



CLONING CALIFORNIANS?

Report of the California Advisory Committee on Human Cloning

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EXECUTIVE SUMMARY

In 1997, when California adopted a five year ban on human reproductive cloning, the legislation required the appointment of an expert group to provide advice to the Governor and Legislature about how to proceed when the five years had ended. This is the report of that California Advisory Committee on Human Cloning. It is not, in any sense, a report *of* the Governor, the Legislature, or the State. Instead, it is our effort to provide useful advice to California, laying out the background on the issues, analyzing the arguments, and presenting our recommendations. The Committee, made up of twelve Californians from a wide range of backgrounds, has studied these issues for over two years. In five public meetings around the State, we have heard testimony from international experts and comments from ordinary Californians. We heard many different views and, indeed, our most fundamental conclusion may be that, on many of these questions, reasonable people can and do disagree. Nonetheless, the Committee has found itself in unanimous agreement on five main recommendations:

- 1. The Committee unanimously agrees that California should ban human reproductive cloning. Many arguments support this position, some dealing with physical and psychological safety, some with ethical or social concerns and some with regulatory and political issues. We all believe, based on current knowledge on physical safety, that California should prohibit human reproductive cloning. Moreover, while not all members of the Committee were persuaded by the same set of arguments, most Committee members have concluded that some combination of the other arguments should also lead to prohibition of human reproductive cloning even if it were proven physically safe.**
- 2. The Committee unanimously agrees that California should not prohibit but should reasonably regulate human non-reproductive cloning. We believe that use of this technology offers potential medical and scientific benefits while not raising many of the same concerns as human reproductive cloning. Such uses might include cloning technology as a source of human stem cells that would not be rejected by a patient's immune system. California should regulate all human non-reproductive cloning in the State, public or private. That regulation should do at least three things: a) prohibit the use of pre-embryos after development of the primitive streak, b) ensure that the persons providing cells for this purpose gave informed consent, and c) require that the research be permitted by an approved Institutional Review Board ("IRB").***
- 3. In banning or regulating human cloning, California may be affected by actions of the federal government. Federal regulation needs to be watched carefully to ensure that California's actions are both necessary and appropriate. The actions of other states, which might provide experience useful to the California regulatory plan, should also be watched.**

* One Committee member, Francis Pizzulli, would go further in stipulating the substance of IRB review. His views on this point are set out separately at page 49.

4. Regulating a scientific field undergoing rapid change is difficult for a legislature. The California Legislature should define the terms of its prohibition on human reproductive cloning carefully and its regulation of human non-reproductive cloning carefully but broadly. It should delegate the implementation, including further definition, of that regulation to a state agency.

5. The Committee strongly believes that California will increasingly face complex challenges arising from genetic and reproductive technologies. “Cloning” by embryo-splitting is one of many such technologies. We recommend that California establish an on-going mechanism to advise the Governor and the Legislature on this and related issues of human biotechnology.

We discuss the reasoning behind these recommendations, and much more, in this report.

INTRODUCTION

This report is the product of over two years of work and meetings by the California Advisory Committee on Human Cloning. The Committee, made up of 12 Californians from different backgrounds and fields (Appendix No. 1), has listened to expert testimony; studied the scientific, ethical, and legal literature; and discussed at length the many issues raised by the possible application to humans of the technique, known as nuclear transfer cloning, used to produce Dolly, the world's most famous sheep.

Members of the Committee began their work with different opinions on various aspects of human cloning. Some of those differences have disappeared; others remain. In spite of our continuing disagreements on some points, though, this group has reached a consensus on several important recommendations. We unanimously agreed that California should not ban non-reproductive human cloning, that California should prohibit reproductive human cloning, and that the State should create a more permanent body to provide advice and expertise on other important ethical, legal, and policy issues that will arise from our increased understanding of human biology.

This report sets out our recommendations and the analysis behind them. It does so, in part, by laying out arguments for and against human cloning. No Committee member agrees with every argument in the report; for most of the arguments, the Committee concluded that reasonable people could reach varying conclusions. Nonetheless, our eventual conclusions are strongly and unanimously held.

The report is organized in four sections. The first section provides background information about the Committee, human cloning, and the legal and public reaction to its prospect. The second section discusses non-reproductive human cloning. The third section analyzes the arguments concerning reproductive human cloning. The final section describes some issues about the implementation of the Committee's recommendations.

I. BACKGROUND

This section of the Committee's report provides background information. It begins with information about the Committee itself, then continues with some basic information about the science of human cloning. It then describes the legal status of human cloning, in the United States and elsewhere. It ends with discussion of the public opinion about human cloning.

A. The California Advisory Committee on Human Cloning

On February 23, 1997, the British newspaper *The Observer* published a report of the successful production of a sheep named Dolly from the nucleus of an adult cell injected into an enucleated egg. The report set off an international debate about the ethical, legal and social ramifications of a powerful new technology for cellular and embryological and related biomedical research, as well as for genetic design of mammalian species, in particular, the human species.

Like many other major scientific discoveries that resulted in major changes in our worldview, cloning was immediately controversial. The next day President Clinton requested a report within 90 days from the National Bioethics Advisory Commission (NBAC) and, without waiting for the report, issued an executive order barring federal funding of cloning research on March 4, 1997.

The NBAC conducted a rapid review of published opinions and reports, held public hearings, and published a report on June 9, 1997.¹ The conclusions of the NBAC were that there were clearly such great safety and efficacy concerns with cloning procedures that had until then been reported that it would be immoral and contrary to good public policy to attempt cloning in humans. They recommended legislation to place a moratorium on attempts to clone humans. They reached no conclusion with respect to the question as to whether, if research improved safety and efficacy, the procedure itself was intrinsically immoral, calling for a broad public dialogue to clarify this issue.

Legislation has been introduced several times in Congress to ban or restrict cloning. Congress has considered such legislation in the aftermath of public announcements of plans to clone humans, first in 1998 by Dr. Seed and then in 2001 by Drs. Zavos and Antinori and by a company called "Clonaid," which is connected to a religious group called the Raelians. As a result of the recent announcements, the House Energy and Commerce subcommittee held a public hearing on human cloning on March 29, 2001. A second hearing on May 2, 2001 was held by the Senate Commerce Subcommittee on Science, Technology and Space. Federal legislation banning reproductive cloning has been introduced and one bill has passed the House of Representatives, but, to date, Congress has not enacted any law on the subject.²

There has also been activity at the state level, which led to legislation banning human cloning in at least four states, including California. In 1997, the California legislature passed two enactments about human cloning: Senate Bill 1344 and Senate Concurrent Resolution 39 (Appendix No.2). S.B. 1344, passed unanimously in the Senate and 44 to 17 in the Assembly, defined cloning as "the practice of creating or attempting to create a human being by transferring the nucleus from a human cell from whatever source into a human egg cell from which the nucleus has been removed for the purpose of, or to implant, the resulting product to initiate a pregnancy that could result in the birth of a human being."

The legislation established "a five year moratorium on cloning of an entire human being." The State Director of Health Services was "called upon to establish a panel of representatives from the fields of medicine, religion, biotechnology, genetics, law, bioethics, and the general public" to evaluate the "medical, ethical and social implications," review public policy and "advise the Legislature and the Governor in this area." Senate Concurrent Resolution 39 required the report to be submitted "not later than December 31, 2001."

Implementation of the legislation was assigned to the Genetic Disease Branch of the California Department of Health Services. On December 23, 1998, the Director of the Department of Health Services, S. Kimberly Belshé, formally appointed a group of twelve individuals with the expertise required by the legislation to be members of the

California Advisory Committee on Human Cloning. No staff or funding was provided for the Committee's work; Committee members were not paid for their work beyond reimbursement of some travel expenses.

