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Issues Regarding Pending Legislation

We emphatically agree with NBAC about the difficulty of drafting legislation to constrain science. We trust that the Subcommittee will agree when it considers the difficult issues raised by the most sophisticated bill proposed on this subject, that of the Clinton Administration. A copy of the Administration bill is printed in Appendix D of my testimony and our detailed analysis is printed in Appendix C.

Let me briefly summarize the twelve issues we have raised with respect to the Administration's draft bill:

1. **"Cloning Prohibition Act":** The proposed short title for the draft bill – "the Cloning Prohibition Act" – is literally misleading. Although the draft bill aims to prohibit the cloning of entire human beings, the bill would not, in fact, prohibit "cloning," a technology which is used to duplicate genes and cells. The draft 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). Thus, the draft defines the term "cloning" to include many technologies other than somatic cell nuclear transfer and urges that all cloning should continue, except for cloning to create entire human beings.

2. **Purposes Section:** Although the bill as drafted includes a section to protect vital biomedical research (see Section 6), this statement should be included in the purposes section -- Section 3. Specifying this purpose in the proper section would enhance the possibilities that the proposed bill would be interpreted and enforced in ways which would not inhibit the use of cloning technologies for beneficial purposes, such as the development of life-saving treatments.

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." One interpretation of this language is that "introducing" is equivalent to "creating a human being." 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.

4. **Acts vs. Intent:** The proposed bill focuses on the 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. There are many scenarios outlined in our analysis which make no sense. For example, 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. It is possible to find oneself in the absurd position of suing individuals even where no human being is created and not suing 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.

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 be required to show that this was the specific "intent" of the researcher?

6. Research vs. Somatic Cell Nuclear Transfer: Because the draft bill is not confined to cases where a human being is actually created, the bill is particularly likely to inhibit a broad spectrum of research, not just research which leads to certain end points. The bill should be drafted to solely restrict the use of somatic cell nuclear transfer to create an entire human being, not to inhibit other types of cloning research.

7. Definition of critical terms: One of the most troubling aspects of the draft bill is that the definitions of key terms, including "somatic cell nuclear transfer," are not correct from a scientific point of view. This creates ambiguity about the conduct which is subject to the prohibition and penalties. 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 definitions are one of the most critical aspects of any bill. They will determine the strength or weakness of this effort.

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 beneficial research well beyond its explicit terms.

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.

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: Given how difficult it is proving to be to craft any statute on this issue, if the Subcommittee determines that enactment of a law is necessary, we believe enactment of one Federal law is essential, as opposed to enactment of many different state laws. The proposed bill fails to include a clause preempting state laws. We believe that one of the reasons why NBAC and the Administration proposed enactment of a Federal statute was concern about the potential for many conflicting state laws on these complex issues.

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. Thus, 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 to avoid confusion.

We agree with NBAC on the imperative of a sunset provision. NBAC stated that a sunset provision is "absolutely needed to ensure an opportunity to re-examine any judgment made today" because 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."

Other Federal Proposals

We have not as yet completed our analysis of the two bills introduced by Representative Ehlers (H.R. 922 and 923) and the bill introduced by Senator Bond (S. 368). Copies of these three bills are included in appendices E, F, and G, respectively, of my

testimony. The Clinton Administration bill is quite sophisticated by comparison to these bills, which were introduced long before NBAC had completed its review.

H.R. 922, sponsored by Rep. Ehlers, which was referred to both the Science and Commerce Committees, states that "None of the funds made available in any Federal law may be expended to conduct or support any project of research that involves the use of a human somatic cell for the process of producing a human clone." The bill does not touch research or other activities which are not funded by the Federal government. As with the Administration bill, this bill uses terms which are not correct from a scientific point of view. It focuses squarely on "research" and not just on prohibiting the act of cloning a human being, chilling vital biomedical research. The bill contains no definitions at all, so there is sure to be a wide range of interpretation of its scope. This broad interpretation adds to the likelihood that the bill would inhibit much research, including research well outside of that intended to be covered.

H.R. 923, also sponsored by Rep. Ehlers, was referred only to the Committee on Commerce and it makes it "unlawful for any person to use a human somatic cell for the process of producing a human clone." This bill applies to all research, not just research funded by the Federal government. Again, this bill uses terms which are not correct from a scientific point of view. It focused on the "process" rather than on the act of cloning a human being. It is not clear how much research might be interpreted to be part of this "process." The focus on "process" implies that the bill covers research and not just on the prohibited act, also chilling vital biomedical research. This bill also contains no definitions, so there is sure to be a wide range of interpretation of its scope and an inhibition of research.

