STATEMENT IN OPPOSITION TO A FEDERAL LEGISLATIVE BAN ON THERAPEUTIC CLONING

The Human Cloning Prohibition Act of 2003 (the "Act"), as passed by the United States House of Representatives in February 2003, would make it a crime punishable by up to 10 years in jail for a scientist in the United States to pursue promising medical research on many currently untreatable diseases using cloning techniques to produce human stem cells. The Act is primarily intended to outlaw the use of cloning techniques for human reproduction ("reproductive cloning"). Although many members of the Committee on Bioethical Issues of the Association of the Bar of the City of New York ("Committee") would support a ban on reproductive cloning, the Committee does not support a ban so broad as to prohibit promising stem cell research that is unrelated to the use of cloning for human reproduction. This research, often referred to as "therapeutic cloning," seeks to apply cloning techniques to derive human stem cells. Stem cell technology, while still in its infancy, holds great promise to cure or treat some of our most tragic and intractable diseases and medical conditions. Cloning techniques could help to realize that promise. It is the strong position of the Committee that the ethical and legal reasons to ban reproductive cloning do not apply to therapeutic cloning, which should be encouraged and welcomed.

Reproductive cloning found its poster child in Dolly the sheep. Dolly demonstrated the extraordinary and disquieting power of modern biology. A single cell from an adult sheep was used to produce an "offspring" that was an exact genetic replica, a clone, of its sole parent. Dolly the clone was different from every other sheep because all of her genes came from her only parent, without the usual intermixing of genes from a mother and a father.

Dolly's cloning was accomplished by taking a female egg cell, prior to fertilization, and replacing its nucleus. The replacement nucleus can be taken from almost any cell of the adult who is to be cloned. Since the cell nucleus carries the principal genetic information of an organism, the egg with its new nucleus has a full set of adult genes. If the egg can now be induced to begin dividing and growing, it could, if implanted into the womb of a volunteer birth mother, be carried to term, be born and continue growing into an adult with the exact genetic make-up of its sole genetic parent. This is reproductive cloning.

If, however, the egg cell with its new adult cell nucleus could be induced to grow in a laboratory dish through only its first half dozen or so cycles of cell division, it would soon reach the stage where much of its tiny mass consists of very special cells called embryonic[1] stem cells. At this stage the embryo is no larger than the period at the end of this sentence. Stem cells can be taken out of this very early stage embryo and grown separately in a laboratory cell culture. Removing these stem cells destroys the embryo, ending any prospect of a "reproductive" clone. But the embyro's genetic material lives on in the cultured stem cells. The prospect of using cloning to produce embryonic stem cells is what is generally referred to as “therapeutic cloning.” While cloned human embryonic stem cells have not yet been reported in the scientific literature, many observers believe the reports could come in the near future. To understand the potential importance of this technology, it is first necessary to understand the scientific excitement surrounding embryonic stem cells.

In November 1998, United States scientists first reported the derivation of human

[1] Throughout this Statement, the Committee uses the term embryo to refer to a fertilized egg before implantation in a mother’s uterus and the term “fetus” to refer to the embryo after implantation.

embryonic stem cells.[2] These cells are remarkable. They have the unusual (and perhaps unique) ability to grow in laboratory culture dishes through successive generations without changing. This means that, in theory, a single embryonic stem cell could start a colony that, by exponential growth, soon could generate a virtually unlimited number of exact copies. This property suggests that stem cells can be mass produced in quantities that would be needed for a practical medical therapy.

Embryonic stem cells also have the unique ability to transform themselves into each of the specialized cells that make up an adult human being. Under the right conditions, embryonic stem cells will transform themselves into brain cells, skin cells, bone cells, blood cells, heart muscle cells or any of the other specialized cellular constituents of a human body.

Both theory and early experimental evidence in animals suggest that this property could be useful in treating many currently untreatable diseases and conditions. Stem cells could replace damaged nerve cells in quadraplegics, Alzheimer's patients or Parkinson's patients. Stem cells could provide new insulin producing cells in diabetics and repair heart tissue damaged during strokes by replacing dead heart muscle cells. These possibilities, and others that are discussed further below, are now only dreams, but they are compelling dreams. Science rarely unfolds as predicted. Usually, progress is slower and more difficult than early dreams suggest. Typically, there are unexpected twists, turns, branches or barricades along the path, but pursuing scientific dreams has repeatedly paid enormous social dividends.

