have had a very full morning, and the two parties have caucuses that start at 12:30, where I see most of our members have gone. I think that by 2:15, they will have ended, and hopefully, we will have some additional participation.

I am very, very grateful to all of our panelists.

Senator FRIST. Mr. Chairman.

The CHAIRMAN. Yes, Senator Frist.

Senator FRIST. Let me just add that this is fascinating based on the discussions this morning. If some of the panelists cannot stay, if we could just submit to them written questions, because we do not know what their schedules are. I do have questions, and I do not think we can spend a long time this afternoon, so if we could be permitted to submit written questions.

The CHAIRMAN. Certainly.

Thank you. We will meet again at 2:15.

The committee stands in recess.

[Whereupon, at 1 p.m., the committee recessed, to reconvene at 2:25 p.m. this same day.]

AFTERNOON SESSION

The CHAIRMAN. The committee will come to order.

I will invite our witnesses to return to the table if they would, please. Thank you very much for adjusting your schedules.

I would like to go through a few questions if I might, and I will start with Dr. Melton. You expressed several concerns about the re-

strictions placed on stem cell research under the President's proposal. Do you believe that the restrictions could significantly impede scientific progress and slow the development of new cures using these cells?

Mr. MELTON. Yes, I do. I do think they will impede progress.

The CHAIRMAN. Do you want to elaborate on that? We talked this morning about the issues of accessibility and reliability and safety, contamination. As a researcher, what are your concerns?

Mr. MELTON. I could give one example. You could imagine that with the cells that are available, scientists discover a means by which they can turn human embryonic stem cells into pancreatic beta cells for the treatment of diabetes. You would then want to use human embryonic stem cells that have been freshly derived in the absence of these potentially contaminating mouse feeders and use those for therapies, because that would eliminate concerns about known and unknown viruses. As I understand it, the new cell lines which would be derived would be ineligible for Federal researchers. That is one example of the possible problems that will likely arise.

The CHAIRMAN. How concerned should we be about contamination? Have you used products from other countries, and what is your own sense or knowledge as to how high you think the risk might be?

Mr. MELTON. I am not really qualified to comment on that, but I would say that the FDA, as I understand it, will treat this as a xenotransplant, which means that the hurdles and the requirements for using a therapy will be much more onerous.

Dr. Chute can probably comment more on the difficulties with using animal products in treating humans.

The CHAIRMAN. Dr. Chute?

Dr. CHUTE. Thank you, Senator Kennedy.

In our laboratory, we worked with a feeder layer that was a porcine feeder to grow adult hematopoietic stem cells. I have had iterations with the FDA both on using a porcine and a human feeder layer, and without question, there is a long series of safety tests that you have to do on the human cells that are cultivated with xeno feeder layers such as mouse/porcine. And even with a human feeder layer, there is still a very, very long list of safety tests that have to be done.

But I would make the comment that I do not think it is impossible if you use a mouse feeder layer that the human cells derived from those cultures could ever be used in the clinic. I think it just makes it more arduous, without question. It might add a year or a two potentially to the time before you get to the clinic.

The CHAIRMAN. Well, you are certainly restricted now, under the August 9 date, so you probably would not get there.

Dr. CHUTE. Correct.

The CHAIRMAN. Dr. Melton, after reviewing the agreement signed by NIH and the University of Wisconsin, I see that it expressly forbids use of the cells for therapeutic or diagnostic purposes. What are the implications of restrictions of this kind for the work you do in trying to find new treatments for juvenile diabetes?

Mr. MELTON. Well, first, I am sort of surprised by that news, because I have not seen the agreement. But if it is the case as you

say that the cells could not be used for treatments, I would think that would be a damning condition. Clearly, there is no point in doing the research that I am doing if it were not for the possibility of treating people. So I would have to see the conditions to comment further.

The CHAIRMAN. Ms. Hersey, the President's plan gives a handful of suppliers control over all the federally-approved stem cell lines. Based on your experience negotiating agreements with private companies, wouldn't you agree that this type of monopoly is likely to make it difficult for NIH-funded researchers to get prompt access to these cells?

Ms. HERSEY. Yes, I think it is going to make it very difficult, Senator.

The CHAIRMAN. Are you familiar with the other types of situations that you know of from the past that are similar to this kind of a monopoly?

Ms. HERSEY. There have been several. Especially where the company holds patent right, we have seen a number of them. In some cases, the NIH has been able to step in as they have this time and try to make a difference for the university researchers. But I would say that at least 20 percent of the time, we cannot get access to the materials we want because of the encumbrances.

The CHAIRMAN. Dr. Childress, I want to underline one point you made in your testimony. Is it fair to say that you see no ethical differences between a stem cell derived from a discarded embryo on August 9 and one derived at a later date?

Mr. CHILDRESS. As long as they meet the kinds of ethical standards that President Bush laid out, and I think those are important ones, about the embryo being left over following efforts at reproduction, that the donors give voluntary informed consent, and that there be no financial inducements. If we go forward and apply the same ethical standards to the derivation of stem cells from embryos in the future, I cannot see an ethical difference. I cannot see that what happened before August 9 and what happens after is ethically different.

The concern that some have expressed, that this might well sanction and encourage the destruction of embryos, I think is also problematic as a concern, because after all, to this point, people may well have made decisions about destruction of embryos and the possibility of privately-funded research, since that research has been going forward.

Furthermore, we really do not have evidence from fertility clinics that people deciding to discard embryos make this a major factor in decisionmaking. So I would be inclined to say that we can build the ethical safeguards to prevent the kind of scenario that has concerned many.

The CHAIRMAN. You have followed the fetal transplantation issue closely.

Mr. CHILDRESS. Yes.

The CHAIRMAN. Have you formed any impression—and maybe I could ask others on the panel as well—in that debate, we had the agreement for the use of certain fetal tissue, but we also established guidelines for utilization in the private sector—have you thought about that issue as well, and can you tell us what your

thinking has been, what the advantages or concerns would be, or perhaps the disadvantages?

Mr. CHILDRESS. First, I think there are significant parallels between the kinds of ethical safeguards one would try to set up, which appear to have been effective, in the area of human fetal tissue transplantation research, and the kinds of guidelines that would be appropriate in two different settings. One would be the use of embryos left over after in vitro fertilization, but also the research that we have not really talked about today, the derivation of embryonic germ cells from aborted fetuses. One could draw a parallel there also, and that area of research has been omitted from much of the recent discussion, and I am not sure whether it merits further attention or not. I have not followed the scientific developments on that side, but one could perhaps make a case for paying some attention to that as well.

The CHAIRMAN. Throughout your distinguished career, you have shown a deep reverence for life. Do you think that allowing federally-funded doctors both to use and derive stem cells from discarded embryos is consistent with those deeply-held beliefs?

Mr. CHILDRESS. I believe so, first of all, if we work with the notion which the National Bioethics Advisory Commission also tried to articulate, that it is very important to recognize that the embryo deserves an appropriate form of respect, appropriate to that stage of developmental life. Now, there will be widespread disagreement in society, as I have mentioned earlier, about the moral status of the embryo and exactly what kind of respect it deserves, what kind of protection is appropriate.

On the National Bioethics Advisory Commission, we drew several implications from the notion of respect for the early embryo. One certainly was that in this area, we should not be buying and selling embryos or, if we go in the direction of fetal tissue, we should not be buying and selling fetal tissue.

One could also argue that we should not use left over embryos unless they are necessary.

Now, there would be considerable debate. I happen to be on the side of those who think that, given the promise of this research for alleviating suffering and reducing the incidence of premature death, we ought to be exploring all sources of stem cells at this point. And I certainly agree with my colleagues who stress that we should not neglect adult stem cells in this process, and just seeing which ones will be most important in developing the kinds of treatments and, we hope, cures that might be possible.

One implication that we drew from this principle of respect for the early embryo was that at this point, we should not deliberately create embryos for purposes of use in research, whether it is through IVF or so-called therapeutic cloning.

We emphasized—and I would agree with this emphasis—that the point we were making was “at this time,” because it may well be necessary to revisit this question of so-called therapeutic cloning if the basic research ends up producing some clinically effective treatments that may well best be done, or perhaps only be done, with matched tissue. So it may be necessary to revisit that at some point. But we have heard from many colleagues, and we still have a long way to go before that becomes a critical question again and

then might raise the issue of the necessity of going in that direction.

I would be opposed, though, at this point to a ban on therapeutic cloning, worrying that that would indeed set an inappropriate limit for future developments.

The CHAIRMAN. Thank you.

We will submit the questions of our colleagues.

[Response to questions from committee members were not available at time of printing.]

The CHAIRMAN. I am grateful to the panel, and I thank all the witnesses for their excellent testimony. It has been an extremely informative and important hearing. It is clear that stem cell research offers a virtually unprecedented opportunity to find cures for a host of dread afflictions from cancer to heart disease, from diabetes to spinal cord injury to Parkinson's disease to Alzheimer's disease.

It is also clear that there are serious concerns in the scientific community about whether the restrictive rules currently imposed by the Bush Administration will allow this research to proceed speedily and effectively. These concerns range from the number, safety and durability of the existing cell lines to whether they will be truly widely available to researchers. The memorandum of understanding that Secretary Thompson announced this morning specifically prohibits the use of the cell lines in clinical research, the research that is done to actually test possible treatments for illnesses.