The Committee had its first orientation and organization meeting on May 8, 1999. Over the next 18 months the Committee held five advertised public meetings at different locations throughout California. The Committee's approach focused each meeting on a specific area of interest and invited knowledgeable speakers to make presentations on that topic, followed by questions from the Committee. Each meeting included a period for public comment and dialogue with the Committee and each public meeting was open to the media. Agendas for all meetings are attached as Appendix No. 3. All meetings were recorded and minutes were produced for each meeting. A selection of articles from the press and scientific publications and any correspondence received were included in the Committee's material for each meeting.

The Committee's task was made more manageable by the fact that a great many of the issues and most of the scientific and ethical arguments had been addressed by the NBAC. The voluminous literature about the issue in books and articles was also available for Committee review. A partial reading list is attached as Appendix No. 4.

After the first round of public hearings was complete, the Committee held a series of five closed meetings to develop the text of a report, including recommendations. This is that report. It represents the consensus of the twelve members of the Committee as to their recommendations to the California government. Probably no member of the Committee agrees with every statement in this report, but it does embody, in general, our unanimous recommendations. This report is **not** a position of the state government and it has not been subject to advance approval by any state body.

Although the NBAC report called for broad public dialogue on the issue, no agency of the federal government undertook the organization or funding of such educational and consensus building effort. None of the other states which passed cloning legislation engaged in any process of public participation in developing the issues, technical, legal and moral, raised by the technology.

Although a large majority of the public continues to oppose human cloning, neither legislatures nor scholars have reached a consensus on the appropriate action. Most of the scientific community continues to echo the findings of the NBAC that reproductive cloning remains a risky and inefficient technology, not ready to be attempted in humans. While the prospect of premature application of current technology has been widely condemned, differing opinions exist on whether human reproductive cloning, if physically safe for the cloned embryo, fetus, and child, should be banned.

The California Committee agrees with the NBAC that there is a need to "provide information and education to the public" and has adopted this concept in the preparation of this report. In the 4 1/2 years since Dolly's birth was announced, there have been innumerable articles about human cloning, but few attempts to work through, in an even-handed way, the arguments on both sides. We believe, whatever the merits of our report, the State of California should be congratulated for making an effort to advance public

understanding and discussion of the issues surrounding human cloning. We hope our report will advance that discussions, among policymakers and among the public.

B. SCIENTIFIC BACKGROUND

In 1997, the report of the production of a newborn lamb by a process that involved the transfer of a nucleus from an adult cell of a donor sheep to a recipient enucleated egg sparked the interest of the world. “Dolly” became an instant celebrity and a public dialogue was rapidly initiated to explore the possibilities of human reproductive cloning and to consider the ethical, legal, and social issues that might be raised should such technology be developed and put to use. While the achievements of Ian Wilmut, Keith Campbell, and their colleagues at the Roslin Institute in Scotland are notable from both a practical and a fundamental scientific standpoint, as with virtually everything else in science, this work rested on the prior contributions of many others.

1. Cloning Before Dolly

Since the beginning of the 20th century, scientists had speculated on the nature of the early events in embryonic growth that result in the differentiation of the various cells’ tissues and organs that constitute a mature animal. The cell’s nucleus was known to be the repository of the genetic program that guided development, but the nature of the changes that took place in the nucleus during differentiation was (and to a considerable extent still is) unknown. The German embryologist August Weismann first theorized that the nucleus of the single cell zygote, i.e., a fertilized egg, must be totipotent, that is, it contains all of the information required to direct the development of a complete animal. 1 He also incorrectly believed that with subsequent cellular and nuclear division, there was a progressive loss of genetic information that resulted in the restriction of developmental potential of the daughter cells. He attempted to demonstrate this experimentally, but inevitably encountered many technical difficulties in an attempt to prove what we now know to be an incorrect hypothesis.

In 1892, Hans Driesch, using sea urchin eggs and embryos, was able to separate the daughter cells resulting from early embryonic cell division and showed that each cell from two and four celled embryos could continue to divide independently and to give rise to a complete and intact sea urchin. 2 This was probably the earliest example of reproductive cloning by the process of embryo splitting. In the 1920’s and 1930’s Hans Spemann carried out some technically extraordinary experiments that demonstrated that totipotency, i.e., the ability to develop into all the cells needed to make an adult, could be retained by embryonic nuclei through a number of cell divisions. 3 Using a “noose” constructed from a human hair, he was able to partition part of the cytoplasm of early developing salamander embryos. Then he was able to coax nuclei that were produced via cell division (mitosis) in another part of the embryo to move into the isolated bud of embryo cytoplasm. Here the “transplanted” nucleus, though in the same embryo, would initiate the development of a second distinct embryo. This work suggested that at the eight or even sixteen cell stage, nuclei still retained the ability to specify the development of a complete new individual. In subsequent experiments, for which he was awarded the Nobel Prize in 1935, Spemann showed that there were changes that determined the fate of cells later in development. Thus transplanted cells and tissues derived from embryos

further along in development retained their differentiated characteristics even when moved to a new location within the embryo. Clearly there were restrictive changes, i.e., loss of totipotency that occurred to the nuclear genetic program as development progressed, but whether these changes could be reversed was still not known.

By the early 1950's techniques had been developed which enabled individual cell nuclei from amphibians to be removed from their surrounding tissues and to be injected into eggs whose own nucleus had been removed or destroyed. With these methods, called "nuclear transfer," new questions could be asked regarding the restrictive changes in the programming of nuclei with development. Briggs and King demonstrated in 1951 that nuclei removed from early frog embryos called blastocysts, which contained several thousand cells, could be introduced into enucleated eggs and direct development at least until the tadpole stage. John Gurdon then carried out some key experiments in which intestinal cell nuclei derived from tadpoles were transferred to enucleated eggs in a similar fashion and gave rise (albeit with low efficiency) to mature adult frogs. This research demonstrated that even the well-differentiated cell nuclei of tadpoles could be reprogrammed to direct full embryonic development. In subsequent experiments, Gurdon used nuclei from adult frog skin cells and showed that these could direct differentiation up to the tadpole stage (although apparently not beyond this point). All of this work suggested that much of differentiation and development was not associated with any irreversible changes in the nucleus.

Success in cloning and nuclear transplantation in mammals required overcoming many new technical hurdles as compared to work with sea urchins or amphibians. Mammalian eggs are much smaller, more fragile, and, unlike the eggs of frogs and sea urchins, which are released by the mother, mammalian eggs need to complete their development internally. By 1979, Willadsen had achieved the artificial production of identical twin sheep by splitting very early embryos.⁴ Although this could be considered a form of cloning, it merely reproduced artificially the natural process that causes identical twins; it did not create a genetic duplicate of a sheep that had already lived.

Throughout the 1980's conflicting results were reported regarding the possibility of achieving embryonic development following nuclear transfer in mice. In retrospect, these results were difficult to interpret because of incomplete scientific understanding and imperfect technique. Subsequent work seems to indicate that, at least in mammals, eggs that are in the process of the second meiotic division are more competent recipients for nuclear transfer studies than are zygotes due to the presence of high levels of a molecule known as maturation promoting factor (MPF). Furthermore, reprogramming of the donor nucleus is markedly facilitated by causing it to stop its progression through the cycle of events required for cell division (the cell division cycle or mitosis) prior to transfer to the enucleated egg. In 1986, Willadsen made use of this new information to produce the first mammals utilizing nuclear transfer technology from eight or sixteen cell embryos into enucleated sheep eggs.⁵ He was able to obtain live born lambs from these experiments that in some instances were genetically identical to one another; that is, they were clones. Shortly thereafter, First and colleagues obtained similar results in cattle in efforts to accelerate genetic improvements in dairy herds. Thus, nuclear transfer technology had been used to create cloned mammals a decade before Dolly, but these clones were all created using cells taken from early stage embryos, not from adult animals. Based on the

work with amphibians, DNA from adult cells was not thought capable of directing the new development of a complete animal.