Embryonic stem cell research can take place without cloning. Most currently existing

[2] Thompson, J.A., Liskovitz-Eldor, J., Shapiro, S.S., Waknitz, M.A., Swiergiel, J.J., Marshall, V.S., and Jones, J.J., "Embryonic stem cell lines derived from human blastoycysts," Science 282: 1145-1147 (1998). A good, short, lay persons account of this technology is set out in Dr. Thompson's essay on "Human Embryonic Stem Cells," included in Holland, et al. The Human Embryonic Stem Cell Debate – Science, Ethics and Public Policy pp. 15-26, (2001).

cultures of adult embryonic stem cells were derived from very early stage embryos created and stored by in vitro fertilization ("IV") clinics. IV clinics typically create for each fertility patient many more fertilized eggs than are ultimately needed. The embryos are frozen for storage and unfrozen as needed. When patients no longer need or want fertility treatment, the excess embryos can be either discarded or, with the patient's consent, used to create embryonic stem cell lines. Current federal policy precludes federal funding for any research involving embryonic stem cells created after August 9, 2001.

Using cloning to create embryonic stem cells would provide some very significant advantages. Through cloning it is possible to precisely control the stem cells' genetic character. For example, it should be possible to create a stem cell culture that is a precise genetic match of the person whose cell nucleus is used. The specialized cells derived from those embryonic stem cells retain this precise genetic match. If those specialized cells are transplanted back into the original nucleus donor, then the clinical problems of immune system "rejection" could be vastly simplified. The transplanted tissue would no longer appear "foreign" to the recipient, since it would be a cloned genetic replica of the recipient's own tissue. Even without fully customizing stem cells to match each individual patient, cloning may permit certain genetic classes or types of stem cells to be cultured that will lessen the tissue rejection problem – much like blood typing and matching is used to avoid adverse reactions to blood transfusions.

Most complex and controversial bioethical issues involve balancing competing ethical principles or concerns. Therapeutic cloning is no exception. The ethical analysis requires us to assess the moral weight of competing considerations – an extremely subjective and imprecise calculation. In performing this balancing process and in using any resulting conclusions to make public policy, it is important to keep in mind that we will be confronted with many very

different, real world factual settings. Also as our scientific knowledge increases, we will be confronted with situations and assumptions that we cannot now foresee. Therefore, we should take care in creating sweeping, absolute rules, particularly when those rules inflexibly ciminalize a broadly defined area of science.

The most significant ethical considerations that weigh in favor of therapeutic cloning are the apparent enormous potential to cure disease and suffering, and the related, but not identical, general interest in advancing fundamental scientific knowledge. Weighing against this are two principal arguments. First, some people believe that a full-fledged human life begins at fertilization. For these people destroying even a very early stage embryo is destroying a human life and is, therefore, ethically impermissible no matter how great the potential medical and scientific benefits. Second, some people are, in principle, uncomfortable with creating a human embryo using cloning techniques which they view as too dangerous a scientific precedent and too profound a manipulation of a human life to be ethically acceptable.

The Potential Benefits
of Therapeutic Cloning

The most promising benefit of therapeutic cloning is its potential contribution to the development of treatments for currently incurable medical conditions. Therapeutic cloning is envisioned as a branch of embryonic stem research, a field that is also in its infancy. Researchers are able to culture human embryonic stem cells although that technology is still not well developed. Precursor research on mice and other animal models is further along. It has demonstrated in principle the ability to culture embryonic stem cells, to transform them into specialized cells and, most significantly, to transplant resulting specialized cells into live organisms with some therapeutic effect.

For example, researchers have shown in mice that embryonic stem cells can be transformed to specialized heart muscle cells which, when, injected into mice with damaged heart tissue, can cause some regeneration. This is significant because heart muscle cells destroyed, for example by a stroke, typically do not regenerate by themselves. Very preliminary work has also shown that human embryonic stem cells can be transformed in a laboratory into heart muscle cells. This research, which is in its very early stages, suggests a new and promising approach to treating heart disease.

Work with mice embryonic stem cells has also shown that they can be induced to transform into insulin-secreting cells. When purified and transplanted into living mice with diabetes, the stem cells returned the mice's insulin levels to normal levels.