By comparison, S. 368, introduced by Senator Bond, was referred to the Senate Committee on Labor and Human Resources and it provides that "No Federal funds may be used for research with respect to the cloning of a human individual." It defines the term "cloning" to mean "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." The term "cloning" is obviously not the appropriate term to use in any such statute and the definition is not accurate from a scientific point of view.

Imprecision Regarding Key Scientific Terms

Because I am a scientist by training, and there is a great deal of imprecision in the terminology used in these bills and the debate, let me spend a few minutes talking about some of the key scientific terms. One of the most troubling aspects of this legislation is that the definition of key terms, including "cloning" and "somatic cell nuclear transfer." The definitions provided tend to be scientifically inaccurate. Since these terms define the bills' violations, the definitions are critical. They determine whether any statute enacted on this subject is appropriately targeted or indiscriminate in prohibiting research.

The draft Administration 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." And 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."

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. This is hardly a reassuring situation. This is, after all, the term which defines the 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.

As I have said, 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

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[1] 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."

cause confusion as they include a zygote as one type of somatic cell.[2] But, upon intensive review, we believe that the glossary definition is not precise and that we need to develop a definition which is more precise and less likely to jeopardize vital biomedical research.

In addition to these unsettling questions about the definition of a "somatic cell" in the Administration bill, no mention is made in the 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

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[2] 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.

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 Roslin 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 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.

I have focused on the bottom line, our legislative analysis, and some of the scientific terms, but I would also like to give you some background on my company, the varieties of cloning technology in use in biotechnology research, and other key issues.

Aquila Biopharmaceuticals and Biotechnology Industry

Aquila Biopharmaceuticals, based in Worcester, Massachusetts, is developing and commercializing products for treatment and prevention of infectious disease and cancer. The organization was formed as a result of the reorganization of the Cambridge Biotech Corporation under the Chapter 11 Bankruptcy Code. The turn around and restructuring of CBC was a $50 million transaction.

Aquila uses advances in biotechnology and immunology to identify and produce antigens for specific diseases. Combining these antigens with Stimulon™ adjuvants enhances their effectiveness and enables the development of new, fairly safe products that achieve specific immune responses. Aquila is developing the following products: Quilimmune-P™ for preventing pneumococcal infections in elderly people, Quilvax-M™ for preventing mastitis in cows, Quilimmune-M™ for malaria in people, Quilvax-L™ for Lyme disease in dogs, Quilimmune-T™ for tick-borne diseases in people and Quilvax-FeLV™ for leukemia in cats. Aquila's corporate partners are developing products that incorporate the company's core technologies for a broad range of indications.

The biotechnology industry is steadily growing in the United States. There are currently 1287 companies comprising the industry and 118,000 employees, a growth of 9 percent from the previous year. This past year, the industry had $10.8 billion in sales, a 16 percent growth, and revenues of $14.6 billion, a 15 percent growth. The industry spent $7.9 billion on research and development, a growth of 3 percent. There are over 40 biotech therapeutic products on the market treating millions of people for a variety of diseases, including multiple sclerosis, diabetes, and various cancers.

Background on Debate on Cloning of Human Beings

BIO has supported President Clinton's call for a voluntary moratorium on research efforts undertaken for the purpose of the cloning an entire human being. BIO also supported the referral of the cloning issue to NBAC for review. We have supported the establishment of NBAC and believe that it is the appropriate body to review these issues.

We also encouraged the U.S. Congress and state legislatures not to enact legislation until NBAC issued its recommendations. BIO submitted a detailed analysis with recommendations to NBAC on April 23, 1997. A summary of BIO's recommendations to NBAC is printed in Appendix B of this testimony.

The world, as well as the biotechnology industry, was riveted by the recent cloning of a sheep, "Dolly," from the genetic material of an adult cell. Previously, researchers had reported using genetic material from animal embryos to develop new animals. This latest scientific development raises important new issues because of its potential impact on research with human subjects.

When two individuals are created by nature from the same embryonic genetic material, identical twins result. We are quite familiar with identical twins in our everyday lives. We know, for example, that such twins have very distinct personalities despite sharing the same genetic makeup. However, Dolly raises new prospects for which we are not so adequately prepared. While we may encounter identical twins of the same age today, we have never experienced identical twins substantially different in age, indeed, perhaps alive during entirely different periods in history. We may decide to conceive 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 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 an individual, a parent, a brother or sister, a family.

