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CLONING

Present Uses and Promises

January 29, 1998

This paper presents background information on cloning. It includes a discussion of how cloning technologies are used today and how they could be used in the future. It also explains somatic cell nuclear transfer and describes the range of applications for this technology.

Cloning and somatic cell nuclear transfer are not synonymous. Cloning is the production of a precise genetic copy of DNA, a cell, or an individual plant or animal. Cloning can be successfully accomplished by using a number of different technologies. Somatic cell nuclear transfer is one specific technology that can be used for cloning. It is important to note that the use of somatic cell nuclear transfer is not limited to cloning an organism; there are other potential applications for both research and medicine that are discussed in this paper.

Definitions

DNA - abbreviation for deoxyribonucleic acid which makes up genes.

Gene - a functional unit of heredity which is a segment of DNA located in a specific site on a chromosome. A gene directs the formation of an enzyme or other protein.

Cloning - the production of a precise genetic copy of a molecule (including DNA), cell, tissue, plant, animal.

Somatic cell - cell of the body other than eggs or sperm.

Somatic cell nuclear transfer - the transfer of a cell nucleus from a somatic cell into an egg from which the nucleus has been removed.

Embryo - the developing organism from the time of fertilization until the end of the eighth week of gestation, when it becomes known as a fetus.

CLONING TODAY

DNA cloning

The simplest and most common form of cloning is DNA cloning, in which pieces of DNA (usually a specific gene) are copied. First, a piece of DNA is inserted into a bacterium. As the bacterium reproduces, identical copies of the DNA sequence are also produced. This process is one form of recombinant DNA technology. The multiple copies of DNA can be used for detailed studies of a specific gene. In addition, because genes direct the production of proteins, the bacteria with the inserted DNA can be triggered to act as miniature factories, churning out large quantities of a particular protein. For example, if the insulin gene was inserted into bacteria, the bacteria would serve as insulin factories, producing large amounts of insulin for therapeutic purposes. DNA cloning has been used in medical research and by the pharmaceutical industry in a number of ways, including the development of diagnostic methods for detecting diseases and disease-causing agents, the production of vaccines for preventing illness, and the development of antibiotics for fighting infections, among others. Specific examples of recombinant DNA

produced products include: human insulin, human growth hormone, erythropoietin for kidney dialysis patients, clotting factor for hemophiliacs, and hepatitis B vaccine.

Tissue culture

Tissue culture is another common form of cloning. In tissue culture, a somatic cell (any cell of the body other than egg or sperm cells) is grown in the laboratory in culture dishes. As the cell divides, the newly replicated cells are clones, or identical copies, of the original cell. For years, cells from both animals and humans have been cultured in the laboratory. Cloned tissue culture cells have allowed scientists to test potential chemotherapies on cancerous cells, to study the cellular events leading to cancer, and to mass-produce drugs and vaccines. The cloning of cells in culture has reduced the use of live animals in research and has allowed studies of human cells that could not be done otherwise.

Growing cells in culture is, however, often difficult and is only successful with a limited number of specific types of cells. Some types of cells are difficult or even impossible to grow in culture. Other types of cells grow successfully in culture, but undergo major changes in their features or functions, i.e., they may no longer be representative of the tissue from which they were removed. Thus, tissue culture has limited usefulness. There is a great need for more effective means to develop human cell lines (cultures of specific types of cells) useful for both research and in the development of new ways to diagnose, treat, cure, or prevent a number of injuries and diseases.

FUTURE POSSIBILITIES FOR CLONING

Understanding normal embryo development

In order to understand the potential of somatic cell nuclear transfer, a simple review of normal embryo formation, cell division, and cell specialization is helpful. First, a sperm and an egg join together to form a fertilized egg. The fertilized egg cell then divides many times forming a cluster of virtually identical unspecialized, embryonic cells. After many divisions, cells are triggered to turn into any one of the many different types of cells that make up the human body, i.e., liver cells, muscle cells, heart cells, nerve cells, etc.

What determines whether a cell becomes a muscle cell or a liver cell? It is now known that cell specialization is determined by gene activation. For example, if the genes that control liver formation are activated, the embryonic cell becomes a liver cell. But, if the "muscle genes" are turned on, that same embryonic cell can become a muscle cell. In fact, early, unspecialized embryo cells can become any kind of cell in response to specific gene activation.

The creation of Dolly using somatic cell nuclear transfer

In the Fall of 1997, the world became aware of a major advance in cloning technology when the cloning of a sheep named Dolly was announced by Scottish researchers. Dolly was created using the technology of somatic cell nuclear transfer. First, researchers took a normal sheep egg cell and removed the nucleus (cell structure containing the genes). This left behind a cell filled with the fluid normally found inside an egg cell which contains nutrients and other energy producing materials that are essential for embryo development. Second, they selected a somatic cell--in this case, a cell from the mammary tissue of an adult sheep. Using carefully worked out laboratory conditions, the mammary cell was placed next to the egg from which the nucleus had been removed, and an electrical stimulus was applied to fuse the two cells. This apparently triggered the genetic material in the fused cell to revert to the embryonic state.

Remarkably, when the resultant fused cell divided, rather than forming mammary cells, unspecialized cells were formed, each with the full potential to become any kind of cell. These cells began to divide, and eventually, as is the case with a normal embryo, the dividing early embryonic cells started to specialize. When implanted into the uterus of a ewe, the embryo developed into a fetus, which went on to become an apparently normal newborn lamb–a lamb that is genetically identical to the adult sheep from which the mammary cell was first taken! Although this may sound straightforward, in fact, it took 277 attempts to produce Dolly.

Significance of and therapeutic uses for somatic cell nuclear transfer

This experiment demonstrated that, when appropriately manipulated and placed in the correct environment, the genetic material of somatic cells can regain its full potential to direct embryonic, fetal, and subsequent development. While news coverage on this finding touted the cloning of an adult animal, scientists were excited about the prospect of using this technology to improve health. Medical researchers realized that if the genetic material of a somatic cell from an individual could be stimulated to return to its embryonic state, with the potential to become any kind of cell, the potential uses of this technology for the study and treatment of disease were remarkable.

Scientists understood that somatic cell nuclear transfer could be used to investigate many of the complex events that occur during normal development of various specialized cells. A better understanding of cell specialization would also provide insight into the development of abnormal cells. For example, some birth defects are caused by abnormal cell specialization. If we knew why specialization went wrong, perhaps we could learn how to prevent some birth defects. Improved understanding of cell specialization could also provide knowledge on cell aging and regulation - these in turn may provide the clues needed for conquering debilitating and deadly diseases such as Alzheimer's disease and even cancer. In particular, researchers understood that if we knew how to turn on specific genes, the technology would permit the much needed creation of cells for transplantation or grafting.

Diabetes

Consider a person with diabetes. These patients have a decreased number of insulin-producing cells in their pancreas. If we could augment these insulin-producing cells, we could potentially cure their diabetes. Cloning technology, using somatic cell nuclear transfer, might permit us to take a somatic cell from a diabetic patient and make that cell revert to its unspecialized state. If we then knew how to activate the genes which code for the production of an insulin-producing cell, we could create a large number of insulin-producing cells. These cells could then be transplanted back into the diabetic patient. Because the replacement cells would be genetically identical to the patient (cloned from the patient), there would be no problem with rejection.

This approach to the treatment of diabetes would be a vast improvement over the therapies available today. Rather than having to take insulin, pancreatic insulin cells could simply be replaced. In fact, a similar strategy is used today, but it has limited effectiveness. Insulin-producing cells are currently transplanted into patients with diabetes, but the only source of these replacement cells is through organ donation. Because these replacement cells are genetically different, the transplant patient must take powerful medications to prevent rejection. These medications to prevent rejection have severe and potentially fatal side effects and, often, rejection occurs despite the medication. Somatic cell nuclear transfer could revolutionize the treatment of this debilitating and often fatal illness.

Skin grafts

Somatic cell nuclear transfer might also be used in the future to create skin grafts for people who are severely burned. Patients with severe burns cannot survive without skin grafting. It is optimal to graft skin taken from unaffected areas of the same person's body. This is desirable, because it is genetically identical to the burn patient and, hence, will not be rejected. Unfortunately, when a patient has a large surface area burn, there is often not enough intact skin to use. Doctors are then forced to use skin from cadavers or skin cells grown in tissue culture. In both cases the skin is genetically different from the burn victim. While these provide material for emergency grafting, this skin is ultimately rejected and the patient must undergo grafting numerous times. Somatic cell nuclear transfer cloning could allow skin to be generated from virtually any of the burn victim's cells. The skin would be genetically identical and, hence, should not be rejected.

Both of these examples demonstrate the potential life-saving applications of somatic cell nuclear transfer--to produce vigorous healthy tissue for therapeutic purposes, not to clone a human being. It is important to note that, absent future research exploring this technology, these possibilities will be unrealized. Today, these are hopes for the future. In fact, there are many possible future applications of this technology. They include, for example:

- nerve stem cells to treat neurodegenerative diseases such as multiple sclerosis, amyotrophic lateral sclerosis (Lou Gehrig's disease), Alzheimer's disease, Parkinson's disease, and to help repair injuries of the spinal cord
- bone marrow stem cells, for the treatment of leukemia or other blood diseases such as sickle cell disease
- liver cells to treat liver damage
- muscle cell precursors to treat muscular dystrophy and heart disease
- cartilage-forming cells to reconstruct joints damaged by injury or arthritis

Gene therapy

Somatic cell nuclear transfer could potentially be used to improve gene therapy. Gene therapy promises to be able to virtually replace a patient's defective gene with a normal gene, thereby curing or preventing disease. Currently, gene therapy researchers are developing ways to insert a copy of a normal gene into a virus which has been altered so that it should not cause disease. This modified virus is then introduced into the patient, where it will hopefully "infect" cells–without causing illness–and in the process "deliver" a normal gene into the cells of the patient. At present, the use of viruses as the courier for a normal gene is proving problematic. There are difficulties in transferring adequate amounts of the normal gene into patient cells and obstacles posed by the patient rejecting the courier virus.

Somatic cell nuclear transfer could potentially facilitate gene therapy by eliminating the need for a courier virus. A somatic cell from a diseased patient could be removed and a normal gene inserted using recombinant DNA techniques. The "corrected" cell could then be cloned using somatic cell nuclear transfer. The identical copies of the corrected cell could then be delivered back into the patient. Because the copies of the corrected cells are genetically identical to the patient, they should not be rejected. This technique would overcome some of the most difficult hurdles facing gene therapy today.

Animal Cloning

As Dolly showed the world, somatic cell nuclear transfer can also be used to clone animals. The advantage of this process is the genetic duplication of an animal. In traditional breeding practices, the offspring of an animal are sexually reproduced from genetically different parents and, therefore, may not share all of the characteristics that made the parent's valuable. In conventional breeding, it takes years to produce many animals with similar genetic characteristics. Cloning could speed up this process and could allow the production of genetically identical animals.

This technique would be particularly valuable for research. The use of genetically identical animals could dramatically reduce the numbers of animals needed for experiments. For the first

time, researchers could be sure that differences in responses to drugs and other interventions are due to the interventions, not to genetic differences between animals.

Cloning could also contribute to animal husbandry and medical research by facilitating transgenic technology. A transgenic animal is one that is genetically altered by inserting a new gene with the desired attributes into the DNA of a fertilized egg. Transgenic animals are valuable for a number of reasons. They can be engineered to have decreased susceptibility to bacterial infection, to have increased milk production, and to have the ability to produce pharmaceutically important proteins in their milk. Recently, calves were cloned with the gene that enabled them to produce in their milk human clotting factors for the treatment of hemophilia. Future advances may also allow the development of animal clones with tissues and organs that are compatible for human transplantation purposes. Cloning the animal that incorporated the gene of interest would be much faster than selective breeding and would decrease the amount of time required to produce transgenic animals.

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In sum, somatic cell nuclear transfer holds many diverse and important possibilities to significantly prevent, treat and maybe cure disease. All of these possibilities can be accomplished without using this technology to create a human being.

CLONING

Present uses and Promises

National Institutes of Health
January 29, 1998

January 30, 1998

With No Other 'Dollys' Yet, Cloning Report Draws Critics

Related Articles

- The New York Times: Cloning Index

By NICHOLAS WADE

The credibility of the experiment reporting the cloning of Dolly the sheep from the cell of an adult ewe is being sharply challenged by a leading biologist, and other eminent scientists agree the experiment needs to be repeated before it can be accepted.

The skepticism is erupting almost a year after the original report. The critics note that no other scientist has yet succeeded in cloning a mammal from an adult cell, although the birth of at least one calf cloned this way is said to be imminent. The cloned calves born earlier this month were generated from fetal cells, not those of an adult cow.

The challenge is in the form of a letter, being published Friday in the journal Science, by Dr. Norton D. Zinder, a microbiologist at Rockefeller University and a member of the National Academy of Sciences, and Dr. Vittorio Sgaramella of the University of Calabria in Italy.

In a response, the chief author of the cloning experiment, Dr. Ian Wilmut of the Roslin Institute in Scotland, dismissed the possibility of error but said that some extra tests suggested are now under way and will be reported when complete.

Zinder's position is not that the cloning of Dolly never occurred, merely that so far there is not enough evidence to prove it.

In their letter, Zinder and Sgaramella note that Wilmut's cloning of an adult sheep was successful only one out of some 400 times and that in science, one success in 400 "is an anecdote, not a result."

They also criticize Wilmut's original report for failing to mention that the adult sheep from which Dolly was cloned had died several years earlier. Its absence

prevented any direct comparison between Dolly and her donor, in particular the decisive test of a skin graft from one to the other. If true clones, each would have accepted the other's skin graft; if not, any graft would have been rejected.

Dolly was cloned from a vial of sheep breast cells that had been frozen away in Wilmut's freezer as part of another project. The critics say it is hard to know what other kinds of sheep cell may have been around in the vial but, since the sheep in question was pregnant at the time, the vial could have contained some of the fetal cells that circulate in the mother's body. If it was a fetal cell that generated the Dolly clone, the outcome would not be startling because Wilmut had already demonstrated that fetal cells could be cloned.

"The most heinous crime was not saving the parent," Zinder said. "I just don't understand that. There could be nothing more exciting than seeing the two twins standing there," he said, referring to the fact that the cloned animals would be like identical twins although of different ages.

Wilmut said Thursday in a phone interview that he had not intended to clone an adult cell when he started the experiment, which originally dealt with fetal cells. Midway through that experiment, Wilmut said he decided to try cloning an adult cell. Instead of working with a live animal, he said he used a cell line that was already available.