Millions of patients and their families expect that stem cell research will move forward as rapidly as possible. It will be unacceptable to offer these patients and families the promise of effective stem cell research but deny them the reality of it. We will continue to examine the questions raised at the hearing, and I am optimistic that Congress will take whatever steps are necessary to ensure that stem cell research proceeds effectively and ethically.

The committee stands in recess. Thank you all very much.

[Additional material follows:]

ADDITIONAL MATERIAL

STATEMENT OF THE ALPHA-1 FOUNDATION

Alpha-1 Foundation supports S. 723: Embryonic Stem Cell Research.

The Alpha-1 Foundation is a national not-for-profit organization dedicated to providing the leadership and resources that will result in increased research, improved health, worldwide detection and a cure for Alpha₁-Antitrypsin Deficiency (Alpha-1). Alpha-1 is a genetic disorder that results in devastating and fatal lung and liver disease. Alpha-1 is a major cause for lung transplantation in adults and a leading cause for pediatric liver transplants. Diagnosed patients can engage in preventative health measures. Treatment of the lung disease associated with Alpha-1 consists of a sole therapy that is derived from human plasma, infused weekly and is in critically short supply. Individuals with the pulmonary destruction associated with Alpha-1 often require supplemental oxygen and suffer the pain known only to those unable to catch their breath.

The Alpha-1 Foundation has joined the Coalition for the Advancement of Medical Research whose membership includes voluntary health organizations, scientific and academic societies, industry, universities, medical organizations, and others to add our voice in support of the initiative to reinstate the Federal guidelines for embryonic stem cell research. The Foundation supports the NIH guidelines in the belief that they were developed with stringent oversight and that Federally funded research will allow for this research to move forward in an ethical manner.

Further the Alpha-1 Foundation Medical and Scientific Advisory Committee (MASAC) passed a resolution supporting S. 723 because embryonic stem cell research may hold great promise in the search for a cure for Alpha-1. The list of Alpha 1 Foundation MASAC members and a copy of the resolution in support of S. 723 is attached.

ALPHA-1 FOUNDATION MEDICAL AND SCIENTIFIC ADVISORY COMMITTEE RESOLUTION
REGARDING STEM CELL RESEARCH

Whereas, the Medical and Scientific Advisory Committee of the Alpha-1 Foundation (MASAC) is aware of the many issues surrounding the use of stems cells in biomedical research and the debate regarding the National Institutes of Health Stem Cell Guidelines, and,

Whereas, MASAC appreciates the potential role of stem cell research in identifying a cure for individuals with the genetic deficiency of Alpha₁-Antitrypsin,

Therefore, MASAC resolves the following:

1. MASAC endorses the current Federal Stem Cell Guidelines as set forth by the National Institutes of Health.

1. MASAC endorses and recommends passage of US Senate bill S. 723, sponsored by Senators Specter and Harkin.

Further, MASAC recommends these resolutions be included in a letter addressed to both Senators Specter and Harkin and recommends that individuals address letters to their Congressional members requesting support of S. 723.

MEDICAL AND SCIENTIFIC ADVISORY COMMITTEE MEMBERS

James K. Stoller, M.D., Chair, Cleveland Clinic Foundation
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 Robert M. Senior, M.D., Washington University School of Medicine
 Edwin K. Silverman, M.D., Ph.D., University of Maryland School of Medicine
 Gordon L. Snider, M.D., Boston VA Medical Center
 Charlie Strange, M.D., Medical University of South Carolina
 Bruce C. Trapnell, M.D., Children's Hospital and Medical Center
 Gerard M. Turino, M.D., Columbia University College of Physicians & Surgeons
 Catherine A. Valenti*, Meridian, ID
 Debbie Waldrop, M.S.N., R.N., C.C.R.C., University of Texas at Tyler
 Thomas B. Witt*, Severn, MD
 Bioethicist Consultant, Evan DeRenzo, Ph.D., Center for Ethics/ Washington Hospital Center
 Ex-Officio, Robert A. Sandhaus, M.D., PhD, FCCP, Alpha-1 Foundation

John W. Walsh*, President and CEO, Alpha-1 Foundation
 *Diagnosed with Alpha₁-Antitrypsin Deficiency

STATEMENT OF DON C. REED

Dear Senator Kennedy, honorable Committee Members: Seven years ago, my son Roman Reed suffered an accident while playing college football. His neck was broken; he became paralyzed from the shoulders down. Since then, our family has become involved in the struggle to find a cure for paralysis. We were fortunate to have a new law passed in California, the Roman Reed Spinal Cord Injury Research Act, setting aside a small amount of money each year for paralysis research.

Imagine our joy, therefore, to hear about the amazing possibilities of embryonic stem cells. If new nerve cells could be therapeutically cloned, and imprinted with Roman's DNA pattern, his own body could regrow nerves to heal the damaged spine. Our son might be able to close the fingers of his hands again, maybe even rise and walk.

Unfortunately, despite President Bush's public commitment to allow embryonic stem cell research, steps are being taken which will effectively kill that research.

1. The President supports and has promised to sign House Resolution 2505. Under this terrifying anti-science law, it will be a Federal crime to make embryonic stem cells: a felony, punishable by a ten-year jail sentence, and a one million dollar fine. H.R. 2505 treats therapeutic cloning of cells as if it was the reproductive cloning of humans. Obviously, to multiply infant copies of ourselves is wrong, and should be illegal. But therapeutic cloning? That is about cure: making cells, healing people, saving lives. Comparing therapeutic and reproductive cloning is like comparing a surgeon's scalpel to a criminal's switchblade. Their purposes are completely different.

Under H.R. 2505, if a researcher found the answer to cancer, paralysis, or AIDS—but cloned just one embryo to make stem cells—he or she would have to receive the Nobel Peace Prize in jail.

2. The President is also shutting off the only other source of embryonic stem cells; he will not allow the scientific use of embryos left over from fertility procedures. Under the Bush guidelines, no more new embryonic stem cell lines can be made. Ever.

3. The Administration's list of 64 viable stem cell lines is neither sufficient nor even accurate. Sweden, for example, is credited with seventeen "robust, vital" lines. The Swedes made a phone call to correct this, stating they have three usable lines, not seventeen. Only ten laboratories in the world even have viable embryonic stem cell lines. America has four.

4. Even these extremely few stem cell lines can never be used to help people. As is the case with all new science, experimental animals—(laboratory mice)—were used to make the lines. Food and Drug Administration guidelines on inter-species experiments disqualifies them for human cure. If we could use therapeutic cloning, this would not be a problem. We could just manufacture some more—but H.R. 2505 makes that illegal.

The President's proposal, then, leaves us with nothing but the promise of what might have been.

This decision will hurt every American. For those who suffer crippling and life-threatening diseases now, and the families who watch them suffer, our most promising possibility of cure has been denied.

For sheer financial self-interest alone, the quest for cure must be allowed. Our country faces an increasingly unpayable mountain of medical debt, public and private. It is overwhelmingly expensive to provide longterm hospitalization and attendant care.

Example: spinal cord injury, which my son Roman has, costs America approximately \$20 billion a year in medical costs and lost wages. That's about \$170 per taxpayer, for just one medical condition. And the cost in suffering to 450,000 paralyzed Americans and their families? That terrible price can never be calculated.

Why would anyone want to deny cure to the injured and critically ill? The problem, conservatives point out, is that when we dissect an embryo to obtain stem cells, we are destroying living tissue. That near-microscopic dot is technically alive.

And there is our choice. Like the battlefield medic who decides which soldier's life to try and save, because he cannot save them all, we too must choose; a 5-7 day old collection of cells in a glass petri dish—or a hundred million suffering people.

Think of folks you know. Like President Ronald Reagan, who has Alzheimer's disease. Or Michael J. Fox, with Parkinson's. Mary Tyler Moore, juvenile diabetes. Magic Johnson, HIV. Elizabeth Montgomery, who died of cancer. Vice President Dick Cheney, heart disease. Christopher Reeve, spinal cord injury. Annette

Funicello, multiple sclerosis. And other folks, out of the public eye, like a soldier terribly burned on the battlefield and living in continual pain, or my sister Patty, who died of leukemia at age 24. Perhaps, God forbid, even someone in your own family.

Whose rights shall we protect—our loved ones, the living people of the world—or a dot in a dish, a collection of cells which can neither think nor feel?

Honored committee members, you who will make this momentous decision: do not feel rushed. Give us your best. For in your hands are the hopes and dreams of those imprisoned by infirmity, confined to a lifetime of wheelchairs and hospital beds, and the endless humiliations of helplessness.

As my paralyzed son Roman puts it: “Take a stand with us today, in favor of research for cure. Take a stand—so 1 day, everybody can.”

Thank you.

Don C.Reed is the father of Roman Reed, and the sponsor of California’s Roman Reed Spinal Cord Injury Research Act.