"Cloning Dolly"

The procedure used to develop "Dolly" is called "nuclear transfer technology." It is one type of cloning technology which involves transferring the nucleus from a donor cell into an egg from which the nucleus has been removed, and implanting the resultant embryo into a surrogate mother for gestation and birth. What makes Dolly so special is that the cell which supplied her genetic material was taken from a mature adult sheep, cultured *in vitro* and frozen in liquid nitrogen. This procedure resulted in the birth of a lamb which is a clone of its mother, who was the source of the genetic material. Thus, the lamb's genetic material is identical to the adult sheep, with the exception of mitochondrial DNA which is inherited through the enucleated egg. Dolly is the first sheep to be born using an adult cell and "somatic cell nuclear transfer" technology. 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.

We believe that the term, "nuclear transfer cloning," as used by NBAC, represents two different types of procedures. "Nuclear transfer" involves transferring the nuclei from one cell to another; "cloning" is merely copying biological material, such as cells. Nuclear transfer is one type of procedure that results in a clone or copy of an organism. We believe the concerns surrounding the cloning experiment revolve around the application of this

technology to human beings, rather than on the types of technologies used to achieve this result. We prefer to precisely identify the type of technology at issue throughout this statement.

Cloning of Animals

Since the announcement of the birth of Dolly, the sheep produced using nuclear transfer technology with the genetic material of an adult sheep cell, the potential benefits to be derived from cloning procedures in agriculture and laboratory animal species have been widely discussed and recognized. For example, cloning technologies are already used in agriculture to produce higher yield, better quality fruits and vegetables.

While livestock animals have been cloned using embryo splitting techniques, the use of nuclear transfer technology is very likely to bring major improvements to the production of transgenic livestock animals. The development of transgenic animals has been occurring for many years. Already, the proteins produced in the milk of these animals are being tested for use in people in clinical trials. Nuclear transfer technology offers the potential for improving the efficiency of developing large numbers of transgenic animals with a wide range of medical benefits.

Examples of ways in which nuclear transfer technology could enhance the development of transgenic animals include the following:

Animal Models for Testing. Biotechnology companies are developing genetically engineered animal models to test potential treatments for various life-threatening diseases. For example, mice are designed to be susceptible to a specific human disease. Medicines to

treat that disease can be tested on these mice, thereby increasing the speed with which human therapeutics can be developed. Through the use of nuclear transfer technology, all -- not just a portion -- of the animals born would be transgenic. This could significantly enhance our ability to test new treatments for human diseases.

Organ Transplantation. Animals are being bred today whose organs may be transplanted into human patients suffering from organ failure or other diseases. These animals have been bred, using transgenic technology, to minimize the risk that the altered animal organ will be rejected by the patient. If a particular animal, such as a pig, is developed which has optimal characteristics as an organ donor, cloning that specific animal will produce identical animals. This could dramatically increase the supply of available organs, including hearts, kidneys and livers, for life-saving transplantation to humans. We are working with the Food and Drug Administration to address concerns regarding this technology.

Production of Medicine in Animal Milk. Nuclear transfer technology could enhance the efficient production of human medicines in the milk of transgenic dairy animals, such as sheep, goats and cattle. Today, transgenic technology is used to produce therapeutic human proteins in animals' milk. The therapeutic protein is then extracted from the milk, purified, and used as a pharmaceutical product. Nuclear transfer technology could enable the selective breeding of a large number of identical offspring from a single female animal chosen for its ability to produce higher concentrations of specific proteins in its milk. This could accelerate the production of a herd and facilitate clinical development of useful drugs. In addition, nuclear transfer technology would ensure that, within a herd, each animal would be

genetically identical. By eliminating the variability in background genetic factors, this method of producing human proteins could be made more efficient and productive. As a result, products could be developed more quickly and would reach patients faster.

We are pleased that the debate occasioned by the birth of Dolly has not involved any serious challenges to the cloning by nuclear transfer of agricultural and laboratory animals. NBAC has affirmed the benefits of animal cloning research and indicated its support for these technologies and we urge the Subcommittee to do the same.

Medical Benefits of Cloning Cells and Genes

Cloning techniques -- the duplication of cells and genes -- are integral to the process used to produce breakthrough medicines, diagnostics and vaccines to treat heart disease, many cancers, kidney disease, diabetes, hepatitis, multiple sclerosis, cystic fibrosis and a host of other diseases. More than 100 million people worldwide have already benefited from biotechnology medicines and vaccines. These techniques have been used in research and development for almost 20 years and are the cornerstone of the biotech industry and almost all modern biological research at academic institutions and the National Institutes of Health.