Zinder's criticisms have resonated among other biologists, in part because of a seminar Wilmut gave recently at the Massachusetts Institute of Technology. The seminar was attended by many of Boston's leading biologists, several of whom were surprised to hear him say he did not intend to repeat the experiment.

It is an article of faith among scientists that an experiment should be replicated in one's own laboratory in case of an error the first time around, as often happens. Also, it is usual to follow up an important result with more experiments.

Wilmut confirmed that he did not intend to replicate his experiment. "I don't perceive a need," he said Thursday. "The principle is established. Repeating experiments is boring and unimaginative." He said he expected his results to be repeated by many other laboratories in the next few months.

So far three laboratories have tried and failed to repeat Wilmut's experiment, but others are still trying and are confident of ultimate success, according to an article in Science.

Other scientists disagree with Wilmut's view that one need not replicate one's own results. "If I have one success in 215 tries and I don't try to duplicate it, then I'm concerned it's not science," said Dr. Philip Sharp, a Nobel Prize-winning biologist at MIT who attended the seminar. He described Wilmut as a "reputable scientist who has worked long and hard in the field."

But, he added, "If you have only one success in an experiment which is so

widely recognized from a public and now political perspective, then I am really leery. Until an experiment is duplicated you never know if someone has mixed up a test tube in the back room, something that happens in the best of laboratories."

Dr. Bruce Alberts, president of the National Academy of Sciences, said he could not comment on Zinder's letter. "However," he added, "it is fair to point out that scientists generally require that a new result be repeated in at least one independent laboratory before they are ready to accept it unambiguously."

The issue of human cloning has received considerable public attention since Wilmut's announcement last February. Politicians from President Clinton, in his State of the Union message this week, to President Jacques Chirac of France have called for a ban on cloning people.

Zinder said he wrote to Science because of his feeling that if there is going to be such an intense public debate over cloning, it would be useful to make sure the underlying facts are true.

"The whole ambiance of this story was that nobody ever questioned whether or not this was true, and that included the 100-odd page report of the President's Commission on Bioethics," Zinder said. "Wilmut sat before Congress with Varmus sitting next to him and nobody ever said, 'Is this possibly not true?'" Dr. Harold Varmus is director of the National Institutes of Health.

For biologists, the cloning of animals from adult cells has been a longstanding barrier, but one founded more on practical than theoretical obstacles. A full-fledged carrot can be cloned from any cell of an adult carrot, whether a root cell or a leaf cell. So it would not in principle be surprising if the same were true of animals.

But the most serious attempt to clone animals, an elaborate series of experiments on frogs in the 1960s, showed that cells from tadpoles could be cloned but that viable offspring could almost never be obtained from the cells of adult frogs.

The inference was that as an animal progresses from egg to embryo to adult, its cells become increasingly committed to specific fates. A skin cell, say, somehow switches off all its genes except those needed to operate a skin cell. The off-switches can be reset in a tadpole's cells to generate a whole frog, but not in a grown frog's cells.

Attempts to clone even fetal cells in mammals failed for many years, and some biologists began to doubt that cloning would ever be possible from specialized adult cells, also known as differentiated cells.

"The cloning of Elvis Presley from fully differentiated cells is not something we should count on," declares a recent textbook on developmental biology. But biologists had been edging ever closer to that goal, or at least its general vicinity, as their techniques improved. By 1986 lambs had been cloned from

very early embryos, and Wilmut in 1996 showed how lambs could be cloned from a later embryo's cells.

His report last February that he had made the leap to cloning adult cells was more credible because of his previous work in the field. To prove that Dolly's and her donor's DNA were identical, however, Wilmut used only a single test, the same DNA typing technique that is now accepted in courts.

Zinder said this test was strong but not conclusive, because domestic animals are often highly inbred, meaning that the DNA from two different sheep could quite possibly be identical. Wilmut said the assertion that sheep are highly inbred was a "silly exaggeration."

The doyen of animal cloning, Dr. John B. Gurdon of Cambridge University in England, who performed the frog cloning experiments of the 1960s, said he believed Wilmut's experiment showed an animal could be cloned from an adult, but whether the cell was differentiated was "a point that has not been shown by Dolly the sheep." The frog evidence was more compelling, Gurdon said.

Wilmut has no doubt that other laboratories will be able to repeat his success.

"Dolly is real," he said. "In the next few months you'll see positive results coming in from other labs and people will accept it for what it is."

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Armey promises to ban all human cloning

By JIM ABRAMS
The Associated Press
01/29/98 5:36 PM Eastern

WASHINGTON (AP) -- Saying President Clinton's proposed ban doesn't go far enough, House Majority Leader Dick Armey said Thursday the House will legislate next month a permanent ban on cloning humans in the United States.

"This is the right thing to do, at the right time, for the sake of human dignity," Armey, R-Texas, said at a news conference.

Clinton issued an executive order last March banning the use of federal funds for human cloning projects.

He also proposed legislation, which Congress did not act on last year, that would outlaw the cloning of humans for at least five years. During that time the National Bioethics Advisory Commission would assess the risks and the ethical and social impact of human cloning.

Armey said Congress will pass a permanent ban. "How can you put a statute of limitations on right and wrong?" he asked.

He also contended that Clinton's plan would allow human cloning in laboratories for experimental purposes but said the Republicans' bill would "have no loopholes."

The legislation is being drafted by Rep. Vernon Ehlers, R-Mich., and Sen. Kit Bond, R-Mo., Armey said. Sen. Dianne Feinstein, D-Calif., is also introducing legislation that would put a 10-year ban on publicly or privately funded human cloning. And Sen. Bill Frist, R-Tenn., is crafting a bill under which a scientist convicted of human cloning could face up to 10 years in prison.

Momentum to outlaw cloning humans has grown since an independent Chicago scientist, Richard Seed, announced earlier this month he was trying to organize a team to do research on the procedure.

Clinton again recommended a ban in his State of the Union address Tuesday.

Armey said it was not the intention of the legislation to ban all experimentation on human embryos. Some scientists are perturbed that a rush to ban human cloning might unintentionally close down related research in such areas as replacement organs, the mending of spinal-cord injuries and infertility treatment.

Armey was joined at the news conference by representatives of the Christian Coalition, the conservative Family Research Council and the National Conference of Catholic Bishops, groups that contend that any manipulation of human embryos is immoral.

"Human life begins at conception," said Gary Bauer of the Family Research Council. "Cloning of human embryos is entirely unacceptable."

Please send any questions or comments to newsflash@nj.com.

December 2, 1997

Human Cloning: Yesterday's Never Is Today's Why Not?

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- Analysis: Commission on Cloning -- Ready-Made Controversy (June 9)
- After Decades and Many Missteps, Cloning Success (March 3)

Forum

- Join a Discussion on Cloning

By GINA KOLATA

Just nine months have passed since an astonished world got its first glimpse of Dolly the lamb, the first animal cloned from a cell taken from an adult. It was a feat that science had declared impossible.

In the hubbub that ensued, scientist after scientist and ethicist after ethicist declared that Dolly should not conjure up fears of a Brave New World. There would be no interest in using the technology to clone people, they said.

They are already being proved wrong. There has been an enormous change in attitudes in just a few months; scientists have become sanguine about the notion of cloning and, in particular, cloning a human being.

Some infertility centers that said last spring they would never clone now say they are considering it. A handful of fertility centers are conducting experiments with human eggs that lay the groundwork for cloning. Moreover, the federal government is supporting new research on the cloning of monkeys, encouraging scientists to perfect techniques that could easily be transferred to humans.

Ultimately, scientists expect cloning to be combined with genetic enhancement, adding genes to give desired traits, which was the fundamental reason cloning was studied in animal research.

Only California has enacted a law making human cloning illegal, and those who

are intrigued by the idea of cloning humans argue that it is no worse, morally, than creating custom embryos from sperm and egg donors. After all, it is an American tradition to allow people the freedom to reproduce in any way they like.

"From my perspective, it's just a matter of time" before the first human is cloned, said Dr. Steen Willadsen, a cloning pioneer who developed the fundamental methods for cloning animals.

Willadsen, whose techniques were used in the cloning of Dolly, now works at an in vitro fertilization center at St. Barnabas Hospital in East Orange, N.J. He said he had no ethical problem with cloning humans.

"It is not for me, as a person who invents techniques, to say how we should use them," Willadsen said.

Lori Andrews, a professor at Chicago-Kent College of Law and an expert on legal issues of reproduction, said she recently got a call from a British scientist who told her the same thing. Another doctor, Ms. Andrews added, told her that "if any of my relatives got cancer, I would clone them," and use the clone as a bone marrow donor to save the cancer patient's life.

"I absolutely think the tenor has changed," Ms. Andrews said. People who said human cloning would never be done "are now saying, 'Well, the risks aren't that great,'" she said.

"I see a total shift in the burden of proof to saying that unless you can prove there is actually going to be harm, then we should allow it," she said.

Ms. Andrews likes to quote two fertility experts, Dr. Sophia Kleegman and Dr. Sherwin Kaufman, who wrote, three decades ago, that new reproductive arrangements pass through several predictable stages, from "horrified negation" to "negation without horror" to "slow and gradual curiosity, study, evaluation, and finally a very slow but steady acceptance."

That happened, she said, with artificial insemination, with in vitro fertilization, with the freezing of human embryos and with surrogate mothers.

And it is happening with cloning, Ms. Andrews said. But what is so striking, she added, is that "the time frame from 'horrified negation' to 'let's do it' is so much shorter.

"This is very, very quick," she said.

Cloning would be fundamentally different from ordinary reproduction. It would involve taking a cell from a living person, slipping it into an egg cell whose genetic material has been removed and allowing the genetic material of the adult cell to direct the development of a new embryo, then fetus, then person who is the identical twin of the person who provided the initial cell. It would allow a living person to be reborn, in a sense, only at a later time.

Scientists and infertility specialists envision certain specialized circumstances in which it might be acceptable to clone humans. Grieving parents may want to reproduce a terminally ill child. Or a woman may want a child but be infertile. Is it worse somehow for her to clone herself than to obtain an embryo made-to-order with donated egg and sperm, the kind that many fertility clinics are already offering the infertile?

In fact, said Dr. Joseph Schulman, director of the Genetics and IVF Institute in Fairfax, Va., if a woman has no eggs and her husband makes no sperm, they might consider cloning both husband and wife.

"Then they could have one of each," Schulman said.

But what cloning really accomplishes, experts said, is to make it possible, for the first time, to think seriously about genetically enhancing human beings. Scientists could grow a person's cells in sheets in the laboratory and sprinkle the cells with genes. Only a very few cells would take up the genes, and use them, but it is relatively easy for scientists to find those cells and pluck them out of the mix.

If they then used those cells to make clones, the clones would contain the added genes in every cell of their body. Already, two such experiments have been completed in animals, using cells from fetuses rather than cells from adults.

Last summer, Dr. Keith Campbell of PPL Therapeutics in Roslin, Scotland, and Dr. Ian Wilmut of the Roslin Institute in Edinburgh, the scientists who created Dolly, announced that they had made Polly, a cloned lamb whose every cell contained a human gene. Shortly afterward, ABS Global Inc., a company in De Forest, Wis., announced the birth of Gene, a calf that was cloned from genetically altered fetal cells.

With humans, predicted Dr. Lee Silver, a molecular biologist at Princeton University, the first genetic enhancements might be genes to protect against diseases, like an AIDS resistance gene or a gene to protect against Alzheimer's disease, both of which have already been identified. In a sense, it would be no different morally from vaccinating a child for a disease, Silver said.

As more and more becomes known about genes, other enhancements become possible.

"At present," Willadsen said, "there is a large effort involved in sorting out the human genome. I don't think they are doing that just to have some nice charts to put on the wall."

Research that lays the groundwork for cloning humans is proceeding rapidly. Dr. James Grifo, the director of the division of reproductive endocrinology at New York University Medical Center, is working on nuclear transfers, the crucial technique for cloning, but with another purpose in mind. His goal is to transfer the genetic material from immature eggs of older women into eggs of

younger women. The egg could finish maturing with the machinery of the younger woman's egg, and that should result in less chromosomal damage, the bane of attempted pregnancies in older women.

So far, Grifo has shown that he can move egg nuclei around, which is, in essence what is required for cloning.

Dr. Jacques Cohen and Willadsen, at St. Barnabas, also have moved nuclei between cells, but for a different reason. They are trying to help women whose eggs are easily fertilized but whose embryos tend to die, probably because there is a defect in the cytoplasm of their eggs.

"It's being used for a different purpose than cloning, but the techniques are very much the same," Willadsen said.

At the same time, Dr. Donald Wolf, a senior scientist at the Oregon Primate Research Center and the director of Oregon's only in vitro fertilization center, at the University of Oregon, has two federal grants to study cloning in rhesus monkeys. One will involve cloning from cells of an adult.

"We're pretty optimistic," Wolf said. "We have every reason to think it will work."

He explained that the National Institutes of Health, which gave him the grants, is interested in genetically identical monkeys for AIDS vaccine research and in clones of rhesus monkeys that, by chance, happened to develop a rare genetic disease, retinitis pigmentosa.

By cloning the animals, Wolf hopes to make enough of them for investigators to use them to study the disease and its treatments. But one consequence of the primate work, Wolf said, is that it will establish methods that could be applied for the cloning of humans.

"We are laying the groundwork," Wolf said.

Society should think about the possible results of all this work "sooner rather than later," Wolf said.

But some experts said the real question was not whether cloning is ethical but whether it is legal.

"The fact is that, in America, cloning may be bad but telling people how they should reproduce is worse," Willadsen said.

In the end, Willadsen said, "America is not ruled by ethics. It is ruled by law."

Jeffrey M. Smith
12/02/97 09:46:53 AM

Record Type: Record

To: Joshua Silverman/WHO/EOP, Michael D. McCurry/WHO/EOP

cc: John H. Gibbons/OSTP/EOP, Rachel E. Levinson/OSTP/EOP, Holly L. Gwin/OSTP/EOP, Clifford J. Gabriel/OSTP/EOP

Subject: cloning issue

Josh -- in response to your request for bullets on the 12/2 *NY Times* front page story on cloning:

This article presents no new breakthroughs in cloning research. It provides one reporter's view on how some scientists' thinking may be changing on the suitability of using cloning techniques to reproduce human beings.