STATEMENT OF CHRISTOPHER C. STRAUB

I am the Executive Director of the Culture of Life Foundation, an educational foundation dedicated to finding and spreading the scientific truths that confirm the dignity and inviolability of every human life from the moment of conception until natural death. I am submitting testimony today in favor of holding to the course set by President Bush in his August 9th statement. In other words, I urge this Committee and the Senate to support robust funding for adult stem cells and stem cells derived from umbilical cord blood and placentas, and to reject any increase in the number or sources of embryonic stem cell lines beyond those already authorized by the President.

Our Foundation was deeply disappointed in the portion of the President’s August 9th statement which permitted Federal funds to be expended on research on stem cell lines which are the fruits of the prior killing of human embryos. We also recognize that the President drew clear lines of limitation, both in the number of embryonic stem cell lines authorized for Federally funded research, and in the prohibition on Federally funded embryo destruction.

In support of maintaining those lines, I will review for you some facts not well covered in the news media: the tremendous advances already made by researchers and clinicians using adult stem cells. But even if adult stem cells were worthless and embryonic stem cells guaranteed immortality, I would still urge you to reject the funding of research on embryonic stem cells.

The embryo is a human being, fully equipped with the 46 chromosomes of a human being and with the complete genetic data that mark its unique humanity. All it needs to develop into a person as apparently independent as the rest of us is to be appropriately protected and provided with food and oxygen. I will not mention the embryo’s size or weight or appearance—to reject its humanity on those superficial grounds is not a serious argument in this age of science. The argument that its humanity is based on its location (e.g., a uterus) rather than its nature is likewise absurd; consider whether or not an embryo would be human if it were placed in some artificial womb of the future. To deny the embryo’s humanity based on the location of the embryo is to determine its humanity based on the intentions of the person who has power over it. In this view, if the embryo is intended to survive and grow, then it is human; if it is intended to be killed, then it is not human. By this reasoning, there are no human persons on the death rows of our penitentiaries.

The embryo’s humanity from fertilization onward is not a matter of religious faith, but of reason applied to scientific data. “The genetic information (DNA), which will determine a person’s physical characteristics and much of his intelligence and personality is present at fertilization. Fertilization is the process during which a male gamete or sperm . . . unites with a female gamete or oocyte . . . to form a single cell called a zygote. This highly specialized, totipotent cell marks the beginning of each of us as a unique individual” (William J. Larsen, *Essentials in Human Embryology*, New York: Churchill Livingstone, 1998, p. 17). To determine the embryo human at any point subsequent to fertilization is arbitrary, subjective, unscientific, and may coincide with the personal interests of those making the determination. All the talk about “treating the embryo with dignity” is nothing more than a nervous tiptoeing around the awesome and simple truth of its human personhood.

To obtain stem cells from an embryo, the embryo—this person—must be killed. Killing innocent people is considered evil in Judeo-Christian morality and in the laws that derive from that morality, the laws by which we govern ourselves. Throughout human history, it has been demonstrated repeatedly that we humans

cannot obtain a good outcome from an evil action. This rule operates with mathematical certitude. That is why embryonic stem cell research is objectionable and why tax dollars should not be used to pay for it.

The President, of course, did not authorize the killing of any embryos, and I am grateful for that. He did authorize Federal funding for research on 64 stem cell lines derived from embryos that had previously been killed, and that was a mistake on his part. I ask you to imagine you are a medical researcher in Germany sixty years ago and the German Army contracts with your laboratory to research a diet and medications to help soldiers resist extremes of cold. The data you are given to work with comes from experiments on condemned prisoners who were forced to participate and who in most cases froze to death in the course of the experiment. If you know the source of the data, it is wrong for you to work on this contract. This is the situation with the stem cell lines upon which Federally funded research is permitted: although the killing was done elsewhere, by another, it is wrong to seek the fruits of it. That is the basis of our Foundation's objection.

The work on the 64 stem cell lines is also the seed of more killing, as scientists State their requirement for more and better embryonic stem cells than those authorized by the Administration. The authorized cell lines may not be sufficient. Many of them may be tainted by contact with feeder cells from mice. More work reportedly remains to be done on some of the cell lines to be sure of their viability. There may be fewer than 64 viable lines among those the Administration has authorized; the August 29 New York Times reported that a hospital in Sweden, which the Administration asserts has nineteen lines, by its own account has only three established lines, four more that are being studied, and twelve that are in early stages. In addition, the ownership of patents and rights to the process by which the cells were derived and developed is not completely clear, and none of the corporate and academic laboratories seem disposed at this point to imitate Dr. Jonas Salk's generosity with his epochal discovery.

If more cell lines are demanded, the *in vitro* fertilization (IVF) industry reportedly has an overstock of at least 100,000 frozen embryos that were supposedly a rich source for stem cell research. But that source may have been a mirage: the August 26 New York Times reported that most parents of frozen embryos created in the IVF process do not want to contribute their embryos to science. The only other source may therefore be embryos specifically created to be destroyed in research. Many of the lines President Bush has authorized for federally funded research are probably in this category, and laboratories like the Jones Institute for Reproductive Medicine are ready to make many more. Against this possibility I again recall to you the human personhood of every embryo, even one destined for destruction within days of creation. No potential good can justify such a killing.

With the destruction of embryos for medical research we see the division of humankind into two parts: those who are destined to be killed for the benefit of others, and those who benefit from the death of another. This is as profound an inequality as has ever existed in human history.

Meanwhile, research on stem cells from postnatal human tissue and from umbilical cords and placentas continues to make spectacular breakthroughs in the treatment of human patients as well as laboratory animals. With exception of the news this summer that adult stem cells reside in one of our Nation's most bountiful resources, human fat, there has been little coverage of the spectacular breakthroughs made using adult stem cells against some of the very conditions and diseases which are used to justify the killing of embryos. Our foundation tracks these discoveries and issues a report each week, and I submit a list of those discoveries. You should know that adult stem cells have already been used to create knee cartilage, heart muscle, liver tissue, kidney cells, and bone mass in real human patients. Adult stem cells have been used to grow restorative tissue around spinal cord injuries, to restore vision, and to help people suffering from diabetes to become insulin-free. Adult stem cells have been used to treat Crohn's disease, to overcome immune deficiency in children, to restore bone marrow in people with leukemia, and to fight a wide variety of cancers. Fresh successes are reported almost daily. For example, the August edition of Archives of Dermatology reported that doctors at the M.D. Anderson Cancer Center in Houston, Texas, used adult stem cells to cure a man with rare but devastating skin disease, scleromyxedema. This disease had stiffened and thickened the patient's skin to the point he could not close his eyelids or eat. His doctors collected adult stem cells from his own bone marrow, then destroyed his immune system with chemotherapy and transplanted his stem cells back into his body to permit them to rebuild his immune system. As a result, the scleromyxedema is now in remission.

There are also spectacular nonstem cell treatments being developed to fight the diseases and disorders most often cited as a rationale for embryonic stem cell re-

search. Against Alzheimer's, for example, a university in Tokyo has discovered a protein with the potential to prevent or reverse the disease, and researchers in Dublin and at New York University have separately discovered what may be an Alzheimer's vaccine. Against cancer, nonstem cell developments include new toxins to be directed against cancer cells, using red blood cells guided by ultrasound to deliver anti-cancer drugs directly to tumors, and developing antibodies to deliver lethal radiation to a tumor.

Adult stem cells have another advantage: when taken from the patient the possibility of tissue rejection is greatly reduced. For this reason, many Americans are now banking their infant's umbilical cords.

The performance and the promise of adult stem cells are so great, and the news blackout and scant attention paid them by elite opinion is so marked, that there may be some motive at work besides concern for health. Whether it is a desire to derive a supposed benefit from the death of an embryo, the attraction of huge grants and concomitant fame, or the urge to smash another traditional human taboo, the embryonic stem cell is supposedly the new hope of mankind and the adult stem cell, which has already accomplished much more, is ignored. Unless we wake up to the facts and respond to them by reinforcing the success of adult stem cells, we will delay the day we conquer some of the cruelest diseases and conditions that afflict us, while at the same time becoming a nation that kills out of utilitarian motives.

STATEMENT OF THE CULTURE OF LIFE FOUNDATION

DIABETES

Adult Stem Cell Research

- **Adult Stem Cells Cure Type I Diabetes in Mice:** Dr. Denise Faustman of Harvard University Medical School has discovered an exciting potential new therapy that could possibly cure type I diabetics. The treatment effectively cured diabetes in mice, and human trials are currently being set up. Patients with type I diabetes have a defect in their immune system wherein their white blood cells (WBC's) inappropriately attack their own "pancreatic islet cells" in their pancreas. These cells are the primary producers of insulin for the body. Dr. Faustman's experiments entailed killing the defective WBC's in mice with diabetes by giving them certain drugs. She then planned to somehow "reprogram" the new WBC's that would be produced, so that they wouldn't attack the pancreatic islet cells again, and then to transplant new islet cells into the mice. However, she found that there was no need to do so. After the defective WBC's were gone, adult stem cells in the mice "took over," and started producing new pancreatic islet cells within 40 days. If the human clinical trials prove effective, this treatment would be helpful for not only diabetics, but also for other diseases that involve similar "autoimmune" symptoms, like lupus, rheumatoid arthritis, multiple sclerosis, and more than 50 other illnesses. All without need of embryonic stem cells.