Scientists also are conducting valuable research into cloning human cells, organs and tissue. This could produce replacement skin, cartilage and bone tissue for burn and accident victims. This avenue of study may produce cells useful for cancer therapy and result in ways to regenerate retinal or spinal cord tissue. As mentioned above, research is also underway to develop replacement internal organs in transgenic animals for human transplantation. Also,

treatment and diagnosis of mitochondrial genetic disorders may be advanced by nuclear transfer technology.

Perhaps even more important, cloning of human cells and genes is essential to research that will provide profound new insights into how genes control human development and contribute to human diseases. These fundamental insights, in the years ahead, will provide the basis for even greater biomedical advances in the service of humanity, such as in identifying treatments for many diseases associated with aging. People of all ages are awaiting the development of these diagnostic tools and cures; their suffering provides strong motivations for researchers pursuing these valuable studies.

Existing Constraints on Cloning of Entire Human Beings

We believe that there is little immediate risk of the application of nuclear transfer technology or other cloning techniques for the purpose of developing an entire human being for several reasons.

Scientific Constraints: First, it may not be feasible to apply this technology to human beings. Second, there are immense scientific hurdles that would need to be overcome before any attempt could be made to apply nuclear transfer technology to humans. We believe it is not currently possible, and will not be possible for some time, to clone an entire human being using nuclear transfer technology.

The reliability of nuclear transfer technology is far from established, as the cloning of a sheep from an adult sheep cell has occurred only once. The first successful use of nuclear transfer technology came in sheep in 1984. This was based on a large body of knowledge

developed over many years by many researchers. It has taken an additional twelve years to yield the imperfect technology that resulted in Dolly. It may take a considerable period of time before this technology is perfected when applied to sheep and other farm animals, so that it can be performed with a greater success rate than this first experiment.

Furthermore, there are risks associated with the technology which we might tolerate in the case of farm animals, but which we would never tolerate were the technology to be applied to entire human beings. Assuming all the scientific procedures were known and optimized, many eggs, as well as surrogate mothers, would be necessary to establish this technique as a reliable method of developing new human beings. This type of research is neither feasible nor ethically acceptable at this time.

FDA and NIH Regulation of Research on Human Subjects: Regulations already exist to protect the individuals who participate in medical research studies. Under these regulations, the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) require informed consent from participants and approval by a national or local review board for medical research. In addition to obtaining FDA or NIH review, research studies also must be approved by institutional review boards (IRBs), in compliance with NIH guidelines and FDA regulations, to assure patient safety.

BIO recommends that medical research, including research using cloning and nuclear transfer technologies, continue to be governed by existing regulations to protect the safety of research subjects, specifically those regulations cited in the Code of Federal Regulations at 21 CFR 50 and 45 CFR 46.

Ethical Obligations of Researchers and Physicians: The scientific and medical communities subscribe to ethical codes which make unlikely their participation in the cloning of entire human beings without an extended scientific, medical, and ethical review process which attains consensus regarding the benefits and risks of this procedure.

Given the existing ethical and regulatory governance of science, a federal or state law to ban the cloning of entire human beings is not necessary. Rather, we recommended that NBAC extend the current moratorium and we urge the Subcommittee to do the same. We believe this moratorium will be sufficient to deter this type of experimentation, while allowing beneficial research to continue.

History of Voluntary Moratoria in Biotechnology Research

The history of strong adherence to moratoria in biotechnology research shows that this moratorium can and should be continued with regard to the cloning of entire human beings and that it will be effective.

Early Biotechnology Research: In the mid 1970s, when the industry was very new, researchers wondered whether their work would pose hazards to human health, and they worried over the potential environmental impact of genetically engineered microorganisms.

There were no easy answers to those early concerns, although most researchers thought their work could be extraordinarily beneficial and would pose no safety risks. Because of these questions, however, a moratorium was declared by academicians and industry itself on all experimentation until there could be a full debate of the issues. In 1974, the NIH began a program to consider the state of knowledge and what risks might be

posed by biotechnology. In 1975, at the Asilomar Conference Center in California, a group of scientists drew up principles to govern biotechnology research and established the NIH Recombinant DNA Advisory Committee. This committee was given the responsibility to review experiments about which there was uncertainty or ethical concern.

These guidelines have been modified over the years as scientific and regulatory experience has shown that most biotechnology procedures pose little or no risk. In fact, high school students now conduct recombinant DNA experiments involving cloning cells in their biology labs.

BIO and its members support the research guidelines and the NIH advisory committee. Even though not specifically required to do so, BIO companies voluntarily adhere to these guidelines. Developing specific guidelines, rather than passing laws to try to determine the areas appropriate for scientific pursuit, allowed the biotechnology industry to grow and develop life-saving medications and vaccines. Hasty legislation could have halted the industry's growth in its infancy. The industry still maintains its promise of beneficial new medications that should not be swept aside.