As spelled out in legislation submitted by the President in June, the Administration is committed to banning the use of certain cloning technologies for the production of human beings until all safety and ethical concerns have been adequately addressed. Our proposed legislation includes all the important elements the President would want in any legislative initiative regarding the cloning of human beings. It would extend to the private sector the current ban observed by the public sector on the cloning of human being. In the meantime, the President has asked the private sector to voluntarily comply with the ban.

The use of federal funds to support cloning research on monkeys is justified. Our proposed legislation is careful not to restrict this type of research, which could have enormous benefits to improving human health such as the development of AIDS treatments and vaccines.

December 2, 1997

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Just nine months have passed since an astonished world got its first glimpse of Dolly the lamb, the first animal cloned from a cell taken from an adult. It was a feat that science had declared impossible.

In the hubbub that ensued, scientist after scientist and ethicist after ethicist declared that Dolly should not conjure up fears of a Brave New World. There would be no interest in using the technology to clone people, they said.

They are already being proved wrong. There has been an enormous change in attitudes in just a few months; scientists have become sanguine about the notion of cloning and, in particular, cloning a human being.

Some infertility centers that said last spring they would never clone now say they are considering it. A handful of fertility centers are conducting experiments with human eggs that lay the groundwork for cloning. Moreover, the federal government is supporting new research on the cloning of monkeys, encouraging scientists to perfect techniques that could easily be transferred to humans.

Ultimately, scientists expect cloning to be combined with genetic enhancement, adding genes to give desired traits, which was the fundamental reason cloning was studied in animal research.

Only California has enacted a law making human cloning illegal, and those who

are intrigued by the idea of cloning humans argue that it is no worse, morally, than creating custom embryos from sperm and egg donors. After all, it is an American tradition to allow people the freedom to reproduce in any way they like.

"From my perspective, it's just a matter of time" before the first human is cloned, said Dr. Steen Willadsen, a cloning pioneer who developed the fundamental methods for cloning animals.

Willadsen, whose techniques were used in the cloning of Dolly, now works at an in vitro fertilization center at St. Barnabas Hospital in East Orange, N.J. He said he had no ethical problem with cloning humans.

"It is not for me, as a person who invents techniques, to say how we should use them," Willadsen said.

Lori Andrews, a professor at Chicago-Kent College of Law and an expert on legal issues of reproduction, said she recently got a call from a British scientist who told her the same thing. Another doctor, Ms. Andrews added, told her that "if any of my relatives got cancer, I would clone them," and use the clone as a bone marrow donor to save the cancer patient's life.

"I absolutely think the tenor has changed," Ms. Andrews said. People who said human cloning would never be done "are now saying, 'Well, the risks aren't that great,'" she said.

"I see a total shift in the burden of proof to saying that unless you can prove there is actually going to be harm, then we should allow it," she said.

Ms. Andrews likes to quote two fertility experts, Dr. Sophia Kleegman and Dr. Sherwin Kaufman, who wrote, three decades ago, that new reproductive arrangements pass through several predictable stages, from "horrified negation" to "negation without horror" to "slow and gradual curiosity, study, evaluation, and finally a very slow but steady acceptance."

That happened, she said, with artificial insemination, with in vitro fertilization, with the freezing of human embryos and with surrogate mothers.

And it is happening with cloning, Ms. Andrews said. But what is so striking, she added, is that "the time frame from 'horrified negation' to 'let's do it' is so much shorter.

"This is very, very quick," she said.

Cloning would be fundamentally different from ordinary reproduction. It would involve taking a cell from a living person, slipping it into an egg cell whose genetic material has been removed and allowing the genetic material of the adult cell to direct the development of a new embryo, then fetus, then person who is the identical twin of the person who provided the initial cell. It would allow a living person to be reborn, in a sense, only at a later time.

Scientists and infertility specialists envision certain specialized circumstances in which it might be acceptable to clone humans. Grieving parents may want to reproduce a terminally ill child. Or a woman may want a child but be infertile. Is it worse somehow for her to clone herself than to obtain an embryo made-to-order with donated egg and sperm, the kind that many fertility clinics are already offering the infertile?

In fact, said Dr. Joseph Schulman, director of the Genetics and IVF Institute in Fairfax, Va., if a woman has no eggs and her husband makes no sperm, they might consider cloning both husband and wife.

"Then they could have one of each," Schulman said.

But what cloning really accomplishes, experts said, is to make it possible, for the first time, to think seriously about genetically enhancing human beings. Scientists could grow a person's cells in sheets in the laboratory and sprinkle the cells with genes. Only a very few cells would take up the genes, and use them, but it is relatively easy for scientists to find those cells and pluck them out of the mix.

If they then used those cells to make clones, the clones would contain the added genes in every cell of their body. Already, two such experiments have been completed in animals, using cells from fetuses rather than cells from adults.

Last summer, Dr. Keith Campbell of PPL Therapeutics in Roslin, Scotland, and Dr. Ian Wilmut of the Roslin Institute in Edinburgh, the scientists who created Dolly, announced that they had made Polly, a cloned lamb whose every cell contained a human gene. Shortly afterward, ABS Global Inc., a company in De Forest, Wis., announced the birth of Gene, a calf that was cloned from genetically altered fetal cells.

With humans, predicted Dr. Lee Silver, a molecular biologist at Princeton University, the first genetic enhancements might be genes to protect against diseases, like an AIDS resistance gene or a gene to protect against Alzheimer's disease, both of which have already been identified. In a sense, it would be no different morally from vaccinating a child for a disease, Silver said.

As more and more becomes known about genes, other enhancements become possible.

"At present," Willadsen said, "there is a large effort involved in sorting out the human genome. I don't think they are doing that just to have some nice charts to put on the wall."

Research that lays the groundwork for cloning humans is proceeding rapidly. Dr. James Grifo, the director of the division of reproductive endocrinology at New York University Medical Center, is working on nuclear transfers, the crucial technique for cloning, but with another purpose in mind. His goal is to transfer the genetic material from immature eggs of older women into eggs of

younger women. The egg could finish maturing with the machinery of the younger woman's egg, and that should result in less chromosomal damage, the bane of attempted pregnancies in older women.

So far, Grifo has shown that he can move egg nuclei around, which is, in essence what is required for cloning.

Dr. Jacques Cohen and Willadsen, at St. Barnabas, also have moved nuclei between cells, but for a different reason. They are trying to help women whose eggs are easily fertilized but whose embryos tend to die, probably because there is a defect in the cytoplasm of their eggs.

"It's being used for a different purpose than cloning, but the techniques are very much the same," Willadsen said.

At the same time, Dr. Donald Wolf, a senior scientist at the Oregon Primate Research Center and the director of Oregon's only in vitro fertilization center, at the University of Oregon, has two federal grants to study cloning in rhesus monkeys. One will involve cloning from cells of an adult.

"We're pretty optimistic," Wolf said. "We have every reason to think it will work."

He explained that the National Institutes of Health, which gave him the grants, is interested in genetically identical monkeys for AIDS vaccine research and in clones of rhesus monkeys that, by chance, happened to develop a rare genetic disease, retinitis pigmentosa.

By cloning the animals, Wolf hopes to make enough of them for investigators to use them to study the disease and its treatments. But one consequence of the primate work, Wolf said, is that it will establish methods that could be applied for the cloning of humans.

"We are laying the groundwork," Wolf said.

Society should think about the possible results of all this work "sooner rather than later," Wolf said.

But some experts said the real question was not whether cloning is ethical but whether it is legal.

"The fact is that, in America, cloning may be bad but telling people how they should reproduce is worse," Willadsen said.

In the end, Willadsen said, "America is not ruled by ethics. It is ruled by law."

1/10

Jenny –

Thanks for your input. At least on target. The statement has disposal. – JFP

THE WHITE HOUSE

Office of the Press Secretary
(Houston, Texas)

Embargoed For Release
Until 10:06 A.M. EST
Saturday, January 10, 1998

RADIO ADDRESS BY THE PRESIDENT
TO THE NATION

Four Seasons Hotel
Houston, Texas

THE PRESIDENT: Good morning. Today I want to talk with you about the extraordinary promise of science and technology, and the extraordinary responsibilities that promise imposes on us.

As we approach the 21st century it is clearer than ever that science and technology are changing the way we live and work and raise our families. The remarkable breakthroughs in biomedical science are helping to unravel the mysteries of life, holding out new hope for lifesaving cures to some of our most dreaded diseases. In recent years, we've made real progress, lengthening the lives of people with HIV, finding the genes that can show heightened risk for breast cancer and diabetes. Now we're on the verge of discovering new treatments for spinal cord and even brain injuries.

For five years I have maintained our nation's solid commitment to scientific research and technological development, because I believe they're essential to our nation's economic growth and to building the right kind of bridge to the 21st century. The balanced budget I will submit in just a few weeks to Congress reflects that continued commitment. And, in my upcoming State of the Union address, I'll talk more about what we're doing to keep America on the cutting edge of the scientific and technological advancements that are driving our new global economy.

Still, it's good to remember that scientific advancement does not occur in a moral vacuum. Technological developments divorced from values will not bring us one step closer to meeting the challenges or reaping the benefits of the 21st century.

This week, like many Americans, I learned the profoundly troubling news that a member of the scientific community is actually laying plans to clone a human being. Personally, I believe that human cloning raises deep concerns, given our cherished concepts of faith and humanity. Beyond that, however, we know there is virtually unanimous consensus in the scientific and medical communities that attempting to use these cloning techniques to actually clone a human being is untested and unsafe and morally unacceptable.

We must continue to maintain our deep commitment to scientific research and technological development. But when it comes to a discovery like cloning, we must move with caution, care and deep concern about the impact of our actions. That is why I banned the use of federal funds for cloning human beings while we study the risks and responsibilities of such a possibility. And that's why I sent legislation to Congress last June that would ban the cloning of human beings for at least five

years while preserving our ability to use the morally and medically acceptable applications of cloning technology.

Unfortunately, Congress has not yet acted on this legislation. Yet, it's now clearer than ever the legislation is exactly what is needed. The vast majority of scientists and physicians in the private sector have refrained from using these techniques improperly, and have risen up to condemn any plans to do so. But we know it's possible for some to ignore the consensus of their colleagues and proceed without regard for our common values. So today, again, I call on Congress to act now to make it illegal for anyone to clone a human being.

Our nation was founded by men and women who firmly believed in the power of science to transform their world for the better. Like them, we're bound together by common dreams and by the values that will drive our own vision for the future. And our commitment to carry those enduring ideals with us will renew their promise in a new century and a new millennium. We must never lose touch with that, no matter what the reason, or we'll lose touch with ourselves as a people.

Thanks for listening.

END

THE WHITE HOUSE

Office of the Press Secretary

For Immediate Release March 4, 1997

March 4, 1997

MEMORANDUM FOR THE HEADS OF EXECUTIVE DEPARTMENTS AND AGENCIES

SUBJECT: Prohibition on Federal Funding for Cloning of Human Beings

Recent accounts of advances in cloning technology, including the first successful cloning of an adult sheep, raise important questions. They potentially represent enormous scientific breakthroughs that could offer benefits in such areas as medicine and agriculture. But the new technology also raises profound ethical issues, particularly with respect to its possible use to clone humans. That is why last week I asked our National Bioethics Advisory Commission to thoroughly review the legal and ethical issues associated with the use of this technology and report back to me in 90 days.

Federal funds should not be used for cloning of human beings. The current restrictions on the use of Federal funds for research involving human embryos do not fully assure this result. In December 1994, I directed the National Institutes of Health not to fund the creation of human embryos for research purposes. The Congress extended this prohibition in FY 1996 and FY 1997 appropriations bills, barring the Department of Health and Human Services from supporting certain human embryo research. However, these restrictions do not explicitly cover human embryos created for implantation and do not cover all Federal agencies. I want to make it absolutely clear that no Federal funds will be used for human cloning. Therefore, I hereby direct that no Federal funds shall be allocated for cloning of human beings.

WILLIAM J. CLINTON

# # #

THE WHITE HOUSE

Office of the Press Secretary

For Immediate Release June 9, 1997

TO THE CONGRESS OF THE UNITED STATES:

I am pleased to transmit today for immediate consideration and prompt enactment the "Cloning Prohibition Act of 1997." This legislative proposal would prohibit any attempt to create a human being using somatic cell nuclear transfer technology, the method that was used to create Dolly the sheep. This proposal will also provide for further review of the ethical and scientific issues associated with the use of somatic cell nuclear transfer in human beings.

Following the February report that a sheep had been successfully cloned using a new technique, I requested my National Bioethics Advisory Commission to examine the ethical and legal implications of applying the same cloning technology to human beings. The Commission concluded that at this time "it is morally unacceptable for anyone in the public or private sector, whether in a research or clinical setting, to attempt to create a child using somatic cell nuclear transfer cloning" and recommended that Federal legislation be enacted to prohibit such activities. I agree with the Commission's conclusion and am transmitting this legislative proposal to implement its recommendation.

Various forms of cloning technology have been used for decades resulting in important biomedical and agricultural advances. Genes, cells, tissues, and even whole plants and animals have been cloned to develop new therapies for treating such disorders as cancer, diabetes, and cystic fibrosis. Cloning technology also holds promise for producing replacement skin, cartilage, or bone tissue for burn or accident victims, and nerve tissue to treat spinal cord injury. Therefore, nothing in the "Cloning Prohibition Act of 1997" restricts activities in other areas of biomedical and agricultural research that involve: (1) the use of somatic cell nuclear transfer or other cloning technologies to clone molecules, DNA, cells, and tissues; or (2) the use of somatic cell nuclear transfer techniques to create animals.

The Commission recommended that such legislation provide for further review of the state of somatic cell nuclear transfer technology and the ethical and social issues attendant to its potential use to create human beings. My legislative proposal would implement this recommendation and assign responsibility for the review, to be completed in the fifth year after passage of the legislation, to the National Bioethics Advisory Commission.

I urge the Congress to give this legislation prompt and favorable consideration.

WILLIAM J. CLINTON

THE WHITE HOUSE,
June 9, 1997.

# # #

OUTLINE OF WHITE HOUSE STATEMENT

In fashioning a law to ban human cloning, we have to be extremely careful to ensure that we do not inadvertently ban research which is vital to developing cures and therapies for deadly diseases.

Let me outline the key principles which should guide us in drafting a law:

1. The law should ban the act of cloning of a human being. It should not ban "research" because that might chill scientists in the conduct of vital basic biomedical research.