2. Dolly

In the early 1990's Drs. Keith Campbell and Ian Wilmut worked together in Scotland to investigate systematically the requirements for successful nuclear transfer by manipulating both donor cells and recipient eggs. This work culminated in the discovery that cultured embryonic epithelial cells could act as nuclear donors if the cells were first induced to leave the active cell division cycle and enter the so-called quiescent (G_0) state. Five live born lambs resulted from the early efforts. 6 Two of the lambs died within minutes of birth and the third succumbed after ten days. However, two other animals that came to be known as Megan and Morag lived well into adulthood. This work was highly significant because it demonstrated for the first time that mammals could be cloned from nuclei derived from well-differentiated cells that had been maintained in tissue culture. Yet, these were still cells that had originally been derived from fetal sheep.

Subsequently, Campbell and Wilmut extended their efforts to the use of cultured cells from an adult donor, and this work produced Dolly. 7 Dolly was part of a wide-ranging experiment that involved the transfer of donor cell nuclei into nearly one thousand enucleated sheep eggs. Roughly a third of the eggs received nuclei from embryonic cells, a third from fetal cells, and a third from a cell line created with cells from the mammary tissue of a six year old ewe. Although the adult cells were used to create numerous embryos that were implanted into ewes, Dolly was the only successful pregnancy. Her distinction is not that she is the first cloned mammal – sheep and cattle had been produced through nuclear transfer cloning since the mid-1980s. Dolly, however, was the first mammal successfully cloned from an adult cell, thus opening, for the first time, a plausible scientific prospect for cloning living humans.

3. Reproductive Cloning Since Dolly

In the 4 1/2 years since the announcement of Dolly's birth, researchers have used nuclear transfer cloning with adult donor cells to produce cattle, goats, pigs, mice, and one gaur (an endangered wild ox native to South Asia). At the same time, research in other species has not been successful. Well-financed efforts to clone house pets – dogs and cats – have thus far been unsuccessful. No primates of any kind have been successfully cloned from adult cells; only two primates (two monkeys) have been successfully cloned by nuclear transfer from embryonic cells. As far as we know, no human clones have been born, or have even been implanted for possible birth. It is not known at this point whether human cloning by nuclear transfer is even possible, although each new mammalian species cloned makes human cloning seem more plausible.

Even if human cloning by nuclear transfer is possible, several scientific issues regarding this kind of cloning need to be emphasized. These affect the relationship between the clone and the source of the donated cell nucleus, as well as the likely safety of such a procedure.

Technically, “clones” produced by these methods are not completely genetically identical to the individual that donated the nucleus. The donor cell has DNA in both the nucleus and in its mitochondria, which are cellular energy producing organelles – structures in the cytoplasm of cells separate from the nucleus. When a nucleus is transferred to an enucleated egg, the donor mitochondria are either left behind entirely or grossly outnumbered by the mitochondria in the recipient egg. As a result, the new embryo derives its mitochondria from the recipient egg. While this is theoretically significant, the size of the nuclear genome is approximately 200,000 times larger than the mitochondria genome, and as far as is known, the mitochondria genes only encode proteins that relate to energy production. Nevertheless, mutations in the mitochondrial genes can produce serious disorders in humans.

Another unresolved scientific issue relates to internal changes, called epigenetic changes, in the nucleus of somatic cells. It is now fairly clear that the DNA in most differentiated somatic cells is not fundamentally different from the DNA in the single celled zygote. It has the same sequence of adenine, cytosine, guanine, and thymine that make up the organism’s genetic code. But a series of chemical changes to the primary structure of DNA, such as the addition of methyl groups to DNA, regularly occurs during development. Another example of such epigenetic changes is genomic imprinting. In mammals, the paternally inherited copy of the genome and the maternally inherited copy of the genome are not functionally equivalent. A heritable “imprint” is created during gametogenesis (the formation of sperm and eggs) so that subsequently certain genes are expressed by only one of these contributions, i.e., only from maternal or only from paternal genome. To be successful in directing development, an adult nucleus would have to have maintained a stable imprinting pattern and this pattern would need to be preserved or replaced following nuclear transfer. The success of producing live-born animals by this procedure suggests that such issues are not insurmountable, but there may be imprinting errors that contribute to the high failure rate seen in cloning experiments to date.

Another issue relates to the possibility that genetic damage (mutations) may have accumulated in the differentiated adult somatic cell selected to be the donor nucleus. The longer cells are maintained in culture and the more divisions that they undergo either *in vitro* or in the body, the greater is the possibility that an error in DNA replication might occur or that some other form of DNA damage might accrue. Any one cell uses only a small fraction of the 30,000 or more genes encoded in a person’s DNA. A skin cell uses the genes it needs to function as a skin cell; a liver cell uses some of the same genes and some different genes. A skin cell could function perfectly well as a skin cell in spite of a crucial mutation in a gene vital to, for example, liver function. A cloned fetus produced from such a cell might not be able to produce a functioning liver and therefore would die. Such mutations might render certain somatic cells incapable of directing full and normal development.

Questions of telomere shortening and cellular senescence are also important and unresolved. 8 Telomeres are the ends of chromosomes that shorten each time a cell divides and that therefore represent a log of the functional age of a somatic cell. There is a lower limit to the size of telomeres that is compatible with cell life, and therefore adult cells that have undergone many rounds of replication during the life of an animal have

fewer additional divisions still available to them – they are “aged cells.” Germ cells and cancer cells seem to evade this problem of cellular aging because they possess an active telomerase enzyme, which repairs and re-elongates the chromosome ends. In the case of the use of an adult, presumably “aged” somatic cell for nuclear transfer and cloning, it is not certain at present what effect such telomere shortening of the chromosome in the donor nuclei might have on the longevity of the resulting animal following nuclear transfer. Conflicting evidence has been presented with respect to the length of the telomeres in Dolly’s cells and it is not yet established whether or not Dolly is aging at a rate different from other sheep her birth-defined age. Yanagamachi’s group has serially cloned mice for up to six generations by using somatic cell nuclei from cloned mice as the donors in subsequent rounds of embryo transfer experiments. 9 This might suggest that telomere shortening will not be a problem, but the normal lifespan of a mouse is only two years, and the scientists did encounter progressive difficulty in creating clones with each succeeding generation.

A final scientific issue, very poorly understood at present, has to do with precisely what is occurring during the so-call reprogramming process when the somatic cell nucleus is first placed inside an egg’s cytoplasm. Normal reprogramming occurs within sperm and egg and takes place over a prolonged period of time. Because cell division is usually triggered shortly after nuclear transfer, in such systems there is a very short period of time in which reprogramming may occur. This may result in incomplete reprogramming in some instances.

Work carried out to date in the various animals that have been the subjects of reproductive cloning experiments suggests that there are important species differences in procedures and outcomes among them. This will be vital to keep in mind before any human cloning attempts might be made. Furthermore, the efficiency of obtaining healthy live born clones is very low (on the order of 1% of attempts implanted) in essentially every species that has been studied to date. Many of the embryos die early in development and others progress to later stages of gestation, but often demonstrate severe defects incompatible with further normal development and life. A significant number of nuclear transfer cloned animals have died in early infancy of either respiratory problems or overwhelming infections. And, in some species, such as cattle, the newborns that result from such pregnancies are larger than normal, giving rise to the so-called large calf syndrome. 10 Finally, and quite disturbingly, more recent work suggests that some animals that appear normal at birth may have significant health issues later in life including the sudden onset of obesity without apparent increase in caloric intake, although other work on cloned cattle indicates that those who appear normal at birth remain normal as they age.

4. Non-Reproductive or Therapeutic Cloning

In addition to the reproductive potential for human cloning, a number of other applications have been described under the general headings of “non-reproductive” or “therapeutic” cloning. These methods would not be intended to produce living, fully developed human beings, but rather to provide a source of what have come to be called embryonic “stem cells” for the cellular treatment of human diseases that otherwise cannot be treated effectively by established drug- or cell-based methods. These

embryonic “stem” cells are found only in the early human and other mammalian embryos or in particular locations in the early fetus. They are called “stem cells” because they have a potential to develop into any and all types of cells that are found in a fully developed human or other mammalian organism. Embryonic stem cells from mice were isolated more than a decade ago; human embryonic stem cells were only isolated in 1998. 1,2 A full discussion of the science of stem cells is beyond the scope of this report. A brief summary follows; one clear and useful reference is a primer on stem cells issued by the Office of the Director of NIH in May 2000.