BIO also has formed a standing, Board of Directors'-level committee on bioethics to further examine bioethical issues as they arise. The industry has long been committed to abide by broad societal concerns as it strives to bring life-saving therapies to patients and their families. For example, BIO supports national legislation to protect the confidentiality of all individually identifiable medical information. We believe that this medical information must be respected, treated confidentially and safeguarded from discriminatory misuse.

Industry's Commitment to Moratorium on Germ Line Gene Therapy: During the past ten years, research and development efforts to perfect somatic cell gene therapy procedures in humans and germ line gene therapy procedures in animals have proceeded at a vigorous pace. At the same time, the academic and industrial research communities have observed a voluntary moratorium on the development and practice of germ line gene therapy procedures in humans; a voluntary moratorium which, to our knowledge, has not been violated. If and when this moratorium is lifted for a particular medical therapy, it will be because an informed public debate has produced a consensus that the benefits of this technology outweigh any potential harms.

We recognize that some may argue that voluntary moratoria will inevitably fail as safeguards and thus would seek to prohibit all research procedures which *if taken to their final possible conclusion* would result in the cloning of entire human beings. We must however, respectfully disagree. Over the last decade the biomedical research community in the U.S. has provided a salutary example of the power of responsible, voluntary restraint, illustrated by honoring this moratorium on germ line gene therapy. The industry has worked closely with the NIH Recombinant DNA Advisory Committee in upholding this moratorium.

As a nation, we should take pride in this experience with a moratorium on germ line gene therapy in humans. We should follow this example in determining how to restrain the cloning of entire human beings, without undermining the use of nuclear transfer and cloning technologies to improve and save the lives of many Americans.

Implementation of a Voluntary Moratorium

Recognizing the industry's experience with moratoria, we urged NBAC to recommend the continuation of the moratorium on the cloning of entire human beings beyond the current ninety day review period. Given the many issues we have raised about the pending bills, we continue to recommend that the moratorium be extended in lieu of legislation.

BIO offers to notify all of our member companies that the moratorium is in effect and request that they notify us if they are conducting any research which might be inconsistent with the moratorium.

BIO offers to work with NBAC and with the Congress to determine what procedures should be followed if and when a specific proposal is made to clone an entire human being. We believe that there is ample time to determine these procedures well before any such proposal is made. We will develop recommendations and share them with the Subcommittee when they are available.

BIO believes any process to evaluate such a proposal must address all the pertinent scientific, medical, legal, cultural, and ethical issues. We believe such procedures should initiate a dialogue which should include all appropriate segments of society, the potential beneficiaries of the research as well as religious leaders and others, to evaluate the ethical implications and acceptability of such a proposal. Furthermore, any such proposal must meet scientific criteria for protecting human subjects in research.

Detrimental Impact of Legislation

As stated, BIO believes the moratorium should be extended, in lieu of legislation, to address any attempts to clone an entire human being. We believe that enacting a law now at the federal or state level to ban the cloning of entire human beings could inhibit beneficial biomedical research.

First, the scientific issues are complicated and these technical terms of art are not well understood by legislative bodies. There is a real risk that any law could ban beneficial research, and delay the development of new diagnostic tests and therapies.

Second, any law which sets civil or criminal penalties for broadly defined research activities would inhibit research remotely connected to the research described in the legislation.

Given the existing regulatory structure for research involving human subjects, our industry's support for a continuation of the current moratorium, the opportunity to develop procedures for reviewing the moratorium in the future, and the many concerns expressed with draft legislation, BIO believes there is no need to rush to establish a federal or state law that could unintentionally inhibit beneficial research.

Importance of Patent Protection

Finally, the issue at hand is primarily the impact of government policies on vital research. Since NBAC in its initial mandate was charged with evaluating the issue of patenting of biotechnology inventions with respect to genes, we stressed in our

recommendations that it should affirm the importance of patenting new technologies for all biotechnology advances. We urge the Subcommittee to do the same.

Patents are critical for the support of this research to ensure continuing investment in and development of new technologies. Biotechnology inventions should receive the same patent protections as other inventions. We recommend that the Subcommittee support the patenting of biotechnology inventions, including genes.

Conclusion

We appreciate the Subcommittee's consideration of our concerns and its recognition of the benefits of cloning technology in improving and saving people's lives. We look forward to working with the Subcommittee and Congress during the consideration of this issue.