In another example, mice embryonic stem cells have been transformed into specialized nerve cells which have demonstrated some therapeutic effect in several neurological diseases including treating paralysis by regenerating damaged nerve tissue and curing Parkinson's symptoms by producing dopamine. These experimental findings suggest the potential to treat spinal cord injuries, stroke, Parkinson's and even Alzheimer's disease.[3]

This embryonic stem cell research has not yet involved cloning to control the genetic make up of transplanted tissue. That step, while plausible in theory, remains to be demonstrated in the laboratory. But if it could be demonstrated, it would, as indicated above, suggest a promising approach for dealing with the immune system rejection phenomenon that currently complicates organ and tissue transplantation.

[3] See Okarma, "Human Embryonic Stem Cells: A Primer on the Technology and Its Medical Applications," included in Holland, et. al. The Human Embryonic Stem Cell Debate (2002).

A separate benefit of research on therapeutic cloning is simply the opportunity it offers to expand our fundamental knowledge of biology. Embryonic stem cells and cloning are both developments that create very powerful new tools for designing experiments that will answer important questions about cellular biology and very early stage development of complex organisms. These developments could also provide important avenues for advancing research on contraception and other women's health issues.

If the United States bans this research, there is certainly no guarantee that other countries will follow. The more likely outcome is that research in the United States will fall behind research in other countries that are more welcoming. In addition, the United States will lose its opportunity to develop sensible regulatory approaches and protections.

The Ethical Concerns[4]

The principal ethical issue raised in opposition to therapeutic cloning arises from the fact that, like all embryonic stem cell research, the initial extraction of the embryonic stem cells for

[4] Several federally appointed national bioethical commissions have published reports on the ethical issues implicated in therapeutic cloning. In 1994, a panel appointed under the auspices of the National Institutes of Health wrote a lengthy report on ethical issues raised by new reproductive technologies that also recommended permitting federal funding for research on very early stage human embryos. National Institutes of Health, Report on Human Embryo Research Panel (Sept. 1994). A fascinating account by a member of that panel of its deliberations and how its conclusions compare to subsequent commissions is set out in Green, The Human Embryo Research Debates (Oxford Univ. Press 2001). In November 1998, President Clinton asked the National Bioethics Advisory Commission, a group he created in 1995, to study stem cell research. In September 1999, the Commission issued a report entitled "Ethical Issues in Stem Cell Research" which recommended that federal funding should be available for research involving the derivation and use of stem cells derived from human embryos remaining after fertility treatment but should not be available for research involving the derivation and use of stem cells from embryos made solely for research purposes, including embryos made using cloning techniques. However, the report recommended that the "progress and medical utility" of research using stem cells from cloned embryos should be "monitored closely" to see if sufficient promise warrants reconsidering the availability of federal funding. Most recently, President Bush's President's Council on Bioethics issued a report in July 2002 with three different views of the bioethical issues. A majority found "cloning for biomedical research" to be, on balance, unethical and recommended a four year moratorium on all research, whether or not federally funded. Two different minority positions disagreed. One minority view found the research ethically warranted with appropriate regulations including a ban on developing research embryos beyond 14 days. Another minority found the research "presents no

culturing involves the destruction of a very early stage human embryo. To some this is the moral equivalent of murder. To others, while not the same as murder, it is ethically unacceptable because it does not accord sufficient respect for an organism that has the potential, if implanted in a birth mother, to develop into an adult human being. Often this ethical debate is posed as asking to what extent a very early stage human embryo, existing in a laboratory, is a "person" entitled to ethical "respect" and legal protection.

Some have sought to answer this question by appealing to biology.[5] Relatively well-accepted biological facts are mustered on each side of the debate. Those who believe that an early stage embryo is entitled to moral and legal respect point out that this embryo, even as maintained in a laboratory, has the full potential to develop into a human being. Further, they argue that the development process is continuous and progressive, from fertilization right up to birth (and after). Proponents of therapeutic cloning respond that the early stage embryo has almost none of the characteristics associated with "humanness." It has no nervous system and thus no feelings or consciousness. It has no distinct organs or body parts. Its development to birth is entirely dependent upon implantation in an adult uterus. It is not yet even associated with a single unique personhood, since the possibility still exists that the single embryo will develop into genetically identical twins. Finally, while the embryo's development would be continuous, there are nonetheless relatively distinct developmental stages that are well established medically.