As a result of extensive studies in other mammals, especially the mouse, researchers believe that only these embryonic stem cells are “pluripotent;” that is, they have been shown to be able to differentiate into all cell types in the adult animal. In the mouse system, such cells can, entirely on their own, develop into all cell types found in a fully developed and normal mouse after they are placed into the properly supportive location in a mouse embryo. Since by most current methods they require such support, they are usually termed “pluripotent” rather than “totipotent.” Totipotent would indicate that they can, without help, develop into a fully mature mouse. While some experiments have suggested that these cells may, in fact, turn out to be totipotent, most researchers still consider that as unproven and therefore prefer the term “pluripotent” to describe the embryonic stem cells.

These embryonic stem cells have exciting therapeutic potential because, when they are exposed in the laboratory to one or another of the many known kinds of “growth factors,” they convert to more adult-like fully differentiated cells such as muscle cells, neurons, glandular cells and others. In the case of the mouse, when these manipulated stem cells are introduced into tissues in a fully developed mouse, they can become part of the tissue into which they have been introduced and take part in the normal structure and function of that tissue. It has therefore become possible to envision the use of “stem cells” to treat serious human disorders such as Parkinson’s disease, muscular dystrophy, cancer, many forms of genetic disease and many other disorders. For example, “stem cells” derived from human embryos might be introduced into the brain of patients with Parkinson’s disease to provide normal neurological functions that are damaged in the disease as the nerve cells degenerate. Similar use can be imagined to restore normal liver cells to patients with life-threatening liver damage, cardiac muscle cells to patients with heart damage, muscle cells to patients with muscular dystrophy, and so on. 3

Embryonic stem cells could be used without any human cloning in the sense used in this report. Nuclear transfer cloning may be attractive for stem cell use, however, because of its implications for a patient’s immune system. If a patient received embryonic stem cells that had been grown into heart muscle cells, his immune system might recognize those cells as invaders and attack them. As a result, the attempted treatment might fail or might require expensive and dangerous suppression of the patient’s immune system. It is plausible that the nucleus from one of the patient’s own cells could provide the DNA for the stem cells. This might be done in one of two ways. First, doctors might create an embryonic clone of the patient, transferring the nucleus of one of his cells into an enucleated egg. That pre-embryo would then be destroyed in order to harvest stem cells from it. Alternatively, it might be possible to insert DNA from the patient into an already isolated embryonic stem cell. In either case, if effective the

procedure would produce heart muscle cells with the patient's DNA. The patient's immune system would presumably consider these cells part of itself, and thus not attack them.

Research has identified other kinds of "stem cells" from the adult tissues in mammals. 4, 5 These cells have been called "adult stem cells" and have been identified in organs such as the bone marrow, the brain, liver, muscle and other tissues. These special cells are rare in each of these organs and their isolation is a difficult task. Some recent evidence indicates that some of these adult stem cells can, in some circumstances, be converted to other cell types when exposed to growth factors or when transplanted into new body environments. For instance, some researchers have found that the best known of these adult stem cell, those found in the bone marrow, can become muscle cells when introduced into adult muscle.

The recently discovered multipotent "stem"-like cells from many kinds of adult tissue can theoretically be used in the same way as embryonic stem cells. Human embryonic or fetal tissue may therefore not be required to isolate functional and therapeutic "stem cells" for the treatment of many human diseases. If adult stem cells from the patient can be used, the immune system problems should not arise. If the adult stem cells used come from another person, cloning by nuclear transfer might still be used to produce adult stem cells with the patient's DNA. At this stage, adult stem cells appear to be more difficult to maintain in culture and their ability to change may not be as unlimited as embryonic stem cells. Research in this area is still limited and much remains to be learned.

C. LEGAL BACKGROUND

The legal status of human cloning is complex and unclear. 1 Although many nations have banned human cloning, variously defined, it has not been banned by the federal government or by most states.

1. Regulation of Cloning by the Federal Government

Federal legislation on human cloning could have serious implications for regulation by California, possibly making it unnecessary or ineffective. Many bills have been introduced in Congress to regulate human cloning but, as of the date of this report, none has been enacted. These bills have had widely differing provisions and would have very different implications for cloning regulation by California.

The federal government has taken some action without new legislation. President Clinton issued an order barring any federal funding for research on human cloning. More significantly, in January 1998, in response to Congressional and public concern over the statement by Dr. Richard Seed that he would soon clone himself, the Food and Drug Administration (FDA) announced that it had regulatory jurisdiction over human cloning under existing federal statutes. 2 This jurisdiction, it said, was the same as its jurisdiction over the use of "more than minimally manipulated" cells for treatment purposes, which includes such fields as gene therapy. The FDA stated that anyone seeking to do human

cloning would need to get permission from the FDA for such experiments; it implied that, on the present state of knowledge, such permission would not be forthcoming.

It is not at all clear that the FDA does have jurisdiction over human reproductive cloning under existing statutes. 3 It has never asserted jurisdiction over similar assisted reproduction procedures even when they also involved “more than minimally manipulated” human cells, such as zygotes that had been fertilized *in vitro* or through intracellular sperm injection. At least two published law review articles have concluded that it does not have jurisdiction over at least human reproductive cloning. 4,5,6 For the FDA to have such jurisdiction, the cloned embryo would have to be, for purposes of the statutory definitions, a “product” that was being used for treatment of a disease or condition. Both conditions are questionable; the second is particularly problematic when reproductive cloning is not being used to overcome infertility but by a fertile couple or person for the purpose of having a child with a particular genotype. Ultimately, whether the FDA has jurisdiction would be a question for the courts; at this point, we know of no lawsuit challenging its authority.

Although the FDA’s power over human reproductive cloning is uncertain, it does clearly have power over non-reproductive cloning when used as a treatment for human diseases or conditions. The use of cloned cells or tissues in such treatments would have to be approved by the FDA; experimentation with such cells or tissues in humans would also be governed by the agency.

Because it would probably require the creation of pre-embryos via cloning technology, non-reproductive cloning is affected by national rules on embryo research. This issue has been extremely controversial at the federal level with regard to federal funding for such research. A 1994 National Institutes of Health Human Embryo Research Panel would have allowed the use of human embryos for federally funded research, including, with specific limitations, the production of embryos for this purpose. 7 The report was not adopted as policy by NIH. Congress, however, in 1996 banned “the creation of a human embryo and embryos for research purposes.” The National Bioethics Advisory Commission issued its report, “Ethical Issues in Human Stem Cell Research,” in January 2000. This was followed by release in August 2000 by NIH of its Guidelines for Research Involving Human Pluripotent Stem Cells. The guidelines allowed NIH funded investigators to conduct research on embryonic stem cells obtained from private services, provided the source is excess embryos produced to treat infertility that are donated without compensation. Federal funding for the creation of stem cells from abortions, their derivation from embryos, and the production of embryos to serve as sources of stem cells, either by sexual combination or by nuclear transfer for research, was prohibited.

These guidelines were in turn limited by President Bush’s August 9, 2001 decision to allow federal funding for embryonic stem cell research only for cell lines established before the date of his announcement. This would prohibit federal funding for research with embryonic stem cells produced through cloning as no such cell lines existed on August 9, 2001.

It is important to note that these rules apply only to research that involves federal funds – privately funded research on non-reproductive cloning is not affected by these policies although it would, at some point, be regulated by the FDA. This limitation was highlighted by the work by Advanced Cell Technologies in using nuclear transfer technology and human eggs to produce what it called early embryos (although none grew to be larger than six cells in size.)