Appendix A: Curriculum Vitae for Dr. Alison Taunton-Rigby and Disclosures Regarding Aquila Biopharmaceuticals and BIO
Appendix B: Summary of BIO Recommendations to National Bioethics Advisory Commission, April 23, 1997
Appendix C: BIO Analysis of Clinton Administration Draft Bill Regarding Cloning of Human Beings
Appendix D: Bill Proposed by Clinton Administration
Appendix E: HR 922 (Ehlers), 105th Congress, 1st Session
Appendix F: HR 923 (Ehlers), 105th Congress, 1st Session
Appendix G: S 368 (Bond), 105th Congress, 1st Session

APPENDIX A:
CURRICULUM VITAE FOR DR. ALISON TAUNTON-RIGBY AND DISCLOSURE REGARDING AQUILA BIOPHARMACEUTICALS AND BIO

Under House Rule XI, clause 2(g)(4), non-governmental witnesses appearing before the Committee or its Subcommittees are required to include as part of their written testimony a curriculum vitae and a disclosure by source and amount of any federal grant, contract, or subcontract received by them or any entity they represent at the hearing, in the current and preceding two fiscal years. This information follows:

CURRICULUM VITAE: DR. ALISON TAUNTON-RIGBY

Alison Taunton-Rigby, Ph.D., is President and Chief Executive Officer of Aquila Biopharmaceuticals, Inc., a public biotechnology company based in Worcester, Massachusetts. It is involved in developing and commercializing products for the treatment and prevention of infectious diseases and cancer. Aquila was formed as a result of the reorganization of Cambridge Biotech Corporation under the Chapter 11 Bankruptcy Code. The turn around and restructuring of CBC was a $50 million transaction. Dr. Taunton-Rigby is a member of the Board of Directors of the Biotechnology Industry Organization (BIO), the national trade organization of biotechnology companies, and Chair of BIO's Emerging Companies Section and a Director and past President of the Massachusetts Biotechnology Council, the trade organization for biotechnology companies in Massachusetts.

Dr. Taunton-Rigby has held senior management positions at several biotech companies. She was Senior Vice-President, Biotherapeutics, of Genzyme Corporation, where she had overall responsibility for Genzyme's biotherapeutics division. She also has served in senior management positions at several other biotechnology companies, including Mitotix, Inc., Vivotech, Biogen, Inc., and Genome Therapeutics, and worked in the Health Industries section at the consulting firm, Arthur D. Little.

Dr. Taunton-Rigby received her doctorate in chemistry from the University of Bristol in England, and is a graduate of the Advanced Management Program of the Harvard Business School. She is a Director of Synaptic Pharmaceutical, Inc., and of the CML Group, a member of the Board of Associates of the Whitehead Institute for Biomedical Research and of the Committee for Economic Development, and a member of Bentley College Ethics Board.

DISCLOSURE REGARDING AQUILA

Federal Grants Received by Aquila, 1995-1997

Saponin Adjuvant Based Vaccines Against Mycobacteria	R29 AI35193 $237,368
Rapid Diagnostic for *Clostridium difficil* toxin B	R44 AI30807 $548,823
Saponin Adjuvant Enhanced Pneumococcal Vaccine	R01 AI33560 $199,218
HIV-1/2 (AIDS) Vaccine Development Using Novel Adjuvants	H01 AI28167 $336,029
Saponin Adjuvant Based HIV-1 Subunit Vaccines	U01 AI33223 $196,558

DISCLOSURE REGARDING BIO

The Biotechnology Industry Organization (BIO) has one federal grant in the current and preceding two fiscal years.

In June 1996, BIO received a $50,000 grant from the Department of Energy to support BIO's Environmental Biotech '96 conference. One of the purposes of the meeting was to initiate a dialogue between companies employing environmental biotechnology and federal agencies using the technology. Sessions during the meeting focused on various issues related to the incorporation of new technologies into the federal government's environmental clean-up programs.

The grant was intended to help pay for the participation of federal officials and/or technical experts from outside of the United States developing innovative environmental treatment and pollution prevention technologies. The National Science and Technology Council co-hosted the meeting with BIO and worked with BIO and the Department of Energy to develop the agenda for the meeting.

BIO has no way of determining the number of grants, contracts, or subcontracts that our 722 members have received from the Federal government.

APPENDIX B:
SUMMARY OF BIO RECOMMENDATIONS TO NATIONAL BIOETHICS ADVISORY COMMISSION APRIL 23, 1997

Following is a summary of BIO's recommendations of April 23, 1997, to the National Bioethics Advisory Commission:

1. BIO recommends that the Commission urge continuation of the current voluntary moratorium on the cloning of entire human beings beyond the current ninety day review period.