2. The law should focus only on the issue addressed by the National Bioethics Advisory Commission (NBAC). NBAC did not review and made no recommendations regarding embryo research, which is already subject to a ban on federally funded research.

> "We do not revisit either the question of the cloning of humans by embryo-splitting or the issues surround embryo research. The latter issue has, of course, recently received careful attention by the National Institutes of Health panel, the Administration, and the Congress." Letter of Harold Shapiro, NBAC Chairman (June 9, 1997).

3. Violation of the ban would be determined based on objective activities, not the "intent" or "purpose" of the scientists. We need to give scientists objective standards to define the prohibited acts. Focusing on their "intent" or "purpose" is open to interpretation and misinterpretation and does not permit scientists to predict how the statute will be enforced.

4. We need a national ban on human cloning. The national law should govern and we need to avoid the enactment of multiple and different state laws. This was one of the recommendations of NBAC.

> "The advantage to federal legislation -- as opposed to state-by-state laws -- lies primarily in its comprehensive coverage and clarity....Besides ensuring interstate uniformity, a federal law would relieve the need to rely on the cooperation of diverse medical and scientific societies, or the actions of diverse IRBs, to achieve the policy objective. As an additional benefit, federal legislation could displace the varied state legislative efforts now ongoing, some of which suffer from ambiguous drafting that could inadvertently prohibit the important cellular and molecular cloning research described...in this report." NBAC report at 100.

5. We need to enact the law for a five year period with a mandatory review at that time to determine whether the ban should be extended.

> "It is notoriously difficult to draft legislation at any particular moment that can serve to both exploit and govern the rapid and unpredictable advances of science. Some mechanism, therefore, such as a sunset provision, is absolutely needed to ensure an opportunity to re-examine any judgment made today about the implications of somatic

cell nuclear transfer cloning of human beings. As scientific information accumulates and public discussion continues, a new judgment may develop and we, as a society, need to retain the flexibility to adjust our course in this manner. A sunset provision...ensures that the question of cloning will be revisited by the legislature in the future, when scientific and medical questions have been clarified, possible uses have been identified, and public discussion of the deeper moral concerns about this practice have matured." NBAC report at 101.

6. We need to make sure the bill sets penalties which will absolutely deter any violations. The penalties should be civil fines in large amounts and we should not threaten the existence of a entire research firm.

7. We need to include a findings section and a explicit list of protected medical research to help ensure that the law does not have unintended consequences in inhibiting biomedical research.

8. Finally, we need to ensure that the Department of Justice enforces the law, not private individuals. We need to prevent the filing of frivolous or harassment law suits.

KEY DRAFTING ISSUES

Ban act of cloning

-- No ban "research"

Do not ban embryo research

Violation should be determined based on objective facts, not "intent" or "purpose"

-- "intent" and "purpose" are criminal law concepts, unpredictable, subjective

Federal preemption -- NBAC recommendation

-- Florida bill would have banned cloning of cells and genes!

Sunset -- NBAC recommendation

Penalties -- fines vs. confiscation

Protected medical research -- findings

No private right of action -- Clinton bill

DEFINING WHEN LIFE BEGINS

BILL PROPOSED BY CLINTON ADMINISTRATION

SECTION 5. PROHIBITION. It shall be unlawful for any person or other legal entity, public or private, to perform or use somatic cell nuclear transfer with the intent of introducing the product of that transfer into a woman's womb **or in any other way creating a human being.**

-- Implies that "introducing" = "creating a human being"

MODEL LEGISLATIVE LANGUAGE REGARDING HUMAN CLONING

The following legislative language is technically accurate from a scientific point-of-view and focuses only on the cloning of a human being.

SECTION 1. TITLE. This act shall be called the "Human Cloning Prohibition Act of 1998."

SECTION 2. PROHIBITION. It shall be unlawful for any person to use federal funds to create a human child identical in terms of nuclear deoxyribonucleic acid (DNA) to an existing or previously existing individual using somatic cell nuclear transfer technology.

SECTION 3. DEFINITIONS. For the purposes of this section, the following definitions apply:

(a) "somatic cell nuclear transfer technology" means transferring the nucleus of a somatic cell of an existing or previously existing human child or adult into an oocyte from which the nucleus has been removed;

(b) "the creation of a human child" means implanting the product of somatic cell nuclear transfer technology for gestation and subsequent birth;

(c) "somatic cell" means a differentiated, diploid cell;

(d) "oocyte" means the mature female germ cell, the egg;

(e) "nucleus" means the cell structure that houses the chromosomes, and thus the genes; and

(f) "gestation" means the period during which an embryo develops into a fetus that is ready to be born.

SECTION 4. PREEMPTION OF STATE LAWS. This law shall preempt any state law which imposes on individuals or institutions using federal funds a prohibition or limitation with respect to research regarding somatic cell nuclear transfer, human cloning, cloning of molecules, DNA, cells, and tissues, to the use of somatic cell nuclear transfer techniques to develop animals, or to related research.

SECTION 5. PROTECTED BIOMEDICAL RESEARCH. Nothing in this Act shall restrict other areas of biomedical and agricultural research, including but not limited to important and promising work that involves:

(a) the use of somatic cell nuclear transfer or other cloning technologies to clone molecules, DNA, cells, and tissues; or

(b) the use of somatic cell nuclear transfer techniques to develop animals.

SECTION 6. EFFECTIVE DATE. This Act shall apply to somatic cell nuclear transfers performed after the date of its enactment.

SECTION 7. REAUTHORIZATION. The prohibition in this legislation shall expire five years from the effective date.

SECTION 8. NATIONAL BIOETHICS ADVISORY COMMISSION REPORT. No later than four and one-half years after the enactment of this Act, the National Bioethics Advisory Commission shall report to the President on

(a) the state of the science of somatic cell nuclear transfer;

(b) the ethical and social issues associated with the potential use of this technology in humans; and

(c) the advisability of continuing the prohibition established by this Act. The Commission is authorized to continue for five years from the date of enactment for this purpose and for other purposes as established in Executive Order 12975 and subsequent amendments to this order.

SECTION 9. RIGHT OF ACTION. Nothing in this Act shall be construed to give any individual or person a private right of action.

Draft3 1-13-98
ASRM

CLONING PROHIBITION AND RESEARCH PROTECTION ACT

SECTION 1. PROHIBITION. It shall be unlawful for any person to create a human child using somatic cell nuclear transfer.

SECTION 2. DEFINITIONS. For the purposes of this section, the following definitions apply:

(a) "somatic cell nuclear transfer" means transferring the nucleus of a somatic cell of an existing or previously existing human child or adult into an oocyte from which the nucleus has been removed;
(b) "the creation of a human child" means implanting into the uterus the product of somatic cell nuclear transfer technology for gestation and subsequent birth;
(c) "somatic cell" means a mature, diploid cell;
(d) "oocyte" means the female germ cell, the egg;
(e) "nucleus" means cell structure that houses the chromosomes, and thus the genes; and
(f) "gestation" means the period during which an embryo develops, inside the uterus, into a fetus that is ready to be born.

SECTION 3. PREEMPTION OF STATE LAWS. This law shall preempt any state law that imposes on individuals or institutions any limitations with respect to nuclear transfer, human cloning, cloning of molecules, DNA, cells, and tissues, or the use of nuclear transfer techniques to develop animals, or to related research.

SECTION 4. PROTECTED BIOMEDICAL RESEARCH. Nothing in this Act shall restrict other areas of biomedical and agricultural research, including but not limited to important and promising work that involves:

(a) the use of somatic cell nuclear transfer or other cloning technologies, to clone molecules, DNA, cells, and tissues; or
(b) the use of somatic cell nuclear transfer techniques to develop animals.

SECTION 5. EFFECTIVE DATE. This Act shall apply to somatic cell nuclear transfer performed after the date of its enactment.

SECTION 6. REAUTHORIZATION. The prohibition in this legislation shall expire five years from the effective date.

SECTION 7. NATIONAL BIOETHICS ADVISORY COMMISSION REPORT. No later than four and one-half years after the enactment of this Act, the National Bioethics Advisory Commission shall report to the President on

(a) the state of the science of somatic cell nuclear transfer;

(b) the ethical and social issues associated with the potential use of this technology in humans; and
(c) the advisability of continuing the prohibition established by this Act. The Commission is authorized to continue for five years from the date of enactment for this purpose and for other purposes as established in Executive Order 12975 and subsequent amendments to this order.

SECTION 8. RIGHT OF ACTION. Nothing in this Act shall be construed to give any individual or person a private right of action.

SECTION 9. PENALTIES.

(a) Any person who intentionally violates Section 1 shall be fined the greater of $250,000 or two times the gross gain or loss from the offense.

California Law Penalties

(a) If the violator is a corporation, firm, clinic, hospital, laboratory, or research facility, by a civil penalty of not more than one million dollars ($1,000,000) or the applicable amount under subdivision (c), whichever is greater.

(b) If the violator is an individual, by a civil penalty of not more than two hundred fifty thousand dollars ($250,000) or the applicable amount under subdivision (c), whichever is greater.

(c) If any violator derives pecuniary gain from a violation of this section, the violator may be assessed a civil penalty of not more than an amount equal to the amount of the gross gain multiplied by two.

BIO
BIOTECHNOLOGY
INDUSTRY
ORGANIZATION

News Release

1625 K Street, N.W. · Suite 1100 · Washington, D.C. 20006 · (202) 857-0244 · FAX: (202) 857-0237

FOR IMMEDIATE RELEASE

CONTACT:
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202-857-0244

BIO Calls For FDA To Assert Its Authority On Cloning

(WASHINGTON, D.C., January 13, 1998)...Carl B. Feldbaum, president of the Biotechnology Industry Organization (BIO) sent the attached letter to Health and Human Services Secretary Donna Shalala asking her to assert the Food and Drug Administration's (FDA) authority and jurisdiction over any possible attempts to clone a human being:

"It is clear that society is not ready for the cloning of a human being. We need to listen carefully, and analyze thoughtfully the ethical, moral and safety issues that have been raised.

"Recognition and assertion of the FDA's regulatory power over human cloning will protect biomedical advances and at the same time will give everybody some breathing room to debate this issue. Bioethics issues will occur with further advances in science. We need to be certain, before we move ahead, that advances will clearly benefit human kind and not set us back into some new age of uncertainty about our values and the quality of human life."

The Biotechnology Industry Organization (BIO) represents over 745 biotechnology companies, academic institutions, and state biotechnology centers in 46 states and more than 25 nations. BIO members are involved in the research and development of health care, agricultural and environmental biotechnology products.

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BIO

BIOTECHNOLOGY INDUSTRY ORGANIZATION

January 13, 1998

The Honorable Donna E. Shalala, Ph.D.
Secretary,
Department of Health and Human Services
615F Hubert H. Humphrey Building
200 Independence Ave., SW
Washington, DC 20201

Dear Secretary Shalala:

The recent announcement from Dr. Richard Seed regarding his proposal to establish a clinic for the cloning of human beings has caused significant controversy. BIO supports President Clinton's and the National Bioethics Advisory Commission's (NBAC) moratorium on the cloning of a human being. Cloning a human being poses major ethical and moral questions, as well as deeply troubling medical safety issues. The experience with "Dolly," in which there were 276 unsuccessful attempts before an apparently healthy sheep was born, points to the experimental nature of this technology in animals. It is plainly inappropriate to attempt to apply this technology to human beings. While these questions remain unresolved, government and public opposition to the cloning of a human being remains strong. Society needs to be heard and respected on this issue.

Several members of Congress have recently expressed interest in legislation that would ban the cloning of human beings. They may not be aware that the Food and Drug Administration (FDA) has broad authority to regulate biological products. Last February, FDA published a regulatory framework for the regulation of cellular and tissue-based products. The level of FDA oversight is dictated by the degree of human manipulation of cells or tissues. Those products which are subject to a low level of oversight are those which are defined as 'minimal manipulation' when the processing does not alter the biological characteristics of the cells or tissue.

But in those cases where there is more than 'minimal manipulation,' FDA has stated its intent to subject such products to formal regulatory review including the investigational new drug (IND) regulations and license review regulations.

BIO believes that the Dr. Seed's proposal to clone humans using nuclear transfer technology is much more than minimal manipulation as the original function of the egg cell is unmistakably altered by the removal of the parental haploid DNA and insertion of DNA from a somatic cell from another person. Thus, any such research along these lines should be subject to the IND regulations that require patient informed consent, review by an institutional review board (IRB) where the research is being conducted, and FDA review under 21 CFR Part 312.

In addition to raising profound ethical issues, nuclear transfer technology has not been reliably proven to work in animal models and raises serious safety issues. We believe that for the foreseeable future, FDA should issue a clinical hold on any IND submission to proceed with such experiments.

A public statement by senior officials within HHS as to the regulatory status of nuclear transfer technology would be welcomed and useful as the public debate continues.

Sincerely,

Carl B. Feldbaum /ag

Carl B. Feldbaum
President

CBF:ag

cc: Michael Friedman, MD, Food and Drug Administration

President Clinton's proposal
(not yet introduced)

POSITIVES:

- Focuses only on the act of cloning a human being using somatic cell nuclear transfer, not on "research."
- Includes a five year "sunset" provision to determine the science and public sentiment on the issue in the future. (Just as public and political views have changed about artificial insemination, heart transplants and test tube babies.)
- Includes "findings" section which describes value of biomedical research.
- Includes clause that describes areas of critical protected biomedical research.

NEGATIVES:

- Definition of violation is over broad. One example is that as written it would limit treatments for mitochondrial disease.
- Violations turn on "intent" of individual to clone. The concept of "intent" comes from the criminal law and has no meaning in the context of a statute with civil penalties. Implementing an "intent" test includes a complex assessment of the psychological state of mind of a researcher, opens up the possibility of abuse by prosecutors and other enforcers, and provides no predictability to researchers.
- Does not preempt state laws.
- Draconian penalties (fine plus confiscation of entire research property).

Bond (S. 368)
(Referred to Senate Labor Committee)

POSITIVE:

- Good intentions.

NEGATIVES:

- Outlaws "research" on cloning a human being, does not focus only on the act of cloning a human being using somatic cell nuclear transfer.
- Scientific terms need further definition or refinement.
    - For example, there is no definition of "replication" — does not require individuals to be genetically identical in terms of nuclear DNA and the bill appears to cover all "cells" taken from any source.
    - It does not appear to require taking of cells from an existing or previously existing human being.
- Definition of violation is over broad. For example it would limit treatments for mitochondrial disease.
- Does not preempt state laws.
- Does not include "findings" section which describes value of biomedical research.
- Does not include clause describing areas of "protected biomedical research."
- Does not bar private right of action to enforce prohibition

Elhers (HR 922)
(Substitute bill reported from House Science Committee: referred to House Commerce Committee).