2. Regulation of Cloning by the States

In the first year after the announcement of Dolly's birth, more than half the state legislatures considered bills that would have banned human cloning. Only five states have, thus far, passed statutes prohibiting human cloning: California in 1997, 8 Michigan, 9 and Rhode Island in 1998, 10 Louisiana in 1999, 11 and, most recently, Virginia in 2001. 12 The California statute, the first one adopted, bans reproductive cloning for a period of five years. It does not deal with non-reproductive cloning, but is restricted to situations where a cloned embryo is implanted in a woman's uterus. The Rhode Island and Louisiana statutes were modeled generally on California's. The Michigan statute is much different. It bans reproductive and non-reproductive cloning and contains no sunset date. Virginia's statute is similarly broad, banning completely the transfer of any human cell nucleus into oocytes. Several other states have passed legislation barring state funding for human cloning research or prohibiting such research at state institutions. It is not clear why more states have not acted. After an initial flurry of introduced bills, four states passed statutes by 1999 and only one since then. The FDA's assertion of jurisdiction in early 1998, along with the clearly early stage of the technology, may have made state action seem less important.

More than 20 states have laws banning or restricting research with human embryos. These laws were typically passed many years ago in response to concerns expressed largely by 'pro-life' groups. These statutes could prohibit certain forms of non-reproductive cloning. They could also be construed to prohibit reproductive cloning at least at its early, experimental, and 'research' stages. In an effort to avoid regulating *in vitro* fertilization and other forms of assisted reproduction, however, many of these statutes expressly state that they do not govern research that seeks to result in the birth of a living child. 13

3. Regulation of Cloning Outside the United States

Since the announcement of Dolly's birth, many countries have banned human cloning, and several international bodies—including the United Nations, the United Nations Educational, Social and Cultural Organization (UNESCO), the Council of Europe, the European Parliament, the G7 (the group of leading economic powers), and the World Health Assembly—have taken strong stands against the cloning of human beings.

In 1997 UNESCO adopted a Declaration on the Human Genome and Human Rights signed by 186 nations. Article 11 of the Declaration prohibits "practices which are contrary to human dignity, such as reproductive cloning of human beings." The

Declaration is not binding and, in any event, the United States is not a member of UNESCO.

The most authoritative multilateral initiative banning human cloning is that of the Council of Europe, an organization made up of European governments but not part of the European Union. In 1998, it approved a protocol to its Convention on Human Rights and Dignity with Regard to Biomedicine. The protocol prohibits “any intervention seeking to create a human being genetically identical to another human being, whether living or dead.” It was opened for signatures on 12 January 1998 in Paris. As of April 2001 it has been signed by 29 of the Council’s 41 member states and has been ratified by six of these (Greece, Slovakia, Slovenia, Georgia, Spain, and most recently, Romania). Ratifying the Protocol commits the nation involved to implement it, but the Protocol is not self-enforcing; national legislation must be passed to make it effective. In a political compromise, the Protocol leaves up to member countries the definition of a human being. This is significant in that different nations might or might not define human beings in ways that include techniques for non-reproductive cloning.

Other countries that have passed national legislation restricting human reproductive cloning include Australia, Austria, Argentina, Belgium, Brazil, Costa Rica, Denmark, France, Germany, India, Israel, Italy, Japan, Mexico, the Netherlands, Norway, Peru, Portugal, Russia, South Africa, Sweden, Switzerland, Trinidad and Tobago, and the United Kingdom. All together, as of April 2001, 38 of the world’s nearly 200 countries have banned human reproductive cloning.

We have not attempted to survey definitively laws and policies outside the United States on non-reproductive human cloning, but we have looked at some countries.

A Canadian Discussion Group on Embryo Research endorsed research on human embryos prior to 14 days after conception. They recommended a ban on “fertilization of human ova for research and research into human cloning chimeras, production of interspecies embryos and transgenic embryos.” However, they also recommended a National Regulatory Body, which, subject to specific limitations, would be empowered to permit and regulate broad use of embryos in research.

In contrast the Human Genetics Advisory Committee and the Human Fertilization and Embryology Authority in the United Kingdom, while limiting research to embryos less than 14 days, would permit the direct production of embryos for research by nuclear transfer when done in licensed facilities.

The Deutsche Forschungsgemeinschaft (DFG), Germany’s main research funding agency, issued guidelines that would allow research on imported human embryonic stem cells. The DFG also endorsed legislation, if needed, to allow use of surplus embryos produced in Germany to be used and to form a commission to study the ethics of public and private research involving embryos. This issue has been extremely controversial in Germany and remains, at this time, unresolved.

D. PUBLIC OPINION

Over the last four years polling in the United States has consistently shown that a large majority of Americans oppose reproductive human cloning. A poll taken by Time/CNN in February 2001 revealed that 90% of respondents think it is a bad idea to clone human beings. An April 2001 poll by the American Museum of Natural History concluded that 92% of Americans would not approve of cloning to reproduce a favorite person. These results are remarkably similar to polls taken four years earlier, shortly after the announcement of Dolly. For example, a February 1997 Time/CNN poll found that 93% of Americans opposed the cloning of humans. All polling results depend on the exact wording and approach of the poll, but it seems indisputable that human reproductive cloning is not popular in the United States. On the other hand, approximately two thirds of Americans support embryonic stem cell research, although there is no agreement on the source of the embryos.

In general, public opinion toward animal cloning is more positive than toward human cloning. However, the majority of Americans still oppose even animal cloning. For example, the 2001 Time/CNN poll showed that 67% believed it was a bad idea to clone animals such as sheep, and the 1997 Time/CNN poll showed that 66% opposed the cloning of animals.

II. CALIFORNIA SHOULD PROHIBIT HUMAN REPRODUCTIVE CLONING

RECOMMENDATION

The Committee unanimously agrees that California should ban human reproductive cloning. Many arguments support this position, some dealing with physical and psychological safety, some with ethical or social concerns and some with regulatory and political issues. We all believe, based on current knowledge on physical safety, that California should prohibit human reproductive cloning. Moreover, while not all members of the Committee were persuaded by the same set of arguments, most Committee members have concluded that some combination of the other arguments should also lead to prohibition of human reproductive cloning even if it were proven physically safe.

The Committee unanimously believes that human reproductive cloning should be prohibited. Every Committee member agrees that grave questions about the physical safety of the cloning process for any resulting children require a prohibition unless and until the method is proven safe. Most Committee members have concluded that some combination of the other arguments should also lead to prohibition of human reproductive cloning even if it were proven physically safe. The Committee has reached these conclusions after reviewing arguments in favor of human reproductive cloning as well as arguments against it. This section of our report discusses those arguments, looking first at the arguments for cloning and then at the arguments against cloning. Each argument is summarized with its counter-arguments. In almost all cases, this section of the report tries to lay out the different positions without choosing among them.

A. ARGUMENTS FAVORING HUMAN REPRODUCTIVE CLONING

The arguments made in favor of human reproductive cloning fall into two categories: an argument for reproductive liberty, as a normative and as a legal matter; and a series of examples of “good” uses of cloning, based primarily on the benefits of its use as a treatment for certain kinds of infertility.

1. Reproductive Liberty

One of the deepest consequences of the American belief in liberty is that whatever is not prohibited is permitted. Implicit in that approach is the idea that actions should not be prohibited without good reasons. This general preference for liberty has special resonance in the area of reproduction. Reproduction is an activity of profound importance both to the individual and to society. Its special significance lies in the fact that it generally commences with the intimacy of coitus and always culminates in the creation of a child who not only forges new relationships among individuals and between families, but also serves to perpetuate society. For this reason, some commentators, notably Professor John Robertson, argue that individuals should possess the freedom to choose whether or not to reproduce by means of somatic cell nuclear transfer cloning so long as their actions do not cause any harm to others or pose a threat to society. “Procreative liberty includes a strong presumptive right to have genetically related

children noncoitally” and “cloning may provide a useful [noncoital] alternative, unless harmful.” Of course, the Robertson test leaves open questions of the extent of the necessary harm or threat, to whom the harm or threat must be directed, and who should bear the burden of proof. Those opposed to a ban on human reproductive cloning argue that this reproductive method has not, or cannot, be shown to fail that test, at least in some circumstances.