Source: Cromie, William; "Adult Stem Cells Effect a Cure: Diabetes cure may eliminate need for embryo cells"; Harvard University Gazette, July 19, 2001, at <http://www.hno.harvard.edu/gazette/index.html/01-stemcells.html>.

Non-ES/Fetal Cell Research

- **Formation of Insulin-Producing Pancreatic Islet Cells from Adult Pancreatic Tissue:** A major goal with scientists studying diabetes is to come up with a good source of pancreatic cells that produce insulin. One of the primary insulin-producing cells in pancreases are "islet cells", which secrete insulin in response to glucose stimulation. In patients with type 1 and type 2 diabetes, a transplant of such cells would be tremendously helpful, since not nearly enough cadaver pancreas transplants for such patients become available on time. In July 2000, scientists at Harvard Medical School announced that they had found that by specially-preparing and nurturing adult pancreatic ductal tissue (which normally does not produce much insulin), they were able to coax the ductal cells to form pancreatic islet cells. These pancreatic islet cells were then further found to produce insulin, with increased amounts produced when stimulated with glucose. If this method of pancreatic cell differentiation and growth can be optimized to produce large amounts of cells, it could mean an important new type of cell replacement therapy for type 1 and type 2 diabetics.

Source: Bonner-Weir, et al.; "In vitro cultivation of human islets from expanded ductal tissue"; *Proceedings of the National Academy of Sciences USA*; July 5, 2000; 97 (410); 7999-8004.

- **Insulin-Producing Pig Cells Are Helping Diabetic Baboons:** Scientists at Duke University have demonstrated that specially-coated, insulin-producing pancreas cells

from pigs are keeping a diabetic baboon off of insulin. The pig pancreas cells were encapsulated within a complex carbohydrate known as alginate. This coating had pores that were large enough to allow insulin to be released, but small enough that the baboon's immune system antibodies and cells were not triggered to give a noticeable response to the foreign cells. The encapsulated pig cells were injected into the baboon's peritoneal cavity. The baboon has not needed extra insulin for 9 months, since the injection. With the success of this treatment, it is estimated by the researchers that human clinical trials could begin within the year. Some organizations dedicated to the treatment of diabetes are supporters of embryonic stem (ES) cell research. However, there have been no such successful studies to date using ES cells to treat diabetes; likewise, no ES cell studies have shown such promise or possibility to move to human clinical trials so quickly.

More information can be found at: <http://www.dukenews.duke.edu/Med/baboon.htm>. (From 6/15/01 Duke University News Release)

- Fat Cell Hormone Controls Diabetes: A hormone naturally produced by fat cells shows promise for treating diabetes. The hormone, called adiponectin, was recently found to be able to reduce the severity of diabetes in mice. It was able to normalize elevated levels of glucose in mice, and was also able to regulate the production of glucose by rat liver cells. Both of these abilities could help to treat diabetes in humans. One biotech company, Genset in Paris, France, is so encouraged by the findings that they are already planning clinical trials in humans using the hormone. There is so much potential with such nonembryonic/nonfetal research, that there is no need to delve into research on diabetes using human embryonic stem cells.

Sources: Science <http://www.sciencemag.org/> (need subscription); article entitled "Hormone Keeps Diabetes in Check" by Josh Chamot in ScienceNow section of journal); also Berg, Anders et al.; "The adipocyte-secreted protein Acrp30 enhances hepatic insulin action"; *Nature Medicine*; August 2001; Vol. 7, No. 8; pp. 947–953.

ALZHEIMER'S DISEASE/PARKINSON'S DISEASE/BRAIN & SPINAL CORD INJURY

Adult Stem Cell Research

- Neural cells isolated from adult cadaver human brains were found to be able to grow into different types of neural cells, including neurons, astrocytes, and oligodendrocytes. (Palmer, et al.; "Cell culture: Progenitor cells from human brain after death"; *Nature*; May 3, 2001 (411); 42–43.)

- Human umbilical cord blood treated with growth factors express markers that indicate that they can give rise to neurons. (University of South Florida Health Science Center Press Release, May 9, 2001 and February 18, 2001; also presented at May 6, 2001 American Academy of Neurology Meeting)

Adult Neural Stem Cells Purified From Mouse Brain Can Differentiate

- Scientists in Australia report in this week's journal *Nature* that they were able to purify adult stem cells from mouse brain. This is normally somewhat difficult, since it has been estimated that stem cells number only 1 for every 300 cells in the adult brain. But they were able to do so via modern cell separation techniques, and have also been able to stimulate their collected neural stem cells to differentiate into muscle cells by growing them together with other muscle cells. If it is found that human neural stem cells can do the same, such adult stem cells could possibly be used to treat spinal cord or muscle (including cardiac) injury and many brain diseases (such as Alzheimer's or Parkinson's), without the use of a single embryonic stem cell.

Source: Rietze, Rodney, et al.; "Purification of a pluripotent neural stem cell from the adult mouse brain"; *Nature*; Vol. 412, Aug. 16, 2001; pp. 736–739; also Pearson, Helen; "No stemming the tide"; *Nature*; Vol. 412, Aug. 16, 2001.

Adult Skin Stem Cells Can Turn Into Brain Tissue

- Researchers at McGill University in Montreal, Canada have found that they can repeatedly isolate adult stem cells from the skin of mice. Repeatability is a necessary objective for researchers with stem cells, and so is versatility—the ability to become more than one type of cell. These skin stem cells, called SKPs (for SKin Precursor cells) have both going for them. Over and over, the scientists were able to coax the isolated stem cells to form other types of cells, from neurons to muscle cells to fat cells. The scientists' studies with adult human scalp tissue have found that similar stem cells can be found in human epidermis. This is extremely encouraging, both from an ethical point of view and from an immunological point of view. If taken from a patient's own skin, SKP adult stem cells would likely provoke little or no immunological response, and would not necessitate the use of strong drugs to suppress the patient's immune system. In contrast, the use of embryonic or fetal stem cells would both be immoral and would likely necessitate the use of such drugs. SKP

stem cells appear to have much potential for use in diseases or disorders of the central nervous system.

Sources: Toma, Jean, et al.; "Isolation of multipotent adult stem cells from the dermis of mammalian skin," pp. 778–784; Sept. 2001, Vol. 3, issue 9 (published online on 13 Aug. 2001), also <http://www.washtimes.com/national/20010814-73539816.htm> (8/14/01 Washington Times article by Carolyn Abraham entitled, "Stem Cells from Skin Grow Into Brain Tissue"); also, <http://www.sciencedaily.com/releases/2001/08/010814063557.htm> (ScienceDaily 8/14/01 report) and <http://www.mcgill.ca/public/releases/2001/august/stemcells/> (McGill University 8/13/01 Media Release)

Other Non-ES/Fetal Cell Research

- At Keio University in Tokyo, scientists have discovered a protein that stops the death of brain cells that occurs in Alzheimer's patients. The findings were reported in the May 22, 2001 edition of the *Proceedings of the National Academy of Sciences*. This protein, called humanin by its discoverers, may not only prevent further deterioration from Alzheimer's, but could be the first step in curing the disease. Alzheimer's is one of the diseases most often mentioned in justifications of embryonic stem cell research.

- NYU Researchers Design Successful Vaccine Against Alzheimer's Disease: Scientists at New York University have created a vaccine against Alzheimer's disease which has proven effective in mouse studies at removing amyloid plaques in the brain. These plaques are aggregated clumps of the protein amyloid in the brains of Alzheimer's patients, which are thought to contribute to the characteristic memory loss, confusion, and mood disturbances in such patients. Like the recent report of an Alzheimer's vaccine produced by the Elan Corporation in Dublin (Adult Stem Cell Research Weekly Highlights #3) this vaccine is also made of a synthetic protein. However, the NYU group believes that their vaccine has less chance of causing later potential plaque formation than the vaccine from the Dublin group. Their experimental results were very promising in mice with plaques: 7 months after injection with the vaccine, a bad form of the amyloid was reduced in their brains by 89 percent in the cortex (the seat of higher thought), and by 81 percent in the hippocampus (the brain's memory center), compared to the control, nonvaccinated groups. In addition, the vaccinated mice had 57 percent less soluble amyloid present. This is yet another promising discovery in treatment options for Alzheimer's disease which does not resort to utilizing embryonic or fetal stem cells.

Source: <http://www.eurekaalert.org/> (from 8/2/01 report)

- Alzheimer's Drug Being Used to Treat Brain Injury: The University of Florida and 14 other centers will soon participate in clinical trials testing a drug, donepezil (more commonly known by the trade name Aricept, and manufactured by Eisai Co. Ltd.), in patients with brain trauma. The drug is currently used to slow memory decline in Alzheimer's disease. It is thought that because patients with brain trauma often have trouble with memory and cognition as with Alzheimer's disease, an effective treatment for Alzheimer's could be helpful for treating brain injury. Likewise, people that have received brain trauma have been found to be more likely to develop Alzheimer's later in life. Thus, a treatment that alleviates the symptoms of brain trauma could also have the effect of stemming the onset of Alzheimer's. This is the first randomized clinical trial ever conducted that treats chronic traumatic brain injury. It does not necessitate the usage of embryonic or fetal stem cells.