The Committee finds that these biological facts are helpful in framing more precisely the ethical issues but do not, alone, provide an answer to the ethical question.

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special moral problems and, therefore, should be endorsed with enthusiasm as a potential new means of gaining knowledge to serve mankind."

[5] An example is provided in the "Personal Statements" included in the July 2002 report of the President's Council on Bioethics entitled "Human Cloning and Human Dignity: An Ethical Inquiry." (Compare statements for William

More persuasive is the degree of ethical respect or legal protection that we have historically provided or not provided to early stage embryos in other contexts.

Certainly the abortion context is relevant. Roe v. Wade, and subsequent cases, have firmly established certain legal principles. One issue that the abortion cases consider is to what extent a woman has a right under the due process clause of the United States Constitution to be free from governmental restrictions if she chooses to undergo an abortion. The starting point of that legal analysis is the legal interest of the woman to control what happens to her body. This liberty interest is "balanced" against state interests that include an interest in protecting an unborn fetus. The liberty interest is not raised in the same fashion by the stem cell research debate because the early stage embryos from which stem cells are typically harvested exist in laboratory dishes – not in any woman's body. However, the abortion analysis is relevant to the stem cell debate in determining the degree of the state's interest. Under the Supreme Court's analysis, the state's interest in protecting a fetus depends upon the fetus' developmental stage. During the first trimester, the state's interest is weakest and is outweighed by the woman's right to autonomy and self-determination. Indeed, the state's protective interest is never strong enough to permit the state to impose significant impediments on a woman's choice to seek an abortion during the first trimester.

Applying these same principles to stem cell harvesting suggests that the state's interest in protecting a one-week-old in vitro embryo is quite weak. More importantly, if the relevant state interest is protecting a human life, that interest seems significantly diminished when there is neither intent nor means to implant the embryo into a uterus. Without implantation, the embryo

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Hurlbut and Robert George in favor of a moratorium on therapeutic cloning research with the statements of David Foster and Michael Gazzoniga in favor of permitting research to proceed).

cannot and will not develop further. In short, there is really no prospect of a birth or subsequent life for the state to protect.

Other legal and medical precedents suggest that the state has not generally provided significant protection to very early stage embryos. Birth control methods, such as intra-uterine devices, that work by preventing the subsequent development of early stage embryos are well accepted. Miscarriages that happen naturally within a week or two after conception are generally not considered a major public health problem worthy of aggressive intervention or therapies. Indeed, the routine and widely accepted practice at IV clinics of destroying unneeded early stage embryos reflects this same pragmatic recognition that a very early stage embryo has not yet sufficiently developed human characteristics to be accorded even attenuated rights of personhood.

When these relatively weak ethical claims for protection of a very early stage embryo are balanced against the strong and legitimate claims of the chronically ill and of all who feel compassion for their plight, the Committee finds the ethical balance tips strongly in favor of permitting embryonic stem cell research – including producing embryos through cloning techniques.

In addition to the ethical concerns raised in opposition to therapeutic cloning that views the destruction of early stage embryos as equivalent or analogous to murder, another ethical objection to therapeutic cloning is that it will catapult society down a "slippery slope" to reproductive cloning. This argument is discussed in the next section, below.

Others raise ethical objections to applying cloning techniques to produce human embryos – without regard to whether or not it will somehow lead to reproductive cloning.

One argument objects to any means of creating an embryo for research or therapeutic purposes. The argument distinguishes between embryos created in IV clinics for reproduction (a "good purpose") and embryos created in medical research laboratories for the purpose of curing diseases or learning how to cure diseases (an "unacceptable" purpose). The Committee simply does not agree with this distinction. We cannot understand why enabling an infertile couple to have a child is any more medically worthy than curing or treating a patient dying of Parkinson's, Alzheimer's or other fatal or disabling diseases.

Other commentators are troubled, in principle, by the power and artificiality of cloning – which does exert an unprecedented degree of control over human genes.[6] The Committee recognizes and respects the profound disquiet that accompanies many important scientific breakthroughs – from Copernicus and Galileo to Darwin and in vitro fertilization. However, we hold the view that these breakthroughs should be celebrated, not feared. Their potential includes the potential to do great "good." History has taught us that scientific knowledge will inevitably advance and we do better to engage and harness that knowledge than to fear and avoid it. Of course, where new scientific technologies represent national security concerns – such as biological or atomic weapons – a ban or severe restrictions is appropriate. But the Committee does not see how any of these national securities issues are implicated in therapeutic cloning research.