This argument from reproductive liberty might be made not only as a general normative position but as a legal argument. Reproduction is not only a basic human urge, but it may also qualify as a fundamental liberty shielded from government intrusion by the Constitution. The Supreme Court has already found a fundamental right to *avoid* reproduction, whether by means of contraception or abortion. 1, 2 Some scholars infer a parallel fundamental right *to* reproduce with the assistance of new technologies, including somatic cell nuclear transfer cloning, an inference that is supported by broad language in a number of contraception and abortion cases. In striking down a statute prohibiting the distribution of contraceptives to unmarried persons, for example, the Supreme Court declared: “If the right of privacy means anything, it is the right of the individual, married or single, to be free from unwarranted governmental intrusion into matters so fundamentally affecting a person as the decision whether to bear or beget a child.” 3 More recently, in reaffirming the right to an abortion in 1992, the Court explained that “[o]ur law affords constitutional protection to personal decisions relating to marriage, procreation, contraception, family relationships, child rearing, and education.” 4

One other Supreme Court precedent offers support for a fundamental right to procreate. In 1942 in *Skinner v. Oklahoma*, 5 the Court invalidated a state statute that authorized the forcible sterilization of persons thrice convicted of a felony involving moral turpitude, declaring that “[m]arriage and procreation are fundamental to the very existence and survival of the race.” But the *Skinner* decision is “indeterminate,” and “may be read in several different ways, all of which are equally consistent with current constitutional doctrine.” 6 The Court’s ruling was quite narrow: because the law permitted the sterilization of chicken thieves but not embezzlers, the Court determined that it discriminated against certain categories of criminals in violation of the Equal Protection Clause. Thus *Skinner* may not even establish a right to be free from compulsory sterilization, so long as the law is administered in a nondiscriminatory fashion. Moreover, compulsory sterilization laws implicate the same concerns regarding bodily integrity and social equality that animated the Court in the contraception and abortion decisions, thus they are distinguishable from laws regulating medically assisted reproduction. 7

At least one federal district court has interpreted these decisions to establish a constitutional right to beget children with the assistance of technology, including in vitro fertilization and embryo transfer using a donated embryo, based upon the following reasoning: “[I]t takes no great leap of logic to see that within the cluster of constitutionally protected choices that includes the right to have access to contraceptives, there must be included within that cluster the right to submit to a medical procedure that may bring about, rather than prevent, pregnancy.” 8

The constitutional argument about human reproductive cloning is not frivolous, but neither is it powerful; it is not generally accepted by constitutional scholars. The proponents of cloning support it as an issue of unwarranted restriction of reproductive freedom. However, it can be argued that the freedom to reproduce should not encompass human reproductive cloning because it lacks the essential elements that give reproduction meaning; it is neither coital nor collaborative, and it does not involve the random recombination of genes to create a child with a new and unique genetic identity. Although human productive cloning may ultimately serve the same function as other modes of reproduction by bringing into being a child, opponents argue that it is radically different because it results in genetic duplication—the replication of existing human beings. On this view, cloning should be classified as “replication” rather than “reproduction.”

The supporters of human reproductive cloning cited the constitutional protection of procreative decisions and methods as justifying cloning. However, one reproductive right, i.e., human reproductive cloning, does not necessarily follow from others, i.e., contraception, abortion. The Supreme Court relied heavily upon two factors in the contraception and abortion cases that are conspicuously missing from the cloning context. Because pregnancy entails a massive invasion and occupation of a woman’s body, constitutional protection for the right to avoid reproduction is essential both to safeguard bodily autonomy and to ensure gender equality. But these precedents erect no constitutional barrier to a ban upon human reproductive cloning, which neither results in invasion of the integrity of the body nor endangers women’s equality. Thus, the contraception and abortion cases cannot be read to guarantee a constitutional right to create a child with the assistance of technology.

Even if there were a fundamental constitutional right to reproduce, such a right might not encompass human reproductive cloning. On the one hand, some argue that cloning is clearly procreative to the extent that it is used “to bear and beget a child.” Indeed, if procreation is important because it involves the passing on of one’s genes, one scholar suggests that “in comparison with the parent who contributes half of the sexually reproduced child’s genetic formula, the clonist is conferred with more than the requisite degree of biological parenthood, since he is the sole genetic parent.”⁹ Under this view, cloning appears to merit at least the same degree of constitutional protection as other assisted reproductive technologies. On the other hand, the Supreme Court has generally looked to history and tradition to determine the contours of constitutional protection. As a matter of history and tradition, sexual reproduction seems to fall within “the private realm of family life which the state cannot enter.”¹⁰ Yet such an approach would probably afford little protection to human reproductive cloning, which is radically different from other technologies that serve as a substitute for reproduction by sexual intercourse because it is not *sexual* reproduction – it does not involve sperm and eggs.

If human reproductive cloning were deemed a fundamental right under the U.S. Constitution, any state or federal laws regulating or prohibiting cloning would be subject to the strictest scrutiny of the judicial system. Governments could restrict cloning only for compelling reasons, and any regulations would need to be narrowly tailored so as not to infringe unnecessarily upon individual rights. As a matter of existing federal constitutional law, however, the argument for a right to human reproductive cloning seems weak. The Supreme Court has never held that there is an affirmative right to

reproduce that is free from government regulation. Indeed, the power of the Food and Drug Administration to regulate the safety of contraceptives and abortifacients and of states to make reasonable safety-based regulations for abortions seem well-established. The California Constitution provides residents of California another source of rights, including an express right to privacy, but, like the U.S. Supreme Court, California's courts have never held that there is a state constitutional right to be free from all regulation of reproductive methods. It seems very unlikely that either the U.S. Supreme Court or the California Supreme Court would rule human reproductive cloning to be a fundamental right or liberty interest. Thus, reasonable regulation of human reproductive cloning, including a ban, would likely be upheld as constitutional if government could show a rational basis for its policy.

2. Examples of “Good” Human Reproductive Cloning

Discussion of human reproductive cloning has often focused on evil or frivolous uses of cloning such as to create clones of Adolph Hitler, of superior warriors, of excellent athletes, or of rich egomaniacs. Supporters of human reproductive cloning have responded by pointing out that, in the real world, cloning may serve compelling human needs. They have drawn attention to more sympathetic possible uses of the process. Three examples are commonly used: human reproductive cloning as a treatment for certain kinds of infertility, as a way of producing transplantable tissue (typically bone marrow) to save another life, and as a way of coping with the grief of a loved one's death. Some advocates for human reproductive cloning have argued that cloning should be limited to only certain approved uses. No one proposed to the Committee a detailed plan for selecting the approved uses of cloning or the approved parents, but at least two witnesses before the Committee, Professors John Robertson and Glenn McGee, argued that cloning should only be allowed for parents with some set of “good reasons.” We discuss below three arguably “good reasons.”

a. Human Reproductive Cloning to Treat Infertility

Cloning could provide an innovative method to treat the problem of infertility. Assisted reproductive technologies can help many infertile couples, but people who do not produce viable gametes – eggs or sperm – cannot produce children who are genetically “their own.” A couple where one member is infertile from such a cause currently must turn to an egg or sperm donor in order to create a child who is biologically connected to at least one prospective parent. But human reproductive cloning affords the power to produce a child with a genetic connection to at least one parent, while simultaneously keeping the couple's relationship free of the ghost of such third parties. (Where one member of the couple produces viable eggs, the clone might even have some genetic contribution from each “parent” – nuclear DNA from one and mitochondrial DNA, found only in the egg, from the other.) Moreover, gay or lesbian couples might choose to clone for the same reasons—in order to have children without relying upon third parties, who may ultimately request parental rights and responsibilities.

Opponents of human reproductive cloning could respond that couples who were infertile because of gametic inadequacy do have other options for having children. They can adopt children. They can use assisted reproduction methods using donated eggs or

sperm. Such donations might be particularly appropriate coming from a first degree relative of the infertile person, who would share 50 percent of his or her genome, thus producing a child who was 50 percent related to one parent and 25 percent related to the other. These possibilities raise both the question of what is meant by a child “genetically their own” and whether such a desire should be supported.