Source: <http://unisci.com/stories/20013/0801012.htm> (from 8/1/01 report)

- Manipulation of a Single Gene in Neurons Can Lead to Profuse Cell Regeneration: Could Lead to New Treatments for Brain and Spinal Cord Patients: A July 1, 2001 News Release from the National Institutes of Health/National Institute of Neurological Disorders and Stroke focuses on the recent work of researcher Maureen L. Condic, Ph.D. (University of Utah School of Medicine in Salt Lake City). She has shown that by genetically modifying adult rat neurons to produce more of a protein called integrin, a dramatic increase in nerve fiber growth could be achieved. The amount of growth was more than 10 times greater than in any other published study of adult neuron regeneration, and was indistinguishable from neuron growth in newborn adult animals. Previous studies had primarily focused on somehow changing the environment around neurons to stimulate them to grow, but this study shows that a key to neuronal growth may be as simple as changing the performance of one gene. This could lead to better treatment strategies (and nonembryonic stem cell research ones) for brain and spinal cord injury, as well as for Parkinson's and Alzheimer's diseases.

Sources: July 1, 2001 News Release from the National Institutes of Health/National Institute of Neurological Disorders and Stroke (original source) and <http://www.sciencedaily.com/releases/2001/07/010702084939.htm>

- Anti-Alzheimer's Antibody Gives Clues to Why it Decreases Development of Plaques in Brain: Researchers at Washington University School of Medicine studying the function of an anti-Alzheimer's antibody have found that the antibody draws a protein called amyloid-beta out of the brain in mice and diverts it to the bloodstream. Amyloid-beta contributes to the formation of "amyloid plaques" in the brains of Alzheimer's disease patients. Scientist David M. Holtzman, M.D. says, "Within hours of injecting the antibody into mice, the concentration of amyloid-beta in the bloodstream rose approximately 1,000 times higher than it had been before the injection." In addition, animals injected with the antibody over a period of months developed less amyloid plaques than control animals did. The difference between the groups was statistically significant. Utilization of such an anti-Alzheimer's antibody could be a useful and nonmorally problematic therapy for Alzheimer's patients.

Sources: News Release from Washington University School of Medicine (original source) and <http://www.sciencedaily.com/releases/2001/07/010704093453.htm> (7/3/01)

- New Hope in Spinal Cord Treatment Utilizing Patients' Own White Blood Cells: Doctors at Proneuron Biotechnologies in Tel Aviv, Israel, are using a promising new technique to treat spinal cord injuries. They inject a patient's own white blood cells directly into their spinal cord, after activating the cells by incubating them with skin cells from the patient's body. So far, results are encouraging. A 19-year old girl who was paralyzed from her chest down by a car accident was treated with the procedure, and a year later, has regained pain sensation in one of her legs, can contract some leg muscles, and can curl her toes. It's not clear right now whether the activated white blood cells are promoting regrowth of the neurons or are simply keeping more neurons from dying. The treatment tries to utilize the knowledge that white blood cells are known to usually play a big role in the healing of injuries. Normally, however, white blood cells do not heal injuries to the spinal cord, because of the "blood-brain barrier." This is a term for the tight cell junctions in the blood vessels in the brain and spinal cord areas, which isolate the brain and spinal cord from the blood cells and potential toxins in the blood. With the new procedure, the doctors get past this barrier by injecting the cells directly into the spinal column. Three other people have been treated by Proneuron with this and other new techniques for paralyzed patients, including a 19-year-old man from Colorado who was injured while using a snowboard. The procedure described here can only be performed within 14 days of the spinal cord injury, and Proneuron is seeking more patients from around the world that are interested in trying the procedure. They are willing to pick up transportation and living expenses, and the cost of the treatment itself for the patient. This type of treatment is especially significant in light of the fact that people who advocate embryonic stem cell research believe that spinal cord injuries can be helped by such research. This white blood cell procedure (also known as "autologous macrophage procedure") is already showing promise in humans, and does not face the ethical or immunological problems that would come from human embryonic stem cell or fetal cell research.

Source: <http://www.cnn.com/2001/HEALTH/conditions/07/20/spinal.cord.injuries.ap/index.html> (from 7/20/01 report); also www.proneuron.com

- Alzheimer's Vaccine Holds Promise and Appears Safe in Human Tests: Scientists at the Elan Corporation, a pharmaceutical company headquartered in Dublin, have found that a vaccine they have been testing to treat Alzheimer's disease has shown promise in mice and appears safe in humans. The vaccine, called AN-1792, is made of a synthetic protein which is a form of the protein beta amyloid that is found in the characteristic "plaques" (protein aggregates) in the brains of Alzheimer's patients. These plaques are thought to be what causes the memory loss and behavior changes which are symptoms of Alzheimer's disease. In mouse experiments, the synthetic protein vaccine was injected into mice that had plaques (i.e., they were a mouse "model" of the human disease). Two groups of mice were studied after such immunization: older mice that had already formed brain plaques and younger mice that had not yet formed plaques. With the older mice, it was found that there had been a significant curbing of plaque formation. With the younger mice, it was found that the immunization had kept virtually all of the mice from even developing plaques. It is thought that the vaccine somehow clears plaques out of the brain. In more recent testing of the vaccine in humans to determine its safety, it was found that the vaccine appeared to have no significant adverse effects. In addition, the patients had developed an immune response to it, which is what should happen if the protein is having any effect in their bodies. Although the patients did not exhibit any cognitive or memory improvements, the scientists hope that the next phase of upcoming human trials, which test for vaccine efficacy, will show positive results as did the mice experiments. This research appears to be much safer than the research reported in the March 8, 2001 *New England Journal of Medicine* in-

volving fetal and possibly embryonic cells injected into the brains of Parkinson's patients (another neural disease). That treatment had disastrous results, such as wild, aberrant movements in the patients. In addition, the research involving this vaccine is an example of one of the moral research routes that can be taken as an alternative to research involving the destruction of embryonic human beings.

Sources: <http://www.cnn.com/2000/HEALTH/aging/07/11/alzheimer.vaccine/> (from 7/11/01 report); also <http://www.cnn.com/2001/HEALTH/07/23/alzheimers.vaccine/index.html> (from 7/23/01 report); also <http://www.elan.ie/alzheimer/pressrelease.asp>; also <http://www.elan.ie/alzheimer/research.asp>

Promising New Treatment for Partial Spinal Cord Injury

- Researchers at the Weizmann Institute of Science in Israel are experimenting with a new therapy intended for patients with partial spinal cord injury. With partial spinal cord injury, the several days immediately following the injury are crucial, because during this time, there is usually further neural damage that occurs in a wave that spreads from the injury site, and can be even more destructive than the initial damage. The goal of the researchers is to find a treatment that will effectively stop this postinjury degeneration. In their recent studies on rats with partial spinal cord injury, they injected the rats postinjury with specific proteins which they had derived from the central nervous system (and which were selected to be able to boost the rats' immune system). The treated rats showed significant recovery of movement, and their spinal cords contained nerve fibers that appeared substantially healthier than those of nontreated rats (which suggests that the proteins halted further neural degeneration). These results are very encouraging, and counteract (with hard data) the hype from pro-embryonic stem (ES) cell research organizations that ES cells are needed for healing of spinal cord injury. This nonES therapy is only one of several we've reported on in the last few weeks which treat neural injury and disease in a completely moral manner.

Sources: <http://wis-wander.weizmann.ac.il/weizmann/doi%20iis.dll/Serve/item/English/1.200.7.5.html> and <http://www.sciencedaily.com/releases/2001/08/010817081453.htm> (8/17/01 report)

HEART DISEASE AND REPAIR

Adult Stem Cell Research

- Bone marrow cells were found to regenerate heart cells after induced heart attack-type damage in mice. (Orlic, et al.; "Bone marrow cells regenerate infarcted myocardium"; *Nature*; April 5, 2001 (410); 701-705.)

- The June 7 edition of the *NEJM* also reported on research that found that human heart muscle cells regenerate after a heart attack. These researchers, at the National Institutes of Health and New York Medical College, now seek to determine why heart muscle cells are dividing. One hypothesis is that these cells originate from stem cells present in the heart. Members of the research team had already shown in mice that adult stem cells from bone can become functioning heart muscle.

- A team at University of California at Los Angeles announced in May of this year that they had injected adult stem cells from a heart attack victim's bicep to replace heart muscle tissue damaged in a heart attack. Separately, also in May, a team at Baylor University announced their discovery that stem cells from the bone marrow of an adult mouse had the capability to transform into blood vessels and cardiac muscle.

Other Non-ES/Fetal Cell Research

- Newly-Discovered Heart Cell Protein Could be Used in Cardiac Treatment or for Conversion of Other Cells to Cardiac Cells: In the June 29, 2001 issue of *Cell*, researchers at the UT Southwestern Medical Center at Dallas report that they have discovered a protein called myocardin in heart cells which is responsible for turning on cardiac genes. Dr. Eric Olson, chairman of molecular biology, says, "The Holy Grail in the heart field is finding the gene or genes that can convert noncardiac cells into cardiac cells." The scientists studied the function of the protein in frog embryos and found that when myocardin is absent, the heart does not develop. It is possible that the gene that controls myocardin is a type of "master gene" for the heart. If so, then it could bode well for all sorts of possible heart treatments, such as changing nonheart cells into heart cells (an alternative to embryonic stem cells), or utilization in heart repair therapies in all ages (babies born with heart defects to adults with heart defects or heart attacks).