POSITIVE:

- Includes clause describing areas of "protected biomedical research."

NEGATIVES:

- Focuses on 'research," not on the act of cloning a human being using somatic cell nuclear transfer technology.
- Focuses only on "creation of..an embryo," not on the act of cloning to produce a baby which, must include implementation and birth of clone.
- Does not include any "sunset" provision to mandate reconsideration.
- Does not preempt state laws (this could result in 51 separate cloning statutes — one federal and 50 state laws that confuse and inhibit valuable biomedical research.)
- Does not bar private right of action to enforce prohibition.

Elhers (HR 923)
(referred to House Commerce Committee)

POSITIVE:

- Focuses on the act of cloning a human being using somatic cell nuclear transfer, not on "research" about cloning.

NEGATIVES:

- No definition of scientific terms.
- Does not include any "sunset" provision to reconsider legislation.
- Does not preempt state laws.
- Does not include "findings" section which describes value of biomedical research.
- Does not include clause describing areas of "protected biomedical research."
- Does not bar private right of action to enforce prohibition.

California Cloning Law

POSITIVES:

- Focuses only on the act of cloning a human being using somatic cell nuclear transfer, not vaguely on "research."
- Includes a five years "sunset" provision.
- Includes a "findings" section which describes value of biomedical research.

NEGATIVES:

- Piecemeal approach to national issue.
- Definition of violation is over broad — for example it would limit treatments for mitochondrial disease.
- Violations turn on "purpose" of individual to clone. The concept of "purpose" comes from the criminal law ans has no meaning in the context of a statute with civil penalties. Implementing a "purpose" test once again involves a complex assessment of the psychological state of mind of a researcher, opens up the possibility of abuse by prosecutors and the enforcers.
- Does not include a description of "protected biomedical research."
- Does not bar private right of action to enforce prohibition.

BILL PROPOSED BY CLINTON ADMINISTRATION

To prohibit any attempt to create a human being using somatic cell nuclear transfer, to provide for further review of the ethical and scientific issues associated with the use of somatic cell nuclear transfer in human beings, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE. This Act may be cited as the "Cloning Prohibition Act of 1997".

SECTION 2. FINDINGS.

(a) It has been reported that an adult sheep has been cloned using a technique called somatic cell nuclear transfer, a form of cloning.

(b) The National Bioethics Advisory Commission (NBAC) has reviewed the scientific and ethical implications of this technology's potential use to clone human beings.

(1) NBAC has found that:

(a) Somatic cell nuclear transfer technology may have many applications for biotechnology, livestock production, and new medical approaches including the production of pharmaceutical proteins and prospects for regeneration and repair of human tissues.

(b) However, the possibility of using somatic cell nuclear transfer for the purposes of creating a child entails significant scientific uncertainty and medical risk. Potential risks, known and unknown, could result in harm to a child.

(2) The NBAC concluded unanimously that at this time it is morally unacceptable for anyone in the public or private sector, whether in a research or clinical setting, to attempt to create a child using somatic cell nuclear transfer cloning. The Commission's consensus is based on current scientific information indicating that this technique is not safe to use in humans at this point.

(3) Moreover, in addition to issues of safety, the Commission identified many additional serious ethical concerns which they agreed require a great deal more widespread and careful public deliberation before this technology may be used.

(4) NBAC recommended a continuation of the current moratorium on the use of Federal funds to support any attempt to create a child by somatic cell nuclear transfer, and an immediate request to all firms, clinicians, investigators, and professional societies to comply voluntarily with the intent of the Federal moratorium.

(5) NBAC further recommended that Federal legislation be enacted to prohibit anyone from attempting, whether in a research or clinical setting, to create a child through somatic cell nuclear transfer cloning.

(6) NBAC also recommended that the United States cooperate with other

countries to enforce mutually supported restrictions on this activity.

(7) NBAC specified that the legislation should include a sunset provision and that, prior to the sunset date, an oversight body should review and report on the status of somatic cell nuclear transfer technology and the ethical and social issues associated with its use and recommend whether the prohibition should be continued.

(8) The Commission concluded that any regulatory or legislative actions undertaken to effect the foregoing prohibition should be carefully written so as not to interfere with other important areas of research, such as the cloning of human DNA sequences and cells, which raise neither the scientific nor the ethical issues that arise from the possible creation of children through somatic cell nuclear transfer techniques.

(9) The Commission also found that cloning animals by somatic cell nuclear transfer does not raise the same issues implicated in attempting to use the technique to create a child, and its continuation should only be subject to existing regulations regarding the humane use of animals.

© Biomedical research facilities, including those conducting cloning, and reproductive services facilities affect interstate commerce.

SECTION 3. PURPOSES. The purposes of this Act are

(a) To prohibit any attempt to create a human being using somatic cell nuclear transfer cloning; and

(b) To provide for further review of the ethical and scientific issues associated with the use of somatic cell nuclear transfer in humans.

SECTION 4. DEFINITIONS.

(a) "Cloning" means the production of a precise genetic copy of a molecule (including DNA), cell, tissue, plant, animal, or human.

(b) "Somatic cell" means any cell of the body other than germ cells (eggs or sperm).

© "Somatic cell nuclear transfer" means the transfer of a cell nucleus from a somatic cell into an egg from which the nucleus has been removed.

SECTION 5. PROHIBITION. **It shall be unlawful for any person or other legal entity, public or private, to perform or use somatic cell nuclear transfer with the intent of introducing the product of that transfer into a woman's womb or in any other way creating a human being.**

SECTION 6. PROTECTED BIOMEDICAL RESEARCH. Nothing in this Act shall restrict other areas of biomedical and agricultural research, including important and promising work that involves:

(1) the use of somatic cell nuclear transfer or other cloning technologies to clone molecules, DNA, cells, and tissues; or

(2) the use of somatic cell nuclear transfer techniques to create animals.

SECTION 7. PENALTIES.

(a) Any person who intentionally violates Section 5 shall be fined the greater of $250,000 or two times the gross gain or loss from the offense.

(b) If a person is violating or about to violate Section 5, the Attorney General may

commence a civil action in Federal district court to enjoin such violation.

© Any property, real or personal, derived from or used to commit a violation or attempted violation of Section 5, or any property traceable to such property, is subject to forfeiture to the United States in accordance with the procedure set forth in Chapter 46 of Title 18 of the United States Code.

(d) The Attorney General of the United States shall have exclusive enforcement authority under this Act.

SECTION 8. EFFECTIVE DATE. This Act shall apply to somatic cell nuclear transfers performed within five years after the date of its enactment.

SECTION 9. NATIONAL BIOETHICS ADVISORY COMMISSION REPORT. No later than four and one-half years after the enactment of this Act, the National Bioethics Advisory Commission shall report to the President on (1) the state of the science of somatic cell nuclear transfer; (2) the ethical and social issues associated with the potential use of this technology in humans; and (3) the advisability of continuing the prohibition established by this Act. The Commission is authorized to continue for five years from the date of enactment for this purpose and for other purposes as established in Executive Order 12975 and subsequent amendments to this order.

SECTION 10. RIGHT OF ACTION. Nothing in this Act shall be construed to give any individual or person a private right of action.

Ehlers Bill (H.R. 922) as Reported From House Science Committee

SECTION 1. SHORT TITLE.

This Act may be cited as the ''Human Cloning Research Prohibition Act''.

SEC. 2. PROHIBITION AGAINST EXPENDITURE OF FEDERAL FUNDS FOR RESEARCH ON CLONING HUMANS.

(a) Prohibition.-- None of the funds made available in any Federal law may be obligated or expended to conduct or support any project of research that includes the use of human somatic cell nuclear transfer technology to produce an embryo.

(b) Definitions.-- For purposes of this section--

(1) the term ''human somatic cell nuclear transfer'' means transferring the nucleus of human somatic cell into an oocyte from which the nucleus has been removed or rendered inert; and

(2) the term ''somatic cell'' means a cell of an embryo, fetus, child, or adult which is not and will not become a sperm or egg cell.

SEC. 3. REVIEW. The Director of the National Science Foundation shall enter into an agreement with the National Research Council for a review of the implementation of this Act. Not later than 5 years after the date of the enactment of this Act, the Director shall transmit to the Congress a report containing the results of that review, including the conclusions of the National Research Council on--

(1) the impact that the implementation of this Act has had on research; and

(2) recommendations for any appropriate changes to this Act.

SEC. 4. PROTECTED SCIENTIFIC RESEARCH. Nothing in this Act shall restrict other areas of scientific research not specifically prohibited by this Act, including important and promising work that involves--

(1) the use of somatic cell nuclear transfer or other cloning technologies to clone molecules, DNA, cells other than human embryo cells, or tissues; or

(2) the use of somatic cell nuclear transfer techniques to create animals other than humans.

HR 923 (EHLERS)
105th CONGRESS
1ST SESSION

To prohibit the cloning of humans.

IN THE HOUSE OF REPRESENTATIVES
March 5, 1997

Mr. EHLERS introduced the following bill; which was referred to the Committee on Commerce

A BILL

To prohibit the cloning of humans.

[Italic->] Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, [<-Italic]

SECTION 1. SHORT TITLE.

This Act may be cited as the 'Human Cloning Prohibition Act'.

SEC. 2. PROHIBITION AGAINST CLONING OF HUMANS.

(a) IN GENERAL- It shall be unlawful for any person to use a human somatic cell for the process of producing a human clone.

(b) CIVIL MONEY PENALTY- Any person who violates subsection (a) is liable to the United States for a civil money penalty in an amount not exceeding $5,000.

S 368 (BOND)
105th CONGRESS
1ST SESSION

To prohibit the use of Federal funds for human cloning research.

IN THE SENATE OF THE UNITED STATES
February 27, 1997

Mr. BOND (for himself and Mr. ASHCROFT) introduced the following bill; which was read twice and referred to the Committee on Labor and Human Resources

A BILL

To prohibit the use of Federal funds for human cloning research.

[Italic->] Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, [<-Italic]

SECTION 1. PROHIBITION ON CLONING RESEARCH.

(a) IN GENERAL- No Federal funds may be used for research with respect to the cloning of a human individual.

(b) DEFINITION- For purposes of this section, the term 'cloning' means the replication of a human individual by the taking of a cell with genetic material and the cultivation of the cell through the egg, embryo, fetal, and newborn stages into a new human individual.

CALIFORNIA LAW
BANNING HUMAN CLONING

BILL NUMBER: SB 1344 CHAPTERED
BILL TEXT

CHAPTER 688
FILED WITH SECRETARY OF STATE OCTOBER 6, 1997
APPROVED BY GOVERNOR OCTOBER 4, 1997
PASSED THE SENATE SEPTEMBER 10, 1997
PASSED THE ASSEMBLY SEPTEMBER 2, 1997
AMENDED IN ASSEMBLY AUGUST 25, 1997
AMENDED IN SENATE APRIL 21, 1997

INTRODUCED BY Senator Johnston and Assembly Member Battin

MARCH 11, 1997

An act to add and repeal Sections 2260.5, 16004, and 16105 to the Business and Professions Code, and to add and repeal Chapter 1.4 (commencing with Section 24185) to Division 20 of the Health and Safety Code, relating to human cloning.

LEGISLATIVE COUNSEL'S DIGEST

SB 1344, Johnston. Human cloning.
Existing law regulates medical experimentation on humans. **This bill would prohibit a person from cloning, as defined, a human being, and from purchasing or selling an ovum, zygote, embryo, or fetus for the purpose of cloning a human being.** The bill would authorize the State Director of Health Services to levy administrative penalties for violation of $1,000,000 on a corporation, firm, clinic, hospital, laboratory, or research facility and $250,000 on an individual, or twice the amount of pecuniary gain from the violation, if greater, to be paid into the General Fund. The bill would provide that violation of the prohibition constitutes unprofessional conduct for purposes of the Medical Practice Act. The bill would require city business licenses and county business licenses to be revoked for violation of the prohibition. The bill would repeal its provisions on January 1, 2003.

THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1. **It is the intent of the Legislature to place a five-year moratorium on the cloning of an entire human being in order to evaluate the profound medical, ethical, and social implications that such a possibility raises. It is not the intent of the Legislature**

that this moratorium apply to the cloning of human cells, human tissue, or human organs that would not result in the replication of an entire human being. During this moratorium period, the State Director of Health Services should be called upon to establish a panel of representatives from the fields of medicine, religion, biotechnology, genetics, law, bioethics, and the general public to evaluate those implications, review public policy, and advise the Legislature and the Governor in this area.

SEC. 2. Section 2260.5 is added to the Business and Professions Code, to read:

2260.5. (a) A violation of Section 24185 of the Health and Safety Code, relating to human cloning, constitutes unprofessional conduct.

(b) This section shall remain in effect only until January 1, 2003, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2003, deletes or extends that date.

SEC. 3. Section 16004 is added to the Business and Professions Code, to read:

16004. (a) Any license issued to a business pursuant to this chapter shall be revoked for a violation of Section 24185 of the Health and Safety Code, relating to human cloning.

(b) This section shall remain in effect only until January 1, 2003, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2003, deletes or extends that date.

SEC. 4. Section 16105 is added to the Business and Professions Code, to read:

16105. (a) Any license issued to a business pursuant to this chapter shall be revoked for violation of Section 24185 of the Health and Safety Code, relating to human cloning.

(b) This section shall remain in effect only until January 1, 2003, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2003, deletes or extends that date.

SEC. 5. Chapter 1.4 (commencing with Section 24185) is added to Division 20 of the Health and Safety Code, to read:

CHAPTER 1.4. HUMAN CLONING

24185. (a) No person shall clone a human being.

(b) No person shall purchase or sell an ovum, zygote, embryo, or fetus for the purpose of cloning a human being.

© For purposes of this section, "clone" means the practice of creating or attempting to create a human being by transferring the nucleus from a human cell from whatever source into a human egg cell from which the nucleus has been removed for the purpose of, or to implant, the resulting product to initiate a pregnancy that could result in the birth of a human being.

24187. For violations of Section 24185, the State Director of Health Services may, after appropriate notice and opportunity for hearing, by order, levy administrative penalties as follows:

(a) If the violator is a corporation, firm, clinic, hospital, laboratory, or research facility, by a civil penalty of not more than one million dollars ($1,000,000) or the applicable amount under subdivision (c), whichever is greater.