2. We recommend that the Commission endorse the continuation of research involving the cloning (i.e., duplication) of human and animal cells, genes and proteins -- as distinct from the cloning of an entire human being -- because this research has already produced enormous medical and agricultural benefits for society, and promises to produce even greater benefits in the future.

3. Although the Commission has not been charged with reviewing the issue of animal cloning, we recommend that the Commission affirm the very evident benefits of this research and express its support for its continuance.

4. While we are not now aware of any practical reason for cloning an entire human being, we recommend that the Commission determine what procedures should be followed if and when a specific, compelling, practical purpose is proposed. We recommend that consideration of any such proposal comprehensively address all pertinent scientific, medical, legal, cultural, and ethical issues. We believe that any such proposal should cause the initiation of a dialogue including all appropriate segments of society, the potential beneficiaries of the research as well as religious leaders and others, to evaluate the ethical implications and acceptability of any such proposal.

5. We recommend that the moratorium not apply to the research examples described in the April 1 letter to BIO from the Commission's Ad-Hoc Cloning Science Working Group. These examples include the use of adult or embryonic cells for nuclear transfer technology used to improve scientific understanding, short of developing an entire human being.

6. We recommend that the moratorium be continued in lieu of any new federal law or regulation regarding the cloning of an entire human being. We recommend that the Commission strongly oppose the enactment of any state law on the subject of human cloning because issues raised by the cloning of entire human beings should be addressed nationally and comprehensively, not

on a state-by-state basis. Continuing the moratorium should obviate the need for any state or federal legislative action.

7. We recommend that the Commission express its concern that a hastily drafted, poorly envisioned federal or state law could inadvertently inhibit or even deter valuable, life-saving research. "Cloning" -- the duplication of specific genes and cells -- is an essential process in biotechnology research; the cloning of a whole organism represents only one type of cloning. Any regulation or law which refers simply or generally to "cloning" could prove devastating to millions of patients relying on research developments leading to new therapies and cures, and could eliminate billions of dollars of biomedical research by biotechnology and pharmaceutical companies, research universities and the federal government.

8. Finally, we recommend that the Commission support the patenting of biotechnology inventions, including genes, as a critical part of the process of developing new treatments.

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.[3]

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.

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[3] 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."

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 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.[4] 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

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[4] 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.

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 Roslin 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 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.

APPENDIX D:
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.

(c) 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).

(c) "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.

(c) 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.

APPENDIX E:
HR 922 (EHLERS)
105th CONGRESS
1ST SESSION

To prohibit the expenditure of Federal funds to conduct or support research on 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, and in addition to the Committee on Science, for a period to be subsequently determined by the Speaker, in each case for consideration of such provisions as fall within the jurisdiction of the committee concerned

A BILL

To prohibit the expenditure of Federal funds to conduct or support research on 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 Research Prohibition Act'.

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

None of the funds made available in any Federal law may be expended to conduct or support any project of research that involves the use of a human somatic cell for the process of producing a human clone.

APPENDIX F:
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.

APPENDIX G:
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.

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.

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HUMAN CLONING

CRITICAL TERMS — CONFLICTING DEFINITIONS

Among biotechnology, pharmaceutical and biomedical research organizations, there is a broad consensus that human cloning is medically unsafe and morally unacceptable. There is an equally broad consensus that many pending proposals are not only unnecessary but also pose an unintended but significant threat to critical, life-saving research.

In some areas of law, there are terms of art that have settled meanings which have been relatively unambiguous for decades. These settled terms of art allow the prohibition of specific acts while posing little risk of accidental "collateral damage".

In the new and rapidly changing field of biotechnology, by contrast, terminology is uncertain and even core terms in pending cloning legislation lack definitive meaning for scientists and lawyers alike. As the attached chart indicates, three key concepts -- "somatic cell nuclear transfer", "cloning", and "somatic cell" -- engender disagreement.

This lack of consensus and clarity has profound real-world consequences. An inadvertently broad ban on "cloning", for example, would cripple the promise of biotechnology to produce breakthrough medicines to treat life-threatening ailments like cancer, kidney disease, diabetes, hepatitis, cystic fibrosis and a host of other diseases.

Vague language threatens the medical benefits of cloning cells and genes. Chilling of research unrelated to any popular conception of human cloning is certain, especially when these unclear definitions of critical terms are combined with an ill-advised focus on the researchers "intent" and prohibitions on broad areas of "research" rather than discrete and readily identifiable acts.

There is time to move carefully and methodically. Congress should oppose legislation which, while well-intentioned, inadvertently threatens to undermine vital biomedical research into deadly and disabling diseases.