Therapeutic Cloning Will Not
Lead to Reproductive Cloning

[6] A short statement of this position (and the "slippery slope" concern) may be found in a New York Times op-ed piece by Leon Kass, the current Chair of the President's Council on Bioethics, that appeared under the title "How One Clone Leads to Another," January 24, 2003 at p. A23. For example, Dr. Kass writes, " . . . saying yes to cloned embryos, even for research, means saying yes, at least in principle, to an ever-expanding genetic mastery of one generation over the next. Once cloned embryos exist in laboratories, the engenic revolution will have begun."

Therapeutic cloning that produces embryonic stem cells cannot lead to reproductive cloning. The very early stage embryo is destroyed as the stem cells are removed. And embryonic stem cells, even in animal models, are not yet sufficient to produce an adult organism.[7]

A more plausible fear is that as the technology to produce cloned embryos develops, someone, somewhere will attempt reproductive cloning.[8] There are several responses to this concern. First, and foremost, reproductive cloning requires implantation of the cloned embryo in a birth mother. This is a distinct event that could be clearly and enforceably prohibited. Implantation is the natural "bright line," the obstacle that prevents therapeutic cloning from leading us down a "slippery slope" to reproductive cloning. While some people may attempt to evade a prohibition against implantation, the same thing can be said about nearly any legal rule. Permitting therapeutic cloning will not make it any more difficult to design and enforce a prohibition against reproductive cloning. Second, reproductive cloning may well occur in some foreign country no matter what legislation the United States enacts. It is simply unrealistic to expect that a ban on United States based research will prevent scientific knowledge and technologies from being developed elsewhere. The best way to prevent reproductive cloning is not to hope against all experience, that the technology needed will never be developed. It is to

[7] However, very recently reported research suggest that mouse stem cells can be transformed into egg cells, like those produced in a female mouse's ovary. N. Wade, "Pennsylvania Researchers Turn Stem Cells to Egg Cells," N.Y. Times, May 2, 2003 at A28. It has been noted that this, in theory, presents the prospect of generating a nearly unlimited number of human egg cells without resort to the somewhat intrusive harvesting procedures used by IV clinics. The egg cells would be an important benefit to therapeutic cloning where they are needed to accept a cell nucleus. Also, cloned embryos produced in this fashion (or by cloning) do not involve fertilization, which some people regard as the start of an individual human life. This may change their ethical concerns. The Times article cited above makes the further point that these extraordinary scientific developments illustrates that any broad bans on research are premature. The article quotes a noted authority on bioethics, Dr. Arthur Caplan, as observing about the Act, "It's as if they were trying to regulate the aviation industry with only the Wright brothers' plane in front of them."

anticipate its development and put in place regulatory approaches and controls that will prevent its improper use.

CONCLUSION

For the reasons discussed above the Committee strongly urges that no legislation should be adopted that bans therapeutic cloning. The Act that is currently before Congress goes well beyond current public policy in an important respect. Public policy debates on embryonic stem cell research in the United States have for the most part addressed whether or not federal government funding should be available to sponsor research. For example, President Bush's directive regarding using stem cell cultures available on August 9, 2001 but not newly created stem cell lines concerned only the availability of federal funding to sponsor the stem cell research. The federal government has historically developed bioethical guidelines in the context of regulating federal funding. It has not typically sought in the first instance to regulate research sponsored by purely private sources.

The Act departs from this pattern by imposing a legal ban on all therapeutic cloning research, whether sponsored by public or private funds. This is a significant extension and a dangerous precedent. Most importantly, it is contrary to the United States' pluralistic tradition of respect for strongly held dissenting views, especially in areas of purely private sponsorship.

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[8] For an eloquent statement of this view by a respected bioethisist and chair of the President's Council on Bioethics, see L. Kass, "How One Clone Leads to Another" N.Y. Times, January 24, 2003 A.23 (OpEd) ("Once cloned embryos exists in laboratories, the engenic revolution will have begun").

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The Committee adopted this Statement unanimously except that Mr. Renehan abstained. John Linville was the principal author of this Statement.