(b) If the violator is an individual, by a civil penalty of not more than two hundred fifty thousand dollars ($250,000) or the applicable amount under subdivision (c), whichever is greater.

© If any violator derives pecuniary gain from a violation of this section, the violator may be assessed a civil penalty of not more than an amount equal to the amount of the gross gain multiplied by two.

(d) The administrative penalties shall be paid to the General Fund.

24189. This chapter shall remain in effect only until January 1, 2003, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2003, deletes or extends that date.

APPENDIX C:
BIO ANALYSIS OF CLINTON ADMINISTRATION DRAFT BILL REGARDING CLONING OF HUMAN BEINGS

A copy of the bill proposed by the Clinton Administration is attached as Appendix D to this testimony. This analysis raises issues about the bill's unintended consequences and other issues.

1. "Cloning Prohibition Act"

The proposed short title for the draft bill -- "the Cloning Prohibition Act" -- is literally misleading. The draft bill would not, in fact, prohibit "cloning" and explicitly states that nothing in the bill should "interfere with other important areas of research, such as the cloning of human DNA sequences and cells, which raise neither the scientific nor the ethical issues that arise from the possible creation of children through somatic cell nuclear transfer techniques." Section 2 (b)(8). The draft also states that "cloning animals by somatic cell nuclear transfer does not raise the same issues implicated in attempting to use the technique to create a child, and its continuation should only be subject to existing regulations regarding the humane use of animals." Section 2(b)(9). The draft defines the term "cloning" to include many technologies other than somatic cell nuclear transfer.

To give the draft bill this title might well increase the possibilities that the bill would be interpreted or enforced in ways which do, in fact, inhibit the use of cloning technologies to produce medicines and other beneficial products to treat deadly and disabling diseases. It would be preferable to have no title for any such law or a title which reflects its substance.

2. Purposes Section

The purposes section, Section 3, does not include as one purpose the protection of vital biomedical research even though the bill as drafted includes -- in Section 6 -- such protections. Including this purpose in Section 3 would reduce the possibilities that the proposed bill would be interpreted and enforced in ways which would, in fact, inhibit the use of cloning technologies for beneficial purposes.

3. "Introducing" and "Creating a Human Being"

The proposed bill refers to "introducing" the product of somatic cell nuclear transfer

"into a woman's womb or in any other way creating a human being."

To begin with it is not clear whether this means that there are two possible violations or one. One violation might be "introducing" and the second might be "creating."

Another interpretation of this language is that "introducing" is equivalent to "creating a human being." It can be read that one way of "creating a human being" is to introduce the product of somatic cell nuclear transfer into a woman's womb. If this is a correct interpretation, this might be the first Federal statute which states or implies that a fertilized embryo in a woman's womb is already a "human being."

The ethical question of when a "human being" has been "created" is not an issue with respect to which our industry has expertise. These are not issues about technology; they are issues for society.

A further interpretation is that the draft bill contemplates that there are ways of "creating a human being" other than "introducing" an egg into a woman's womb. It might, for example, be interpreted to mean that a "human being" has already been created when an egg is fertilized outside the womb -- the standard practice with *in vitro* fertilization.

In addition, the word "introducing" is ambiguous. The term is not defined in the proposed bill and could refer to any number of different acts.

We are not aware of "any other way" of creating a human being other than birth. If the authors of the draft bill are aware of other ways, perhaps they should be specified. If there are no other ways, then this language is superfluous.

We only point out that this proposed bill has far reaching implications which go way beyond the issue of somatic cell nuclear transfer technology and go to the fundamental ethical question of what constitutes a "human being."

4. <u>Acts vs. Intent</u>

The proposed bill focuses on use of somatic cell nuclear transfer "with the intent of introducing the product of that transfer into a woman's womb or in any other way creating a human being."

The use of the word "intent" here is quite confusing and troubling. Consider four possible scenarios:

(1) If an individual has no intent to "introduce" or otherwise create a human being, then there is no violation even if the cell is, in fact, later introduced into a woman's womb by that individual. In this sense the proposed language does not violate the act of introducing or creating as long as there is no intent.

(2) If an individual has no intent to "introduce" but a third party does, in fact, "introduce," then the first party is presumably not liable even if the introduction does, in fact, take place.

(3) If an individual has the requisite intent, but does nothing to actually "introduce" the cell into a woman's womb, then the individual may be found liable. Read carefully, the draft bill does not require the actual "introduction" of the cell into a woman's womb, but only the "intent" to do so.

(4) Finally, it is possible for an individual to "intend" to do something which is not only not done, but which is likely to be impossible to be done. If an individual announces that he "intends" to use nuclear transfer technology to create a human child, makes no attempts to do so, and then finds out that it is quite impossible to do so, he or she still might be liable.

None of these results makes sense.

The point is that the wording of the proposed bill does not focus solely on the final act of creating a human being. As a result, it is impossible to avoid the absurdity of prosecuting individuals even where no human being is created and not prosecuting individuals even though human beings have, in fact, been created.

If the gravamen of the violation is the act of using somatic cell nuclear transfer technology to create a human being, then intent should not be relevant. If no such act occurs, then there should be no violation no matter what the intent may be.

The only way to avoid these absurdities is to focus exclusively on the act of creating a human being. Any focus on intent will very likely lead to unintended results.

5. Implementation of "Intent" Requirement

We are concerned that a focus on "intent" would lead to unpredictable explorations of the psyche of researchers. What evidence would have to be produced to prove the "intent" of the individual? Would it be sufficient to demonstrate that the introduction or creation took place, or would additional evidence required to show that this was the specific "intent" of the researcher?

If "intent" is an element of the offense, would the individual be entitled to produce evidence to show that he or she has the equivalent of an insanity defense or is not able to recognize the consequences of the act?

It is particularly strange to focus on "intent" if the violation is that of a "legal entity" rather than a "person." There are many different legal entities -- universities, non-profit foundations, and companies. What evidence would be needed to prove that such an entity had the requisite "intent" to violate the prohibition? The concept of "intent" is not normally one

which is relevant to the conduct of a "legal entity." If the requisite "intent" is that of the "legal entity," would that require that the "intent" be that of an officer of the entity who had legal authority to bind the entity, rather than that of an employee with no legal authority to bind the entity?

We believe that these are not quibbles over semantics given the fact that one of the penalties is confiscation of the entire legal entity by the government when a violation has been proven.

6. Research vs. Somatic Cell Nuclear Transfer

As explained above, the draft bill focuses on the use of a specified technology with a specified intent. The gravamen of the violation is not, using the words of the draft bill, "creating a human being." Violations can occur even if a human being is not, in fact, created. This raises very serious issues about the potential chilling impact of the draft bill on biomedical research.

The fact that the bill is not confined to cases where a human being is created means that the draft bill is particularly likely to inhibit a broad spectrum of research, not just research which leads to certain end points. There are many intermediate points in the research process short of, say, infusing a drug into a human subject. Every one of the acts short of infusing the drug may be critical to the research and discovery process. This research can have totally different, non-controversial purposes, and involve no actual infusion of the drug. The reference to "intent" can give rise to fears that every act of research concerning somatic cell nuclear transfer is vulnerable to misinterpretation and that every researcher or institution involved with this technology is vulnerable to suit for research.

It may be that the authors of this proposed bill mean to prohibit unsuccessful as well as successful "attempts" to create a child. There are several other places in the draft bill which refer to the "attempt" to use this technology, rather than to the concept of "intent." (See Section 3, Purposes, where it refers to any "attempt" to create a human being.) The word "attempt" is quite different than the word "intent." "Attempts" involve specific acts, not mental states, and it would be easier to determine when a violation occurs. The determination would be less subjective.

Even if the proposed bill were to refer to "attempts" rather than "intent," it may still inhibit research. Every act of research might be characterized as an "attempt," just as it might be seen as evidence of "intent." Every act of research which might, after many additional steps, lead to creation of a human being could be questioned.

Again, the only way to avoid this unintended effect is to focus the proposed bill on the final and definitive act of creating a child using a specified technology, not on the intent or attempt to create a human being using the technology. Any statute which focuses on the technology, as distinct from the end use and application of the technology, inherently and necessarily inhibits research. The only way to avoid this result is to make the "creation of a

human child" using this technology the violation.

7. Definition of "somatic cell nuclear transfer"

The complexity of the issues raised by this draft bill are evident in the definitions of the key scientific terms it uses to specify the reach and impact of the prohibition and penalties. Some of the definitions are not correct from a scientific point of view. This creates ambiguity about the conduct which is subject to the prohibition and penalties and casts doubt on the wisdom of enacting this proposal. Ultimately this is a proposed bill which seeks to regulate scientists and, if it is not possible to draft it to include scientifically accurate terminology, it may well fail to deter conduct which is intended to be covered and deter conduct which is not controversial.

The draft bill would make it unlawful for a person or legal entity to "perform or use somatic cell nuclear transfer" for certain purposes. The draft bill's definition of a "somatic cell" excludes cells which are "germ cells (eggs or sperm)." Then the draft defines "somatic cell nuclear transfer" to mean the "transfer of a cell nucleus from a somatic cell to an egg from which the nucleus has been removed." The terms "germ cells, "eggs" and "sperm" are not defined in the draft bill.[1]

To add to the confusion the NBAC report glossary defines "somatic cells" as "any cell of an embryo, fetus, child or adult not destined to become a sperm or egg cell." The first footnote in the NBAC report defines "somatic cell" as "any cell of the embryo, fetus, child, or adult which contains a full complement of two sets of chromosomes; in contrast with a germ cell, i.e. an egg or a sperm, which contains only one set of chromosomes." And the text of the NBAC report provides a third definition. It recommends that the prohibition apply to "banning nuclear transfer using the nuclei derived from somatic cells other than those of an embryo or fetus" and defines this nuclear transplantation as "transplanting the genetic material from a differentiated somatic cell into an egg from which the nucleus had been removed." Thus, the somatic cell comes from a non-embryonic, non-fetal source.

At a minimum this means that the Administration's draft bill differs from the legislation which the NBAC report recommends be enacted.

It also means that we have three definitions of the critical term "somatic cell," one in the bill, and two in the NBAC report. (And two more definitions in the Ehlers and Bond bills.) This is hardly a reassuring situation. This is, after all, the term which defines the

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The glossary in the appendix to the NBAC report defines an "egg" as "the mature female germ cell; also called ovum, or oocyte." The glossary provides other interrelated definitions: a "germ cell" is defined as "a sperm or egg (all other body cells are known as somatic cells)"; "sperm" as "mature male reproductive cells, an egg as the mature female germ cell"; and a "gamete" as a "mature sperm or egg."

violation and with respect to which extreme penalties are prescribed. The fact that there is such wide disagreement about how to define this term casts doubt on the wisdom of enacting the draft bill.

We believe that none of the three definitions is accurate. Our initial view was the definition in the NBAC glossary is closest to the mark -- with its reference to cells which are "not destined to become a sperm or egg cell." The other two definitions will cause confusion as they include a zygote as one type of somatic cell.[2] We need a definition which is more precise than the glossary definition and is less likely to jeopardize vital biomedical research.

In addition to these unsettling questions about the definition of a "somatic cell, " no mention is made in the draft bill of the cells which are destined to become gametes, which are not somatic cells (at least under two of the above definitions). These cells are not fully differentiated and therefore they are not gametes per se. Many researchers refer to the types of cells that will become eggs and sperms as "germ cells"; the terms "pre-meiotic germ cells," "primordial germ cells" or "progenitor germ cells" are also often used. These cells can be isolated from embryos which are only eight days old (in mice) and they are destined to become sperm or eggs when the diploid (double) cells split into haploid (single) cells. Thus, by these definitions diploid germ cells are present in adult animals.

We don't know if these pre-meiotic germ cells can be used for the purpose of nuclear transfer, but in mice it is possible to isolate these cells from fetuses, grow them *in vitro* (tissue culture) and maintain their totipotency, allowing them to contribute to all cell types in a new animal. The fact that the definitions of cell types mentioned in the draft bill are not scientifically precise and are defined differently by different scientists illustrates the extreme difficulty of drafting a bill on this subject.

The NBAC definition of an "egg" is not included in the draft bill although it appears to be correct from a scientific point of view. But there have been instances, in the murine and bovine systems, where two cell embryos, rather than eggs, have been enucleated and used as hosts for the donor nucleus. A "two cell embryo" is not an egg. An egg is an unfertilized, haploid gamete which when combined with a sperm forms a zygote. An embryo is created when the zygote divides for the first time. Although progenitor germ cells and two cell embryos were not mentioned in the Roblin Institute paper and are not covered in the draft bill, many different protocols and procedures could be adapted for use in this context. Again, we

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The NBAC report includes the following interrelated definitions of "embryo," "fertilization," "oocyte," and "zygote": "embryo" is defined as "the developing organism from the time of fertilization until significant differentiation has occurred, when the organism becomes known as a fetus"; "fertilization" as "the process whereby male and female gametes unite [which] begins when a sperm contacts the outside of the egg cell and ends with the formation of a zygote"; "oocyte" as "the mature female germ cell, the egg"; and "zygote' as "the single-celled, fertilized egg." None of these definitions is included in the draft bill.

point out that the proposed bill is deficient from the point of view of science and that it is extremely difficult to draft a bill on this complex issue.

8. Penalties

The penalties proposed by the Administration for violation of the ban can only be described as draconian. This fact, combined with the vagueness of the description of the prohibited conduct, is likely to discourage research well beyond its explicit terms.

The penalties include a fine which is the greater of "$250,000 or two times the gross gain or loss from the offense" and confiscation of "any property, real or personal, derived from or used to commit a violation...or any property traceable to such property..."

If the violation occurs at a university, would the proposed bill permit confiscation of the entire university? If the violation were to occur at a company, would the proposed bill permit the confiscation of the entire company even if only one researcher were involved?

Researchers who are seeking grants from the National Science Foundation or other foundations would tend to avoid any research with any potential or possible connection, real or perceived, to this technology. No funding agency would dare to fund such research.

The draft bill refers also to penalties being imposed on "public" legal entities. By this we assume that the draft bill could refer to the National Institutes of Health or another public agency which performs biomedical research. We find it odd to contemplate the possibility of the Attorney General seeking to impose a fine on NIH or to confiscate its property.

It is obvious to us that the vagueness of the draft bill and the severity of the penalties could lead any prudent university or company or NIH institute to cease doing research even remotely connected to the type of technology covered by the statute.