Sources: Wang, Da-Zhi, et al.; "Activation of Cardiac Gene Expression by Myocardin, a Transcriptional Cofactor for Serum Response Factor"; *Cell*, Vol. 105, 851-862, June 29, 2001; also, <http://unisci.com/stories/20012/0629013.htm>

Heart Cells Divide, Enlarge, and Live Longer With Special Enzyme

- Scientists at Baylor College of Medicine in Houston have found a way to increase heart cell division, increase heart cell size, and make heart cells live longer. This is great news for people prone to heart attacks or other heart ailments. The researchers genetically engineered their laboratory mice to produce a specific enzyme called TERT (Telomerase Reverse Transcriptase) in their heart muscles. This enzyme is normally only produced in very young mice, and is involved in the process of chromosome duplication during cell division. The engineered mice continued to produce the enzyme even after they grew older. At first, the mice produced many more heart cells than normal mice. Several weeks later, cell division ceased and the cells grew larger (hypertrophy). In addition, the cells appeared to be more resistant to cell death than normal cells. Usually, the condition of hypertrophy confers a weakness to the heart. With these mice, however, their hearts did not have impaired functioning. One of the scientists in the group, Dr. Michael Schneider, said that the scientists involved believe that adding TERT to an adult heart could offer protection against the type of cell death experienced during a heart attack. In addition, TERT could possibly be added to cells that have been grafted onto an injured heart. This could probably aid in cell growth and protection from cell death. It is just one more example of the exciting research being done without using embryonic stem cells.

Source: <http://www.sciencedaily.com/releases/2001/08/010821074944.htm> (8/22/01 report) and Oh, et al., "Telomerase reverse transcriptase promotes cardiac muscle cell proliferation, hypertrophy, and survival", Proceedings of the National Academy of Sciences, published online August 21, 2001 www.pnas.org/cgi/doi/10.1073/pnas.191169098 [Need subscription].

KIDNEY DISEASE/RENAL FAILURE

Adult Stem Cell Research

- Bone Marrow Cells Can Become Kidney Cells: Scientists at the Imperial Cancer Research Fund and Imperial College School of Medicine in the UK have recently discovered that bone marrow stem cells (which are adult stem cells) can change into kidney cells in both mice and humans. For the mice that they studied, they examined the kidneys of *female* mice which had been given bone marrow transplants from *male* mouse bone marrow. For the humans, they analyzed kidneys of *male* patients who had been given transplants of *female* kidneys. The researchers utilized a special DNA probe technique on the kidneys, which can detect if a cell originated from a male or female. For both groups, it was found that the mouse and the human kidneys contained male kidney cells as well as female kidney cells. It was determined that these male cells had come from the mouse's or patient's own bone marrow, had implanted into the new kidneys, and had literally become kidney cells. This finding opens up many promising possibilities. People whose kidneys are damaged or failing because of disease or injury could be treated with their own bone marrow cells to form new kidney cells and possibly whole new kidneys (which would help solve the desperate current shortage of kidney transplants). This is especially beneficial for the realm of kidney treatment, because as organs, they are particularly bad at repairing themselves. Also, there would be less immune rejection, because the repairing cells would be coming from the patients' own bone marrow. Professor Nick Wright, one of the authors of the paper in the *Journal of Pathology Online* which describes the experiments, says that an additional possibility using this knowledge could be to genetically engineer bone marrow stem cells to contain genes "resistant to cancer or other disease, to protect the kidneys from further damage." Says Dr. Poulson, lead author on the paper, "The potential for advances in medicine from using adult stem cells is enormous. They can give rise to many different types of cells so any organ may 1 day be repaired. Using adult stem cells also avoids the ethical dilemmas associated with embryonic stem cell work."

Sources: Poulson, et al., *Journal of Pathology Online*; "Bone marrow contributes to renal parenchymal turnover and regeneration"; 25 July 2001; also Pro-Life Infonet 7/25/01 #2486 (contact: infolnet@prolifeinfo.org); also <http://unisci.com/stories/20013/0725011.htm> (from 7/25/01 report)

HEMOPHILIA

Non-ES/Fetal Cell Research

- Research showing that the genetic modification of cells could fight hemophilia, announced in the June 7, 2001 edition of the *New England Journal of Medicine* (NEJM), used adult cells taken from the skin of the patients' arms. The cells were

then modified to add the gene for a missing clotting factor, grown in the laboratory, and injected in to the patient.

CANCER

Placental Stem Cell Research

- Placental blood was found to be a useful source of stem cells for bone marrow reconstitution in patients with leukemia and other diseases. (Rubinstein, et al.; "Outcomes among 562 recipients of placental-blood transplants from unrelated donors"; *New England Journal of Medicine*; November 26, 1998; 339 (22); 1565–1577.)

Non-ES/Fetal Cell Research

- Cancer Treatment Made Better Through "Sticky" Antibodies: A team of scientists at the University of California, Davis, has developed a new method for altering antibodies for targeting the destruction of tumors. Antibodies are molecules within the body's immune system which normally hone in on foreign elements in the body, to fight infections. It has been found that they can also be directed to fight cancerous tumors. When they are connected with a radioactive element (which is joined to a small carrier molecule), the special antibodies not only hone in on the tumor, but also deliver lethal radiation to the tumor. Radiation is a commonly-used therapy to fight cancer. When used in this way, the radiation goes straight to the cancerous cells, rather than to other parts of the body as well (which is a frequent side-effect of usual radiation therapy). Previous studies have combined the antibody-radiation complex in a rather temporary manner, using methods that unfortunately allow the radiation carrier molecule to unhinge from the antibody. The scientists at UC Davis have come up with a new method which engineers the binding region of the antibody to adhere permanently to the radiation carrier molecule. In effect, the antibody-radiation juncture is "stickier". This should allow for a cancer treatment regimen that is more precise, delivering the radiation directly to the tumor site without potential radiation leakage in other parts of the body. This is yet another cancer therapy which does not utilize embryonic stem cells (which have been touted as being a possibility for use in cancer research).

Source: Chmura, et al.; "Antibodies with infinite affinity," *Proc. Natl. Acad. Sci. USA*, Vol. 98, Issue 15, 84808484, July 17, 2001; also, <http://unisci.com/stories/20013/0717015.htm>

- Drug Capable of Destroying Only Oxygen-Starved Cells Within Tumors: Researchers at the University of Ulster in the UK have developed a promising new drug for cancer treatment. It is different from other current drugs on the market in that it targets hypoxic cancerous cells, which are cells deep within tumors that are not receiving much oxygen. These types of cells have proven to be particularly difficult to treat with the normal range of cancer drugs and radiation therapy, which are generally only good at killing cancer cells on the exterior of a tumor (and which do receive oxygen). The hypoxic cancerous cells within tumors are also known to be especially malignant, and have been found to be one of the prime instigators of secondary bouts of cancer, after the external tumor cells have been killed off. The new drug, called AQ4N, is also different from standard chemotherapy drugs, in that when administered, it is not toxic to the body. It only becomes toxic when it reaches the tumor cells deep inside the tumor, and is only toxic to those particular cells. This would avoid the common side-effect of the current chemotherapy drugs to kill other, noncancerous cells in the body (in doing so, they cause hair loss and extreme nausea to cancer patients). It is thought that perhaps this new drug can eventually be used in combination with current modes of drug and radiation therapy to be an effective cancer treatment regimen. The development of drugs such as this is a moral and effective alternative to cancer research involving embryonic stem cells.

Source: <http://unisci.com/stories/20013/0719012.htm>

- Making Deadly Acute Myeloid Leukemia (AML) Treatable: Scientists at Johns Hopkins University have found that drug called AG1295 can treat acute myeloid leukemia (AML), which is the most common form of adult leukemia. At least 40% of patients with AML have a genetic mutation wherein the gene called "FLT3" is altered. This gene is normally involved in the growth and maturation of blood cells, and when it is altered, uncontrolled division (causing leukemia) can occur. The researchers discovered that the drug AG1295 specifically interferes with the action of the altered FLT3 protein, blocking the uncontrolled growth and causing the leukemia cells to die. Safety and efficacy trials in animals and humans will need to be done, but it is a big step that the investigators have been able to pin down the genetic abnormalities related to this type of leukemia. This is good news, and another exciting prospect that doesn't involve embryonic stem cell research.