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CRITICAL TERMS — CONFLICTING DEFINITIONS

	Somatic Cell Nuclear Transfer	Cloning	Somatic Cell
S. 1599, Senator Bond's "Human Cloning Prohibition Act of 1998"	taking the nuclear material of a human somatic cell and incorporating it into an oocyte from which the nucleus has been removed or rendered inert and producing an embryo (including a preimplantation embryo)	while entitled "Human Cloning Prohibition Act of 1998", "cloning" is not expressly defined	although making it unlawful to use human somatic cell nuclear transfer technology, "somatic cell" is not expressly defined
National Bioethics Advisory Commission (NBAC) -Glossary	"somatic cell" defined as any cell of an embryo, fetus, child or adult not destined to become a sperm or egg cell-- "nuclear transplantation cloning" defined as a type of cloning in which the nucleus from a diploid cell is fused with an egg from which the nucleus has been removed	"clone" defined as a precise copy of a molecule, cell, or individual plant or animal	any cell of an embryo, fetus, child, or adult not destined to become a sperm or egg cell
NBAC-Footnotes	"somatic cell" defined 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	--	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

	Somatic Cell Nuclear Transfer	Cloning	Somatic Cell
NBAC-Text	recommends prohibition apply to banning nuclear transfer using the nuclei derived from somatic cells other than those of an embryo or fetus-- "nuclear transplantation" defined as transplanting the genetic material from a differentiated somatic cell into an egg from which the nucleus has been removed	the word "clone" is used in many different contexts in biological research but in its most simple and strict sense, it refers to a precise genetic copy of a molecule, cell, plant, animal, or human being	--
H.R. 922, Congressman Ehlers' "Human Cloning Research Prohibition Act", as reported from the House Science Committee	transferring the nucleus of a human somatic cell into an oocyte from which the nucleus has been removed or rendered inert	although entitled "Human Cloning Research Prohibition Act", "cloning" is not expressly defined	cell of an embryo, fetus, child, or adult which is not and will not become a sperm or egg cell
H.R. 922, Congresswoman Rivers' Amendment (not adopted)	"the creation of a human being using somatic cell nuclear transfer technology" means transferring the nucleus of a somatic cell of an existing or previously existing person into an oocyte from which the nucleus has been removed and implanting the resulting product for gestation and subsequent birth	--	a differentiated, diploid cell

	Somatic Cell Nuclear Transfer	Cloning	Somatic Cell
H.R. 923, Congressman Ehlers' "Human Cloning Prohibition Act"	it shall be unlawful for any person to use a human somatic cell for the process of producing a human clone	while entitled "Human Cloning Prohibition Act", "cloning" is not expressly defined	although making it unlawful for any person to use a human somatic cell for the process of producing a human clone, "somatic cell" is not expressly defined
S.368, Senator Bond's bill to prohibit the use of federal funds for human cloning research	no federal funds may be used for research with respect to the cloning of a human individual	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	--

"SOMATIC CELL NUCLEAR TRANSFER": NINE DEFINITIONS OF CRITICAL TERM

The term which defines the research prohibition -- "somatic cell nuclear transfer" -- is defined in nine different ways in pending bills, the NBAC report, and other sources. The subtle differences among these definitions are critical and each prohibits a different class of research.

H.R. 922 (Ehlers):

None of the funds made available in any Federal law may be expended to conduct or support any project of research that involves the use of a human somatic cell for the process of producing a human clone.

H.R. 923 (Ehlers):

It shall be unlawful for any person to use a human somatic cell for the process of producing a human clone.

S. 368 (Bond):

No Federal funds may be used for research with respect to the cloning of a human individual.

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.

National Bioethics Advisory Commission:

Glossary Definition: defines "somatic cells" as "any cell of an embryo, fetus, child or adult not destined to become a sperm or egg cell."

National Bioethics Advisory Commission:

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."

National Bioethics Advisory Commission:

Text of the NBAC report 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.

Administration Proposed Legislation:

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.

(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).

(c) "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.

July 18, Discussion Draft, Technology Subcommittee:

None of the funds made available in any Federal law may be obligated or expended to conduct or support any project of research that involves the use of a human somatic cell to produce an embryo.

For purposes of this section, the term "somatic cell" means a cell of an embryo, fetus, child, or adult which will not become a sperm or egg cell.

Testimony of Association for Reproductive Medicine, June 22:

Human cloning means the duplication of an existing or previously existing person by transferring the nucleus of a differentiated, somatic cell into an oocyte from which the nucleus has been removed and implanting the resulting product for gestation and subsequent birth.

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