Even if a company avoided this technology entirely, there is a danger that investors might misinterpret the company's research focus and be unwilling to put their capital at risk with that company. This is a clear case where the existence of even a narrowly crafted bill will have a chilling effect far beyond its specific terms.

In addition, the terms of the proposed penalties are vague. It appears that the proposed bill does not call for incarceration, but we are confused given the repeated use of the term "intent" in the proposed bill, a concept which is often associated with criminal law.

The penalty section provides for the payment of the greater of $250,000 or "two times the gross gain or loss from the offense." The concept of imposing a fine based on the "gross gain" of a firm, university, or institute presumably refers to its gross receipts or revenue and the concept of "gross...loss" presumably refers to its gross expenses. We know of no precedent for imposing a fine based on a multiple of the expenses incurred.

The concept of imposing fines based on gains and losses "from the offense" is also vague. Would it be a fine based on the receipts or expenses of the entire firm, university, or institute or a subset of that? The manner in which this provision might be implemented has potentially dire consequences.

The final ambiguity is how the proposed bill would be interpreted in the case of an individual researcher, acting without authorization. Would the firm, university, or Institute where the individual is employed or where he or she conducted the unauthorized research be fined or subject to confiscation? Would a failure to exercise reasonable supervision be evidence of "intent"?

9. Advisory Opinions

Were a law to be enacted, we recommend that a mechanism be established to enable scientists to secure advisory opinions regarding the scope, interpretation and possible enforcement of the law with regard to specific research projects.

This would require the Justice Department to establish sufficient expertise and staff to respond to requests for advisory opinions. It could defer to the expertise of the National Institutes of Health, Institute of Medicine, National Science Foundation, and other bodies which have expertise on these issues or experts in the private sector.

To the extent that it would not compromise the confidentiality of research projects, the privacy interests of patients, or the intellectual property rights of the researchers, these advisory opinions should be published so that other researchers could benefit from the information.

To be clear, we do not believe that such a mechanism would entirely eliminate the inevitable chilling impact of a law on this subject.

10. Exclusive Remedy

The proposed bill provides that the Attorney General will have "exclusive enforcement authority under this Act." We suggest that this clause be interpreted to mean that the authority to seek enforcement cannot be delegated by the Attorney General to another official.

The draft bill also provides that it shall not be "construed to give any individual or person a private right of action." We are concerned that this language is not parallel to language elsewhere in the draft bill referring to a "person or other legal entity." This section should use this same language to clarify that the draft bill cannot be construed to confer a right of action on any "legal entity," not just any "person or individual."

11. Preemption

The proposed bill fails to include a clause preempting state laws. We had thought that

one of the reasons why NBAC and the Administration have proposed enactment of a Federal statute was concern about the potential for many conflicting state laws on these complex issues. Given how difficult it is proving to be to craft any statute on this issue, if enactment of a law is considered to be necessary, we believe enactment of one Federal law is essential, as opposed to enactment of many different state laws. The possibilities for differential interpretation and enforcement of state laws would have a particularly chilling impact on vital biomedical research.

To be effective the preemption clause must refer to all types of laws on the subject of cloning, including the cloning of cells and genes, not just somatic cell nuclear transfer, so that it covers appropriate laws even if they do not use any of the terms in the proposed Federal statute.

12. Effective Date

We interpret the "effective date" section of the proposed bill to include both an effective date and a sunset provision. The proposed bill states that it "shall apply" to acts "performed within five years after the date of enactment." This implies that acts of this type performed thereafter would not be covered by the statue. It would be preferable and clearer if the effective date and sunset provisions were stated separately in distinct sections so there is no confusion.

If a statue is to be enacted, it should certainly include a sunset provision, as NBAC has emphasized. This area of science is new and we need to reevaluate the impact of any law on the subject. Enactment of a permanent law without a sunset provision will increase the likelihood that the law will chill vital biomedical research. A sunset provision will at least focus the attention of the researchers and others on a process towards the end of the five year period when all of these issues can again be reviewed.

Draft Letter Regarding Legislation to Ban Cloning of Human Beings

We are writing to express our concern about legislation pending in the Congress to ban the cloning of entire human beings.

Let us be clear. We oppose the cloning of a human being. We see no ethical or medical justification for the cloning of a human being and agree with the conclusions of the National Bioethics Advisory Commission (NBAC) that it is unacceptable at this time for anyone in the public or private sector, whether in a research or clinical setting, to create a human child using somatic cell nuclear transfer technology. We recognize that this application of the technology raises fundamental ethical and social issues. This technology is not currently safe to use in humans.

The American Society for Reproductive Medicine, the Biotechnology Industry Organization, and the Federation of American Societies of Experimental Biology have all pledged that their members will not seek to clone a human being. These three associations include essentially every researcher or practitioner in the United States who has the scientific capability to clone a human being.

We agree with NBAC in its report on cloning that: "It is notoriously difficult to draft legislation at any particular moment that can serve to both exploit and govern the rapid and unpredictable advances of science." Poorly crafted legislation to ban the cloning of human beings may put at risk biomedical research which is vital to finding the cures to the diseases and ailments which our organizations champion. Cancer, diabetes, (list specific disease of signatories here) and many others will benefit from the advances achieved by biomedical researchers.

We urge the Congress to proceed with extreme caution and adhere to the ethical standard for physicians, "first do no harm." We believe that there are two distinct issues here, cloning of a human being and the healing which comes from biomedical research. Congress must be sure that any legislation which it considers does no harm to biomedical research which can heal those with deadly and debilitating diseases.

Please keep patients' concerns in mind as you proceed in analyzing this very complicated issue.

Sincerely,

PATIENT ADVOCACY GROUPS
PROFESSIONAL MEDICAL SOCIETIES

CURRENT BAN ON FEDERAL FUNDING OF BOTH EMBRYO AND CLONING RESEARCH

The Fiscal Year 1996 and 1997 Labor, HHS Appropriations bills have included a broad ban on funding for **embryo** research. The text of this ban follows:

> (a) None of the funds made available in this Act may be used for -- (1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero... (b) For purposes of this section, the term 'human embryo or embryos' include any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning or any other means from one or more human gametes.

The Fiscal Year 1998 Labor, HHS Appropriations bill, H.R. 2264, as passed by the House and Senate, and signed into law, was **amended in both bodies to provide that this ban be extended to any embryo or embryos that is derived by "human diploid cells." Human diploid cells are precisely the type of cells used in the sheep cloning experiment which led to the human cloning debate.** The new language in both bills reads as follows:

> (a) None of the funds made available in this Act may be used for -- (1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero... (b) For purposes of this section, the term 'human embryo or embryos' include any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning or any other means from one or more human gametes **or human diploid cells.**[1]

Neither the National Bioethics Advisory Commission (NBAC) nor the President have reviewed or made any recommendations regarding enactment of any legislation regarding embryo and fetal tissue research.

> We do not revisit either the question of the cloning of humans by embryo-splitting or the issues surround embryo research. The latter issue has, of course, recently received

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[1] This reference to "human diploid cells" may be over broad and prevent use of any human cell line -- say cancer cells lines -- in research, not just use of these cells for somatic cell nuclear transfer cloning.

careful attention by the National Institutes of Health panel, the Administration, and the Congress. Letter of Harold Shapiro, NBAC Chairman (June 9, 1997).

The bill reported in July by the House Science Committee, H.R. 922, focuses only on Federal funding of embryo research. The substitute amendment adopted by the Committee in reporting the bill provides that "None of the funds made available in any Federal law may be obligated or expended to conduct or support any project of research that includes the use of human somatic cell nuclear transfer technology to produce an embryo." This would, in effect, make the current ban on embryo research permanent.

The House Commerce Committee and Senate Labor Committees have jurisdiction over bills, H.R. 922 (Ehlers) and S. 368 (Bond), respectively, which could ban all embryo research, irrespective of Federal funding.

IMPORTANCE OF "CLONING" TECHNOLOGY TO MEDICAL RESEARCH

Introduction

"Cloning" is an essential tool in biomedical research. Cloning techniques -- the isolation of and duplication of genes or cell lines -- have proved to be a cornerstone of scientists' ability to use biotechnology to develop new drugs for previously intractable diseases. Scientists have used cloning as a standard laboratory technique for several decades. Scientifically, cloning animal and human cells and genes provides greater quantities of these identical materials for study.

Over the past 20 years, cloning has been an invaluable research tool leading to the production of breakthrough medicines, diagnostics and vaccines to treat heart attacks, various cancers, kidney disease, diabetes, hepatitis, multiple sclerosis, cystic fibrosis, and other diseases. More than 100 million people worldwide have already benefited from biotechnology medicines and vaccines. Cloning techniques are critical to the biomedical research that holds the promise of many more treatments to come.

The development of the sheep named Dolly has raised new questions about one specific type of cloning techniques and the implications of using this technology to clone entire human beings. Dolly is determined to be a "clone" because her genetic makeup duplicates almost entirely the genetic makeup of another sheep. We would like to distinguish the ways in which cloning can be used to create identical copies of genes and cells and the benefits these technologies are bringing to research and drug development.

Gene Cloning

Scientists routinely isolate and make copies of DNA (deoxyribonucleic acid), the molecular basis of genes; segments of DNA comprise genes. Genes are isolated, copied and inserted into bacteria where they are amplified. The gene is duplicated – or cloned -- when the bacteria reproduces.

Scientists developed ways to greatly amplify the DNA using "PCR" to improve the speed and efficiency with which DNA can be cloned in the lab, in effect "xeroxing" the DNA. PCR is valuable to researchers because it allows them to multiply unique regions of DNA. Many scientific experiments would not be possible without the availability of large quantities of identical copies of DNA.

Medical Benefits of Gene Cloning

Cloning genes is useful to develop diagnostic tests and eventually therapies for genetically-based disorders. The human genes that direct the production of factor VIII to treat hemophilia, of human insulin and of human growth hormone have each been incorporated into the DNA of certain bacteria. These bacteria are then used commercially to make sufficient quantities of these medicines to treat patients. The cloning of genes also has contributed to the development of important medicines, such as tissue plasminogen activator (tPA) to dissolve clots after a heart attack, and erythropoietin (EPO) to treat anemia associated with dialysis for kidney disease.

Cell Cloning

Cells can be cloned by isolating them from the body through a biopsy, and culturing them in a laboratory. The original cells start to grow and divide, producing new cells that are identical to the original cells. The genetic makeup of the resulting collection of cells, called a "cell line," is identical to that of the original cell. Cell cloning is a highly reliable procedure that is used to test and sometimes to develop new medicines.

Medical Benefits of Cell Cloning

Scientists are using cloning technology to study the regeneration of damaged or diseased tissues and organs. There are many areas where this technology would be invaluable, such as research focusing on: nerve cells to address spinal cord injuries or in diseases where nerves degenerate, muscle cells to address some types of heart disease or diseases in which the muscles are wasting, and skin cells to treat burn victims. Researchers are investigating transplantation of bone marrow stem cells to treat blood disorders and cancer, transplantation of pancreatic beta cells to treat diabetes and neurons to treat brain disorders. Other research is underway to develop cell lines that could help to generate cells for organ transplantation and tissue repair. For instance, one of our companies treats knee damage by taking a biopsy of the patient's knee cartilage, propagating additional cartilage cells and transplanting the new cells back into the patient's knee.

With a better understanding of early cell growth and specialization, scientists may be able to reverse the degenerative processes in conditions such as Alzheimer's, Parkinson's, and Huntington's diseases. Scientists may also learn more about the process by which cancerous tumors spread throughout the body, and examine ways to control and eliminate the growth of cancer cells. There are other types of research to help us learn more about genetic birth defects and infertility.

The Journey from Single Cell to Whole Organism

In normal development of a human being, a sperm containing DNA from the male, and an egg with DNA from the female, fuse to form a new cell, a zygote, with a full genetic complement from two parents. The zygote divides into many more cells, forming a cluster of identical cells. Then, the cells start to grow and differentiate into various types of cells, such as cells that will form the nervous system, or cells that will form the heart. The cells differentiate through genetic regulation with different genes switching off and on, depending on the type of cell they are becoming. As more cells divide and differentiate, the cell cluster grows into an embryo and eventually into a baby.

How Was "Dolly" Cloned?

The procedure used to produce "Dolly" is called "somatic cell nuclear transfer technology." This type of cloning technology involves transferring the nucleus containing DNA from a somatic cell (i.e., any cell of the body, except the egg or sperm) into an egg from which the nucleus has been removed and implanting the resultant embryo into a surrogate mother for gestation and birth.

This procedure resulted in the birth of a sheep whose genetic material is identical to the adult sheep who donated the nucleus, with the exception of the DNA in the mitochondria which is inherited through the cytoplasm with the enucleated egg. Dolly is a clone because her genes are identical to the genes in the first sheep, her mother. It is important to note that this process is extremely difficult and inefficient at this time. This experiment was carried out on 277 eggs before the one success that resulted in the birth of Dolly.

BIO
BIOTECHNOLOGY
INDUSTRY
ORGANIZATION

PLEDGE BY BIOTECHNOLOGY INDUSTRY ORGANIZATION (BIO) TO SUPPORT MORATORIUM ON CLONING OF A HUMAN BEING

March 27, 1997

The Honorable William J. Clinton
President of the United States
The White House
Washington, D.C. 20500

Dear Mr. President:

The recent cloning of a sheep from the genetic material of an adult cell has riveted the world. Previously, researchers had reported using genetic material from animal embryos to create new organisms. But, as you observed, this latest development raises profound new issues. When two individuals are created from the same embryonic genetic material, identical twins result. We are quite familiar with identical twins in our everyday lives. However, "Dolly" raises new prospects for which we are not so adequately prepared. While our everyday lives may include identical twins of the same age, we have never experienced identical twins substantially different in age, indeed, perhaps alive during entirely different periods in history. In our everyday lives we may decide to procreate a child and wait in wonder and awe to see the unique individual he or she will turn out to be. We do not, on the other hand, have experience creating a child where part of that decision may include an evaluation of the life, health, character and accomplishments of an adult from whom we will take the genetic material that will become the child's entire genetic makeup.

These new prospects challenge some of the most fundamental concepts we hold about ourselves as social and spiritual beings. These concepts include what it means to be a parent, a brother or sister, a family. We believe that it was in response

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to this moral and spiritual challenge that you requested the nation's biomedical research community to agree to a voluntary moratorium on the cloning of human beings until the National Bioethics Advisory Commission can review the meaning of this scientific breakthrough. We share your desire for a reflective examination of the moral issues raised by Dolly. We support this moratorium on cloning human beings.