Sources: <http://unisci.com/stories/20013/0727012.htm> (from 7/27/01 report) and <http://www.sciencedaily.com/releases/2001/07/010726102007.htm> (from 7/26/01 report)

- **Teaching the Immune System to Fight Cancer and Other Diseases:** Researchers at Oxford University's Department of Clinical Medicine have developed a modified adenovirus that can teach the body's immune system how to fight tumors, malaria, and hepatitis. The vaccine-type method uses two sequential types of immunization. The first, called the "prime," introduces bits of the tumor or pathogen into the body. This allows the body to be able to identify and recognize the antigen. Later, a second immunization, called the "boost," involves injecting a modified adenovirus. This adenovirus elicits a larger immune response which includes production of special "CD8+ killer T cells" by the body. Because of the first "prime" injection, these killer T-cells are specifically made to hone in on the tumor or pathogen. Clinical trials of such vaccines are currently being started by Oxford's spinout company, Oxxon Pharmaccines. Such research is encouraging and is yet another type of cancer research that doesn't involve human embryonic stem cells or fetal cells.

Source: <http://unisci.com/stories/20013/0724011.htm> (from 7/24/01 report)

- **Red Blood Cells Can Deliver Anti-Cancer Drugs With Great Accuracy:** A scientist at the University of Ulster, Professor Tony McHale, has developed an ingenious way to deliver drugs to target tumors with precision. He uses normal red blood cells (RBC's). RBC's, which routinely carry oxygen throughout the body, have been used in past studies in an attempt to deliver drugs throughout the body before, without much success. This is because it is difficult to get the cells to deliver the drugs to the exact point in the body that one is interested in targeting. Professor McHale, however, has discovered a way to get around this. He found a way to sensitize red blood cells so that they will explode when they come in contact with an ultrasound beam. After sensitizing the RBC's and loading them up with the desired drug, doctors focus an ultrasound beam on the targeted tumor. Once the RBC's reach this area, they explode, delivering the drugs in a precise manner. In this way, surrounding tissue is left unaffected, which is also a key benefit to his procedure, since most current cancer drugs have a way of affecting other, noncancerous cells in the body (which can cause hair loss and nausea in cancer patients). This is yet another great cancer research discovery that does not use a single embryonic stem cell.

Source: <http://unisci.com/stories/20013/0724012.htm> (from 7/24/01 report)

- **Inactivating Cancer Cells:** Scientists at the Lautenberg Center for General and Tumor Immunology of the Hebrew University—Hadassah Medical School say that they have a new and safer way to battle cancer. They say that doctors should induce cancer to remain in a dormant State, rather than treat it by massive chemotherapy treatment (which normally kills both cancerous and normal cells). The researchers have developed a technique whereby they link a toxic molecule with an antibody directed against specific receptors on cancer cells. After injecting this complex into the blood stream, the cancer cells can be induced to internalize the complex. The toxin portion of the complex then inactivates the cancer cell, and prevents it from replicating. In mouse experiments, the scientists caused a human tumor to grow on an immunologically-deficient strain of mice. When treated with the human antibody-toxin complex, the cancer cells in the mice became dormant. The mice stayed healthy for as long as they were being treated. If this treatment proves effective in human clinical trials, it could be used as a therapy for many different kinds of cancer. Importantly, it does not necessitate the use of human embryonic stem cells.

Source: <http://www.eurekalert.org/> (8/7/01 report entitled "Hebrew University researchers seek to 'inactivate' cancer cells")

CROHN'S DISEASE

Adult Stem Cell Research

- **Adult Stem Cells Used to Treat Crohn's Disease:** Crohn's disease, which affects more than 50,000 Americans, is an autoimmune disorder wherein a patient's white blood cells attack their own stomach. It can cause extreme pain, chronic diarrhea, and an inability to digest food. Ten weeks ago, Northwestern Memorial Hospital in Chicago, Illinois performed the first stem-cell transplant to treat Crohn's disease, with successful results. The outcome was so encouraging that they performed a second transplant on a 16-year-old boy on Monday (8/6/01). The first transplant involved a 22-year-old woman who had suffered from Crohn's disease since childhood. The doctors first collected some of her own blood stem cells. They then used powerful chemotherapeutic drugs to destroy her faulty immune system, and afterwards injected the blood stem cells back into her circulatory system. The stem cells traveled to her bone marrow and immediately began producing new immune system

cells. After previously failing all other treatments, the patient now has no diarrhea or abdominal pain. Similar procedures have been used successfully to treat lupus (another autoimmune disease) and with promising results to treat multiple sclerosis. All with the use of a patient's own stem cells, not embryonic stem cells.

Source: <http://www.suntimes.com/output/news/cst-nws-stem07.html> (Golab, Art; Chicago-Sun Times; 8/7/01; "Stem Cells Used to Treat Crohn's")

SKIN DISORDER

Adult Stem Cells Successful in Treating Rare Skin Disorder

- A team of doctors at the University of Texas M.D. Anderson Cancer Center in Houston recently performed the first known adult stem cell transplant to treat a rare skin disorder called scleromyxedema. The disorder is characterized by waxy, stiff, thickened skin. In the Houston patient, it had progressed so far that the skin on his face had a "cobblestone appearance," and he could not close his eyelids completely or eat. The doctors first collected stem cells from the patient's own bone marrow, and then purposely destroyed his immune system with chemotherapy. They then transplanted his stem cells back into his system in order to allow the cells to reconstruct his immune system. Three months after the transplant, the patient's face does not have the cobblestone appearance anymore, and he can now close his eyes and open his mouth. This is another example of highly encouraging results from adult stem cells in clinical work on human patients.

Sources: Prolife Infonet 8/20/01, #2509; Reuters Health, Aug. 17, 2001; also Feasel, et al., "Complete Remission of Scleromyxedema Following Autologous Stem Cell Transplantation", *Archives of Dermatology*; August 2001, Vol. 137, No. 8, pp. 1071-1072.

THALASSEMIA

Umbilical Cord Cell Transplant Successfully Used To Treat Thalassemia

- Doctors from Singapore's National University Hospital and Singapore General Hospital have succeeded in the first known case of an umbilical cord cell transplant into a patient with Thalassemia Major. Thalassemia is a rare genetic blood disorder wherein the patient's red blood cells are unusually small and contain defective hemoglobin, and can lead to anemia. If left untreated, it is fatal for children. Thalassemia Major is one of the most severe forms of the disease. Usually, thalassemia is treated with bone marrow transplants. If a matching bone marrow donor cannot be found, the patient can be given numerous blood transfusions (which carry with them the risk of infections or development of diabetes or liver cirrhosis due to overdose of iron). In this recent case, the patient was given the umbilical cord blood of an unrelated donor. 28 days after the transplant, the patient was producing normal red blood cells, and was released 8 days after that. Umbilical cord cell transplants offer patients an opportunity for an alternative source to bone marrow transplants; it offers more versatility as well, since the umbilical cord donor does not appear to need to even be related.

Source: Agence France Press; August 14, 2001; International News Section; "Singapore scores medical first in treatment of thalassaemia."

APPLICABLE TO VARIOUS DISEASES

Non-ES/Fetal Cell Research

- Blocking Programmed Cell Death and Engulfment of Cells Could Have Potential for Treating Various Diseases: Researchers at Cold Spring Harbor Laboratory have found methods for decreasing cell death in the developing nervous system of the nematode worm known as *C. elegans*. They have been studying the cell survival and cell death processes in the worm, since it has a transparent body and such cell activities can be monitored with a microscope. Like in other animals, the normal process of cell death involves a signal inside of cells that are about to die, which causes a programmed death response in the cells. Soon afterwards, neighboring cells "engulf" the dying cell to complete the process. The scientists have found that when they were able to weaken the "death signal" within the cell slated to die, they were able to save a percentage of the cells. In addition, when they were able to weaken the "engulfment machinery" in the engulfing neighbor cells at the same time, an even greater number of cells were saved from death. The researchers suggest that similarly modifying the engulfment machinery in some cells in humans could prove to be an effective therapy for patients with neurodegenerative disease, stroke, and cancer.

Sources: Daniel J. Hoepfner, et al.; "Engulfment genes cooperate with ced-3 to promote cell death in *Caenorhabditis elegans*"; Vol. 412; July 12, 2001; pp. 202-206;

also News Release from Cold Spring Harbor Laboratory (original source) and <http://www.sciencedaily.com/releases/2001/07/010712080935.htm>

- **Some Mouse Tissue Capable Of Regeneration:** A special strain of mouse may contain secrets for rapid regeneration of injured bodily tissue. These laboratory mice, called "MRL mice," have been noted to have a special ability to heal themselves with minimal scarring. Recent studies by researchers at the Wistar Institute in Philadelphia have shown that even after serious heart injury, these mice show a fascinating ability to heal their own heart tissue without the use of drugs, injections of stem cells, or other intervention. Their experiments showed that in control mice, only 1-3% of the heart cells in the region of cardiac injury were capable of dividing. In the MRL mice, however, up to 20% of cells in the damaged heart area were capable of dividing after the injury. Further studies on these mice will possibly be aimed at identifying specific genetic and molecular markers which are the cause of such rapid regeneration ability. In doing so, scientists can potentially design drugs and treatments that can lead to improved healing in many types of injuries and illnesses. All without necessitating the use of embryonic stem cells.