On the other hand, whatever “children genetically their own” means, the United States currently allows infertile couples to take many steps to try to have such children. Proponents of human reproductive cloning argue that it is unfair to single out one particular group of the infertile and forbid them to use an advanced reproductive technology that would help.

b. Human Reproductive Cloning to Provide Transplants

The desire to clone is not confined to the infertile. A fertile couple may resort to cloning in order to save the life of an existing child, who desperately needs compatible cellular transplantation, e.g., bone-marrow, in order to survive. The parents may remove cells from the dying child to clone another child who will be a perfect match, resulting in two healthy children who happen to be identical twins of different ages. (Of course, if the dying child’s illness had been caused by his genes, cloning would, in most cases, not be useful.)

Opponents of human reproductive cloning sometimes invoke the image of “organ farms” populated by “spare parts clones,” who would be a source for hearts, lungs, and other essential organs. Killing or harming one human, whether or not a clone, for the purpose of providing organs for another, they argue, is wrong. More fundamentally, creating a child for that purpose is using that child as a means to an end, not as an end in itself, and that, they contend, is also wrong.

Proponents of human reproductive cloning present this scenario not for irreplaceable organs like the heart, but instead about transplants that involve little risk, notably bone marrow transplants. Furthermore, they note that children already have been conceived and born for the purpose of providing bone marrow or stem cell transplants to their older siblings, either through conventional conception or through *in vitro* fertilization. In at least one reported case, parents used *in vitro* fertilization with pre-implantation genetic diagnosis in order to ensure that the implanted embryos would be able to provide matching tissue to their ill sibling. Proponents of human reproductive cloning argue that if we allow the creation of tissue donor children in those ways, we should not ban their creation through cloning. Proponents can also point out that children are conceived from a wide variety of intentions or, in many cases, accidentally, with no intention to start a pregnancy. The desire to create a tissue donor child to save the life of its sibling is, they claim, certainly better than many of the other reasons children are conceived.

It is not clear how often this scenario would arise given the availability of other treatments and other sources for bone marrow and other tissues or organs. It might also be the case that, if successful, non-reproductive human cloning could provide simpler

solutions to this problem by creating histocompatible cells or tissues for transplantation into the patient whose cells provided the DNA used to make the cloned cells.

c. Human Reproductive Cloning to Replace a Loved-One

The first two examples are cases where human reproductive cloning would be used for some motive other than, or in addition to, creating a whole person who was genetically identical to another. The couple that is infertile because of gametic inadequacy just wants a child “of their own” and reproductive cloning might provide, they think, the best way to reach that goal. Parents seeking a tissue transplant want genetically identical tissue, but are not motivated by the goal of having a genetically identical child. For them human reproductive cloning is a means to a goal other than the production of a child genetically identical to an existing person. The third example, however, is motivated by a desire for such an identical child. One sympathetic version of the example might involve a couple with a beloved young child. The child dies and the parents, in their grief, wish to have another child quickly, seeking perhaps in some way to “replace” their dead child. Human reproductive cloning might allow them to have a new child that was genetically identical to the first child. They might believe that this genetic identity would help assuage their grief and so seek to clone the first child.

Opponents point out that inherited genes are not overwhelmingly powerful and that, therefore, the clone would not be the same as the dead loved one. Furthermore, they argue that this kind of “replacement” is not psychologically healthy for the parents or for the second child. They also note that, when the second child turns out not to be exactly the same as the first, the consequences for the parents and the child could be negative. On the other hand, proponents would counter that those who have not lived through the tragedy of a dead child may not feel in a position to judge the actions of parents who have.

B. ARGUMENTS AGAINST HUMAN REPRODUCTIVE CLONING

In contrast to the arguments in favor of human reproductive cloning, the arguments against it are both varied and numerous. They fall into six broad categories: (1) possible physical harms to the cloned embryos, fetuses, children, and gestational mothers; (2) possible psychological harms to cloned children and others; (3) possible harms to human society; (4) an inherent immorality or impermissible unnaturalness of human reproductive cloning; (5) pragmatic difficulties in allowing cloning for only some reasons; and (6) a majoritarian political argument. Each is discussed below.

1. Physical Harms

All new drugs and biologics and many new medical devices must be proven “safe and effective” to the satisfaction of the FDA before they can be marketed in the United States. “Procedures,” unlike drugs, biologics, and medical devices, are not regulated by the FDA and need not be demonstrated, to anyone, to be safe or effective before their use.

There is, as yet, no direct evidence concerning the safety of human reproductive cloning. As far as is known publicly, such cloning has never been tried. And, although the Dolly technique for cloning has now been used regularly for cattle, sheep, goats, and mice, it has never been successfully used in any primates. Researchers at Oregon State University cloned two monkeys using somatic cell nuclear transfer with the cell nuclei taken from embryonic monkey cells; no monkeys or other primates have been cloned using nuclei from born primates. In spite of hundreds of efforts, those researchers have been unable to establish another pregnancy by somatic cell nuclear transfer using monkey nuclei from any source. As of June 2000, more than 400 efforts had failed after the first embryonic donor success. 2

There are serious theoretical reasons to be concerned about the safety of reproductive cloning. These include, among others, epigenetic changes in the donor cell's DNA, 3 which might not be reversed in the cloning process; problems with maternal and paternal imprinting of DNA in a clone; 4 accumulated damage in the DNA of the donor somatic cell; 5 telomere length; 6 and problems with reprogramming of the donor cell's DNA. 7 None of these concerns apply to natural reproduction or to the various existing forms of assisted reproduction. Practical experience adds to these theoretical concerns. In cattle and sheep, animals produced by somatic cell nuclear transfer processes have shown a high level of deformity and early death, as well as a very high rate of miscarriage. More than 90 percent of the embryos implanted fail to reach term; over 15 percent of the animals born alive have serious birth defects. This compares with a rate of serious birth defects of about 3 percent in humans. And even apparently "normal" clones may have abnormal gene regulation, leading Rudolf Jaenisch to testify to a National Academy of Sciences panel that "most adult clones may have (at least subtle) abnormalities. Completely 'normal' clones may be the exception." 8

In addition, in other cloned mammalian species the cloned fetuses grow overly large *in utero*. This may pose a significant risk to the woman carrying the fetus during gestation and at birth. Why the fetuses grow so large is not known; some think it may be a result of faulty nuclear reprogramming during the process of nuclear transfer.

Present evidence thus indicates but does not prove that human reproductive cloning would be substantially less safe than either natural reproduction or existing forms of assisted reproduction. But it quite clearly does not prove that it *is* safe and it does raise very serious questions about the procedure's safety.

On the other hand, these standards of safety have not been applied to other forms of advanced reproductive technology. *In vitro* fertilization was not approved by the FDA before its use, nor was it extensively tested in animals before experiments began in humans. The same is true of many medical procedures that do not involve new drugs or devices. Proponents argue that it is unfair and inappropriate to subject this one procedure to a higher standard than similar procedures – although that begs the question whether such proof of safety should, in fact, be required broadly for reproductive technologies.

Human reproduction is not entirely safe, for the child or for the mother. Although modern medicine has greatly reduced infant and maternal mortality rates, about half of one percent of newborns die within a month of their birth. One or two percent live but

have serious birth defects. Furthermore, in the United States parents are not forbidden to reproduce even when the children (or the mother) will be at very high risk. A couple where each member carries a gene for an autosomal recessive disorder – like cystic fibrosis, sickle cell anemia, or Tay-Sachs disease – runs a 25 percent risk of having an affected child. A couple where one member carries a gene for an autosomal dominant disorder, like Huntington’s disease, faces a 50 percent risk that each of their children will inherit that gene. Similarly, parents with non-genetic health conditions that might be transmitted to a child (HIV infection provides one example) are allowed to put themselves and their future children in jeopardy by becoming pregnant. Human reproductive cloning may be less risky than at least some existing, and allowed, childbearing; advocates argue that it should not be banned on this account as long as the parents understand and accept the risks. On the other hand, reproductive cloning involves a degree of premeditation that is often missing from sexual reproduction and a substantial medical intervention, which might distinguish it meaningfully from normally commenced “at risk” pregnancies.