In the days since the announcement of Dolly, the potential benefits to be derived from cloning procedures in agricultural and laboratory animal species have been widely discussed. Cloning, the duplication of specific genes and individual types of cells -- is an essential tool in biotechnology. The techniques involved are integral to the process used to produce breakthrough medicines, diagnostics and vaccines to treat heart attacks, various cancers, kidney disease, diabetes, hepatitis, multiple sclerosis, cystic fibrosis and other diseases. More than 100 million people worldwide have already benefited from biotechnology medicines and vaccines.

There is also valuable research into cloning human cells, organs and other tissue. This could produce replacement skin, cartilage and bone tissue for burn and accident victims. This avenue of study may produce cells for cancer therapy and result in ways to regenerate retinal or spinal cord tissue. Research is also under way to develop replacement internal organs in transgenic animals for human transplantation.

Perhaps even more important, human cells used in a subset of the cloning procedures -- that is, procedures that by themselves could not create a new human being -- could provide profound new insights into how genes control human development. These fundamental insights, in the decades ahead, will provide the basis for even greater biomedical advances in the service of humanity.

Mr. President, we are pleased to report that the Board of Directors of the Biotechnology Industry Organization fully supports your call for a moratorium on research efforts undertaken for the purpose of cloning a human being while the National Bioethics Advisory Commission considers the implications of Dolly. But we firmly believe that research involving duplication of cellular material has such enormous potential benefits for society that it should proceed without hindrance. Accordingly, we ask you to oppose, as we do, any hastily drafted laws to ban the cloning of human beings that may, however well intentioned, inadvertently also ban this valuable research.

Sincerely,

Henri A. Termeer
Chairman

Carl B. Feldbaum
President

PLEDGE BY AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM) TO SUPPORT MORATORIUM ON CLONING OF A HUMAN BEING

At its October 18, 1997 meeting, The Board of Directors of The American Society for Reproductive Medicine approved a voluntary moratorium on cloning human beings.

Resolved: The American Society for Reproductive Medicine declares a voluntary five-year moratorium on cloning human beings, where "cloning human beings" is defined as the duplication of an existing or previously existing human being by transferring the nucleus of a differentiated, somatic cell into an enucleated human oocyte, and implanting the resulting product for intrauterine gestation and subsequent birth.

In addition, the following statement was issued on June 5 (date of releaase of NBAC report)

FOR IMMEDIATE RELEASE: CONTACT: Heather E. Kowalski June 5, 1997
(202) 863-2439 Hkowalski@asrm.com

ASRM STATEMENT ON HUMAN CLONING THROUGH NUCLEAR TRANSPLANTATION

(Washington, DC) -- The American Society for Reproductive Medicine (ASRM) is issuing the following statement:

The American Society for Reproductive Medicine (ASRM) finds the practice of cloning an existing human being unacceptable. However, ASRM believes that the broader field of human embryo research is acceptable and important, and guidelines both promoting and limiting the research should be set on the national level. The current moratorium on federal funding of human embryo research should be overturned and oversight for such research should be given to the National Institutes of Health.

The American Society for Reproductive Medicine (ASRM)), founded in 1944, has more than 10,000 members who are devoted to advancing knowledge and expertise in reproductive medicine and biology, including obstetrician-gynecologists, urologists, endocrinologists, research scientists, medical technologists, and allied health professionals.

# # #

PLEDGE BY THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY (FASEB) TO SUPPORT MORATORIUM ON CLONING OF A HUMAN BEING

For more information, contact:
Howard Garrison, 301/571-0657

September 18, 1997

FASEB ENDORSES VOLUNTARY MORATORIUM ON CLONING HUMAN BEINGS

Bethesda, Md -- Federation of American Societies for Experimental Biology (FASEB) President Ralph G. Yount announced the adoption of a voluntary moratorium on cloning human beings. Members of FASEB's Public Affairs Executive Committee, representing the 14 member societies of the Federation, unanimously voted in favor of the following statement at a recent meeting:

> RESOLVED: The Federation of American Societies for Experimental Biology (FASEB) adopts a voluntary five year moratorium on cloning human beings, where "cloning human beings" is defined as the duplication of an existing or previously existing human being by transferring the nucleus of a differentiated, somatic cell into an enucleated human oocyte, and implanting the resulting product for intrauterine gestation and subsequent birth.

In accord with the recommendations by the National Bioethics Advisory Commission, this moratorium will be in effect for a period of five years, with subsequent reconsideration for possible extension.

Yount, a Professor of Biochemistry and Chemistry at Washington State University, noted that the Federation adopted this moratorium for several important reasons.

> "First and foremost," stated Yount, "we seek to reassure Americans that biologists have no intentions of cloning human beings. Indeed, we would regard cloning a human being as an unethical and reprehensible act. But, we have also recognized that there is a role for us -- as scientists -- to play in this debate. We need to ensure that imprecise or misused technical language is not included in legislation designed to prevent the cloning of human beings. If

enacted, such laws could hinder vital biomedical research that can lead to the repair of diseased and damaged human tissues and organs, and to possible cures for diabetes, cancer, Parkinson's Disease and other neurodegenerative diseases."

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

January 13, 1998

MEMORANDUM FOR DISTRIBUTION

FROM: JOHN H. GIBBONS

SUBJECT: Briefing on Cloning-Related Activities

The Biotechnology Industry Organization (BIO) is concerned that legislation intended to prohibit attempts to clone human beings may curtail a broader sphere of activities that are commonly used in biomedical and agricultural research. BIO is holding a number of meetings on the Hill, preparing op-ed pieces and working with patient advocacy groups to enlist support for carefully circumscribed legislation, such as the measure the President sent to the Hill last June. BIO issued a press release supporting the President's moratorium and the recommendations of the President's National Bioethics Advisory Commission.

BIO has offered to present a briefing to interested EOP staff on their ongoing efforts related to cloning. In light of the recent report that a private individual is eager to attempt to use cloning technology to produce a child, there is renewed interest in a legislative deterrent to such efforts. It would be useful to gain BIO's perspective, as well as that of the Pharmaceutical Research and Manufacturers of America and the American Society for Reproductive Medicine, on possible legislative initiatives and reactions from the biotechnology and health care communities.

OSTP has scheduled this briefing for tomorrow, Jan. 14, at 1 p.m., in Room 472, OEOB. Please contact Rachel Levinson (x66137) and indicate if you or your designee would be interested in attending.

Distribution:
Rahm Emanuel
John Podesta
Paul Begala
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DRAFT MEMORANDUM FOR THE PRESIDENT

FROM:

SUBJECT: Cloning: Legislative Options

Interest in cloning legislation was renewed by reports that a Chicago physicist plans to attempt to use this technology to create a child. Your January 10 radio address challenged Congress to enact a ban on private sector activities like the one you have imposed on the use of public funds. Congressional staff inquiries indicate that your challenge will be accepted. Both critics and supporters of your draft bill agree that this issue raises complex drafting problems. You have the opportunity at this juncture to stay with existing language or, alternatively, propose new wording that clarifies your position. Given the strong possibility that Congressional measures may deviate from the principles outlined in your draft bill, it may be desirable to assert your leadership and encourage your allies by providing more specific language.

Your June 9, 1997 draft legislation (Tab A): 1) prohibits the production of a child using somatic cell nuclear transfer, 2) protects valuable research, especially embryo research conducted without the use of Federal funds, 3) provides no new incentives for abortion, and 4) establishes a sunset provision. We believe these principles should underpin any cloning legislation. The prohibition wording options presented below are designed to clarify our position.

Whichever option you choose, you will have to struggle with the dichotomy between allowing most embryo research in the private sector, while maintaining a ban on the use of Federal funds with which much valuable science might be conducted. You addressed this issue in developing the current draft bill and might refer to the June 8 decision memorandum for useful discussion (Tab B). It is probable that cloning legislation will viewed by some members of Congress as a vehicle for extending a more permanent, broad ban on embryo research.

The memorandum also presents the pros and cons associated with a clause pre-empting state legislation of human cloning, and a possible legislative strategy.

I. Prohibition Wording Options

A. Support current language without changes

Current language:

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It shall be unlawful for any person or other legal entity, public
or private, to perform or use somatic cell nuclear transfer with
the intent of introducing the product of that transfer into a
woman's womb or in any other way creating a human being.
```

Your bill has been praised by the biomedical industry and professional societies for its narrow focus on the act of creating a human being through somatic cell nuclear transfer--the technology used to create Dolly the sheep--and the absence of any mention of embryo research. These groups also applaud your protection of noncontroversial biomedical research and the 5-year sunset provision. Current language maintains the status quo with respect to freedom to carry out

embryo research in the private sector under existing (albeit limited) Federal oversight, and does not affect nor address the ban on Federal funding for a much broader class of embryo research.

The biotechnology industry and fertility research community have identified three problems with this language: (1) it appears to equate introduction into the womb with creating a human being, (2) the meaning of the word "intent" is ambiguous, and (3) the meaning of the phrase "or in any other way" is unclear. Option B describes a solution for these problems, while continuing to uphold the principles expressed in your draft bill .

B. Refine current language

Suggested modification:
It shall be unlawful for any person or other legal entity, public or private, to introduce the product of somatic cell nuclear transfer into a woman's womb in order to create a child.

This language is an improvement in that it makes it clear that violation would occur at the time of introduction into the womb of the product of cloning. However, the phrase "in order to create child" carries with it two problems: (1) defining a child and when life begins, and (2) "in order to" still implies intent. Option C avoids these pitfalls/difficulties.

C. Continue to support the principles in the existing bill, but clarify its scope

Suggested modification:
It shall be unlawful for any person or other legal entity, public or private, to introduce the product of somatic cell nuclear transfer into a woman's womb.

You have been sensitive to the need to be very careful in setting a boundary around permissible biomedical research; hence this bills narrow focus. The phrase "in order to create a child" maintains that view. However, it suggests two potentially troubling scenarios of which you should be aware. First, it could be interpreted that it encourages abortion because transfer of the product of cloning would be prohibited only if it was done to create a child, but not if it was done with the intention to abort. Second, someone caught in the act of attempting to create a child using this method could avoid liability simply by aborting the cloned embryo or fetus. Therefore, we would suggest that "in order to create a child" be deleted.

This clear language means that during the time this law is in effect, no one in the public or private sectors may perform somatic cell nuclear transfer and implant the resulting product in a woman's uterus. Today, this is legal in the private sector, although it may be possible to exert some regulatory oversight, as discussed in the background attachment. Some fertility research would be precluded under this option, although it is difficult to determine how much because efforts are generally made to sustain a pregnancy after implantation, not to perform experiments with the intention of aborting. Your National Bioethics Advisory Commission recommended a temporary

ban on the use of somatic cell nuclear transfer to create child only after hearing testimony that a 3-5 year prohibition would not impede medical research progress, as long as animal cloning experiments were permitted. We have been told that the fertility research community would not object to this approach.

The right-to-life community has criticized your bill based on their interpretation that it would allow the creation of embryos for research purposes using private funds as long as those embryos were aborted subsequently. Option C still permits the creation of embryos, but removes the incentive for abortion. While the scientific and medical communities supported your earlier version, it is likely that you will retain their support even with this change in view of the larger threats that Congress might impose on research. However, it does make retention of the **sunset clause** all the more crucial. Sen. Bond, Rep. Ehlers, and others will oppose a sunset clause.

D. Adopt a more general prohibition

Your bill is intended to prevent anyone from creating a child who is a genetically identical copy of an existing or previously existing person. Somatic cell nuclear transfer is one way of accomplishing this feat and you endorsed the recommendation of your National Bioethics Advisory Commission in limiting the scope of your bill to the use of such technology to create a child. However, other groups including the American Society for Reproductive Medicine and Council of Europe have proposed more general, non-technology specific bans. One example might be the following:

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It shall be unlawful to create a child who is genetically identical
to an existing or previously existing child or adult.
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We oppose this approach because it raises many of the same problems addressed in Options A and B; namely, defining a child and when life begins. It would also bar reproductive technology currently in use in the U.S.

Recommendation:

We propose that you select Option C so as to: maintain a narrowly focused prohibition, thus protecting the widest possible range of biomedical research while not creating any new incentives for abortion.

Approve: _____ Disapprove: _____ Discuss: _____

II. Federal Pre-emption of State Regulation

The industry is strongly advocating that the Administration use this bill to pre-empt state laws restricting cloning research. The industry cites the California Bill as an example of the type of provision that would prohibit appropriate biomedical research on cloning and they fear that the

political climate would likely pressure states to adopt unduly restrictive measures.

There are also a number of reasons arguing against pre-emption at this time. For example, federalism concerns would normally militate against preemption unless it could be shown that such action is necessary (e.g. when there is a need for national standards). In this case, although the industry might be inconvenienced by the existence of differing laws, there is no clear reason why uniform standards are required. Indeed, in the area of biomedical research, there is a strong argument in favor of allowing the states to experiment with a wide range of options because no single correct approach to this issue is immediately obvious. Moreover, the industry's fears that the states would act in concert to preclude important biomedical research, beyond the use of cloning to create a child, seem unwarranted. It is not likely that every state would choose to ban all research because the states that elect to forego restrictive regulation would be likely, on that account, to attract new industry. Finally, using this particular bill to preclude all state regulation of biomedical research is inconsistent with our position that this bill is designed to address only the limited issue of cloning and is not an attempt to address broader research issues.

Recommendation:

We recommend against adding a pre-emption clause.

Approve: _____ Disapprove: _____ Discuss: _____

III. Legislative Strategy

Because the amendment process is difficult to control and extreme amendments may make ultimate support of transmitted Administration legislation undesirable, we recommend encouraging our allies in Congress to incorporate your improved language into their legislation. Senator Diane Feinstein is currently drafting legislation and might be receptive.

Cloning legislation already introduced:
HR 922 by Ehlers - prohibition of Federal funds to conduct or support research on the cloning of humans. Passed out of House Science Committee. Jurisdiction claimed by House Commerce. No hearing date set.
HR 923 by Ehlers - prohibition on cloning humans. House Judiciary Committee. No hearing date.
S 368 by Bond - prohibition of use of Federal funds for human cloning research. No action to date.

Tabs:

A. June 9, 1997 draft Administration bill

B. June 8, 1997 Decision memorandum
C. Discussion of Impact of FDA Regulatory Authority on Legislative Strategy