Source: <http://unisci.com/stories/20013/0807014.htm> (8/7/01 report)

- **Platelets Have Ability to Produce Proteins In Response To Signals:** Scientists at the University of Utah have found out some new things about platelets—they are much more versatile than once thought. Platelets are one of the components of blood (besides red blood cells and plasma), and are known to be involved in wound healing, by sticking together to form plugs at wound sites to help close the wounds up. They have been long thought to have a relatively limited ability to produce proteins in response to cellular signals as normal cells do, because they lack a cell nucleus (which is usually the interpreter of cellular signals). However, the Utah scientists have found that platelets really do have the capacity for significant production of proteins for wound repair, in response to cellular signals. They found that platelets contain RNA transcripts inside them. These portions of cellular machinery are involved in the production of proteins. Specifically, it was discovered that with these RNA transcripts, platelets can produce "interleukin -1 -beta", which is a protein that signals the cells in damaged blood vessels to display receptors for white blood cells (so that the white blood cells can hone in on the injury). These discoveries offer new insights into ways that blood vessels are repaired, and could lead to the development of drugs and treatments that can be more specifically-targeted. Platelets are involved in many illnesses (heart attacks, circulation problems, strokes, gangrene). This new knowledge could be utilized to treat all of them, with no need for embryonic stem cells.

Source: <http://unisci.com/stories/20013/0806011.htm> (8/6/01 report)

More Umbilical Cord Cell Possibilities

- **ViaCell Inc., an Umbilical Cord Blood Research and Banking Company, Comments on Bush Decision to Fund Alternatives.** ViaCell, Inc., commenting on a portion of the recent Bush Administration's decision regarding stem cells, expressed approval at the Administration's decision to increase funding for alternatives to human embryonic stem cells such as adult and umbilical cord cells. ViaCell has developed a new technology which they call "Selective Amplification™", which allows the expansion of stem cell populations from umbilical cords. In addition, they are "preparing and Investigational New Drug (IND) application to initiate human clinical trials designed to demonstrate the safety, efficacy, and clinical benefits of selectively amplified stem cells from umbilical cord blood." They mention that some key advantages of umbilical cord stem cells include their use in the therapy of over 45 diseases; their ability to not cause as many immunological problems as other types of cells when transplanted into donors; and the fact that they can differentiate into various cell types (including hematopoietic, mesenchymal, and neural cells). Of course, one of the primary advantages is that they do not involve the ethical and moral concerns that the use of human embryonic stem cells do.

Source: <http://www.eurekalert.org/> (8/10/01 report); Contacts include Ernie Knewitz (Media Contact for Noonan/Russo Communications; e.knewitz@noonanrusso.com or 212-696-4455 ext. 204) or Marc Beer (Chief Executive Officer of ViaCell, Inc.; mbeer@viacellinc.com or 800-766-0966 ext. 4650)

ADULT STEM CELLS' ABILITY TO CHANGE INTO MANY OTHER TYPES OF CELLS

Adult Stem Cell Research

- A group of researchers at Johns Hopkins University has found that mouse bone marrow cells can change *in vivo* into the cells which line the lungs, intestines, and skin. Dr. Sharkis, the leader of the research team, was quoted in the May 4, 2001, issue of *Cell* as saying that "an infusion of stem cells after toxic cancer treatments

may be able to repair damaged tissue throughout the body, and serve as treatments for a variety of diseases characterized by tissue and organ damage, such as diabetes and cystic fibrosis." (Krause, et al.; "Multi-Organ, Multi-Lineage Engraftment by a Single Bone Marrow-Derived Stem Cell"; *Cell*; May 4, 2001: 105 (3); 369–377.)

- Fat cells taken from liposuction were able to change into cells resembling cartilage, bone, and muscle. (Zuk, et al.; "Multilineage cells from human adipose tissue: implications for cell-based therapies"; *Tissue Engineering*; 97 (410) 2001; 211–228.)

- Skin Of Adult Mammals Contains Multipotent Stem Cells (1/26/01 www.unisci.com article). A French research team published in the January 26, 2001 issue of *Cell* that the skin of adult mammals contains stem cells which can give rise to the epidermis, sebaceous glands, and hair follicles. They found that the stem cells are mainly located within the hair follicles. This discovery can aid in research and treatment in dermatology, oncology, and cosmetology. In dermatology, these adult stem cells have the potential to help in the areas of wound healing and in improving the results of skin grafts in burn patients. In oncology, the adult stem cells show promise in helping to understand the origins of some skin cancers. In cosmetology, it is thought that research on the cells could help to treat hair loss or excess body hair.

Sources: Oshima, et al.; "Morphogenesis and Renewal of Hair Follicles from Adult Multipotent Stem Cells;" *Cell*; Vol. 104 (2), pp. 233–245, January 26, 2001; also, <http://unisci.com/stories/20011/0126015.htm>.

ALTERNATIVES TO USING EMBRYONIC STEM CELLS

Adult Stem Cells

- Numerous recent studies have revealed the potential of adult stem cells to become several different types of tissue. This capability defeats the accepted scientific knowledge of decades past; it was formerly thought that once a stem cell within a developing embryo had differentiated and committed itself into one cell type, it couldn't re-differentiate later in life from an adult cell into another cell type. It has now been found that adult neural murine stem cells can transform themselves into blood cells,¹ adult muscle stem cells can convert into large quantities of blood cells,² adult bone marrow cells can become liver cells.³

- This progress on adult stem cells is wonderful for potential patient recipients, because there would not be the problem of immune rejection of the cells that one would find with embryonic stem cells. Adult stem cell lines could be grown from the patients' own body, thus overcoming any potential graft-versus-host disease and any need for strong immunosuppressive drug therapy.

- Likewise, adult stem cells are much more accessible than embryonic stem cells. They are located throughout the human body, even in adipose (fat) tissue.

Umbilical Cord and Placental Cells

- Umbilical cord blood banks and placenta banks are in operation in several states and are being organized in others. These cells have shown promise in being used to combat leukemia.⁴

DETRIMENTAL FINDINGS WITH ES AND FETAL CELL RESEARCH

- A study in *Science* (Humpherys, et al.; "Epigenetic Instability in ES Cells and Cloned Mice"; Volume 293 (5527); July 6, 2001; pp. 95–97; or <http://www.sciencemag.org/> [subscription necessary]) shows that embryonic stem cells and cloned cells are extremely genetically unstable. The researchers examined the gene expression (the production of proteins from genes) of the cells of mice obtained by cloning. The clones were obtained by performing a transfer of an embryonic stem cell into a de-nucleated egg and then implanting the embryo into a surrogate mother. The original donor embryonic stem cells were also examined. It was found that gene expression by both sets of cells was very different when compared from cell to cell. This implies that "even apparently normal cloned animals may have subtle abnormalities in gene expression." (p. 95) It also implies that if embryonic stem cells would 1 day be able to be coaxed adequately into cells of interest (i.e., cardiac,

¹Bjornson, et al., "Turning Brain into Blood: A Hematopoietic Fate Adopted by Adult Neural Stem Cells in Vivo," *Science* [January 22, 1999] 534–7.

²Jackson, Mi and Goodell, *Proceedings of the National Academy of the Sciences* [December 7, 1999] 14193–5.

³Thiese, Krause, et al., *Hepatology* [January, 2000] 235–40.

⁴Rubinstein, et al., "Outcomes among 562 Recipients of Placental-Blood Transplants from Unrelated Donors," *New England Journal of Medicine*, 339 [Nov. 26, 1998] 1565–1577.

neuronal, etc.) for transplant purposes, the cells may exhibit aberrant behavior due to each cell being wildly different in the proteins they produce.

- Injection of fetal cells into the brains of Parkinson's disease patients was found to cause wild, aberrant movements such as arm swinging and head-jerking. It is thought that these fetal cells produced too much dopamine, and were difficult to control. (Freed, et al.; "Transplantation of Embryonic Dopamine Neurons for Severe Parkinson's Disease"; *New England Journal of Medicine*; March 8, 2001; Vol. 344 (10); pp. 710–719).

- Unstable Gene Expression Found in Both Clones and Embryonic Stem Cells: Scientists have just published a study in *Science* in which they have found that embryonic stem cells and cloned cells are extremely genetically unstable. The researchers examined the gene expression (the production of proteins from genes) of the cells of mice obtained by cloning. The clones were obtained by performing a transfer of an embryonic stem cell into a de-nucleated egg and then implanting the embryo into a surrogate mother. The original donor embryonic stem cells were also examined. It was found that gene expression by both sets of cells was very different when compared from cell to cell. This implies that "even apparently normal cloned animals may have subtle abnormalities in gene expression." (p. 95) It also implies that if embryonic stem cells would 1 day be able to be coaxed adequately into cells of interest (i.e., cardiac, neuronal, etc.) for transplant purposes, the cells may exhibit aberrant behavior due to each cell being wildly different in the proteins they produce.

This is a further reason for not utilizing human embryonic stem cells or human clones in research. There are alternative cells which are morally, and as this new finding shows, *scientifically and medically*, more acceptable: adult stem cells, placental cells, and umbilical cord cells.

Sources: Humpherys, et al.; "Epigenetic Instability in ES Cells and Cloned Mice"; Volume 293 (5527); July 6, 2001; pp. 95–97; or <http://www.sciencemag.org/> [subscription necessary]

[Whereupon, at 2:40 p.m., the committee was adjourned.]

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