2. Psychological Harms

a. Psychological Harms to the Cloned Child

Cloning by means of somatic cell nuclear transfer would make it possible to produce a child who is virtually genetically identical to an existing or previously existing person, i.e., a delayed genetic twin. Many fear that this would inflict deep and lasting psychological damage upon such a child. Some children may suffer from a loss of uniqueness and a diminished sense of individuality and self esteem grounded in the fact that he or she is the genetic copy of another person. Others may be unduly burdened by heightened expectations of parents and others. Thus cloning, it is argued, deprives the child of the right to a unique identity and denies the child the right to an open future.

Proponents of human reproductive cloning argue that common experience with identical (or ‘monozygous’) twins, whether reared together or apart, provides a compelling counterexample to this argument, for identical twins do not necessarily suffer psychological injury as a result of their genetic similarity. A child who is created by reproductive cloning would be no less unique than an identical twin. To the contrary, clones are likely to differ much more than identical twins. Although a cloned child would possess almost the same genotype as the genetic donor, he or she would result from a different egg (with distinct mitochondrial DNA), gestate in a different womb, and grow up in a different environment. The process of cloning requires reprogramming of the genes of a specialized donor nucleus. This process is apparently incomplete and is thought to contribute to the high frequency of birth defects and miscarriages. The result is there may be real differences in the ultimate DNA of the clone.

Although identical twins share the same genome, opponents of human reproductive cloning point to differences between clones who are born and raised years apart and identical twins. Identical twins begin life with a blank slate, equally ignorant of each other’s destiny. A cloned child, on the other hand, may start life with some knowledge of what his genetic predecessor has already become. He may feel much about himself or his fate is pre-determined, losing the sense of freely constructing his own identity and choosing his own future. Even if the clone does not believe in genetic

determinism—that our fate lies only in our genes—some people nevertheless fear that the life of a cloned child would always be haunted by the shadow of the original and unduly shaped and constrained by the expectations of others. Hence, the child clone could be denied the ‘right to an open future’ by having his future autonomy undermined by unfair and over-zealous parental expectations.

A related concern is that the cloned child would become the prisoner of these pre-set expectations that she will possess particular traits or resemble the genetic donor in important ways. Even if such expectations proved to be false, if they are widely shared by the child’s parents and by society, they risk becoming a self-fulfilling prophecy.

In addition, because human reproductive cloning offers the prospect of total control over reproduction—over the child’s specific genome—some fear that it would not only cause parents to harbor unrealistic expectations but also to view their children more as objects manufactured according to precise specifications than as independent persons. To the extent that reproductive cloning fosters such social attitudes, it may ultimately lead to the objectification of children who will be treated as mere means to parental fulfillment, rather than as ends to be loved and cherished for themselves.

Proponents of human reproductive cloning say it is difficult to argue that cloning should be banned to protect against this speculative harm. Parents of clones might have unrealistic expectations of the clone, but this problem of “expectations” is not unique to cloned children. Furthermore, it can be argued that parents who go through the expensive and burdensome process of assisted reproduction, including nuclear transfer, have a strong desire to lavish parental love and care on any child that results. Many parents whose children are the unwanted product of sexual conception are objectified and treated as commodities the world over. The motivations and behavior of a few parents are not a reason to ban a neutral technology that is compatible with both good and bad outcomes. What would be the consequences for the children if they fail to live up to unrealistic expectations? Would they face the rejection of their parents and the disappointment of society? This concern, proponents would argue, is not different in quality or quantity from unreasonable expectations placed on some children who are normally conceived. These harms are abuses that can be combated by education and are not intrinsic to the technology.

Opponents, however, urge that the differences in expectations between cloned children and other children are differences of kind, not of degree. Regardless of one’s belief in the role of genetics behavior, parents who want to clone a child usually would do so in order to have a child with a precise genetic make-up. Common sense, it is argued, suggests that a parent, particularly if the child is the parent’s own clone, is unlikely to forget about that the child carries his or her genome. For the cloned child to have such a parent may threaten the cloned child’s own self-image, as well as her sense of privacy. The argument that cloning deprives a child of the right to an open future is based not simply on genetic determinism, but in part on experience with genetic testing. Clinical geneticists and genetic counselors often counsel against testing children for late onset genetic disorders because a child who tests positive might grow up in a world of limited horizons or suffer psychological harm. Insurers and employers could hardly be

expected to ignore information about the clone's "genetic parent-twin". A basic family history of the cloned child would take on much greater significance.

Some have expressed concern about the possible abusive nature of certain utilitarian purposes for reproductive cloning, once the procedure is considered safe for purposes of physical safety. Examples could include creating a cloned child to provide organ and tissue transplants, or to replicate an unusual or rare genotype primarily to benefit the biomedical research community. In response to this concern, others have pointed to the current laws against child abuse which provide a basis for deterring abusive cases of reproductive cloning. However, cases in which, for example, multiple clones of a distinctive genotype are created, may present harms which are not readily remediable after the fact by typical child abuse statutes. To take an extreme example, if the parents of a dying child—or researchers—wanted to clone a series of equally short-lived children as replacements of a loved one until a cure could be found, the state could consider asserting a legitimate preventive interest.

b. Psychological Harms to the DNA Donor

Some argue that the fact that there exists another individual who share the same genetic identity may inflict psychological harm not only upon the cloned child, but also upon the person who provides the genetic material. The person who is the source of the genetic material (if still alive) may experience a loss of self worth rooted in the knowledge that he or she is no longer unique, but now has a genetic copy. Some genetic donors might see themselves reflected and diminished in the body of the clone, thus producing a harm to him that is the mirror image of the harm suffered by the clone. On the other hand, some genetic donors may have opposite negative psychological effects; a high sense of self-worth that led the donor to want to clone himself might be reinforced in unhealthy ways.

One mechanism to avoid or minimize such potential injuries is to ensure that no one is cloned without first discussing the procedure with an objective professional and obtaining informed consent. Indeed, human reproductive cloning performed in the absence of prior consent could even violate a moral or legal right.

c. Psychological Harms to Other Participants

Opponents of human reproductive cloning could argue that it permits parenthood to be deconstructed into its component parts, making it possible to separate the genetic, gestational, and rearing functions. As a consequence, other participants in the cloning process, such as egg donors, gestational surrogates, and the individuals who intend to rear the child, could also suffer psychological harms associated with the splintering of parenthood. One might also worry about the possibilities of coercion or duress in the procurement of somatic cells, egg cells, or surrogate mothers. Indeed, it is even possible that people could be cloned without their consent, which could cause substantial psychological damage.

On the other hand, proponents could note that many modes of assisted reproduction pose the same risks, thus this objection is not unique to cloning. It cannot

justify a law singling out cloning for special treatment while leaving artificial insemination, egg donation, and gestational surrogacy entirely unregulated. They would argue that, as with other forms of assisted reproduction, these risks should be regulated by counseling, screening, informed consent, and so forth, and not by prohibition.

3. Harms to Society

Opponents argue that human reproductive cloning would have a wide range of possible negative consequences for human society. These include confusion of family relationships; encouragement of genetic enhancement of children; distributive injustice; encouragement of commodification of children; the loss of human genetic diversity; overpopulation; and threats to democratic values of individuality, privacy, and autonomy.

a. Confusing Family and Generational Structures

The fact that human reproductive cloning would make it possible to separate the genetic, gestational, and rearing functions also means that there could be, on rare occasions, as many as five different individuals who claim some biological connection to the child; the genetic donor, the woman who provides the egg (which also includes mitochondrial DNA), the woman in whose womb the clone is gestated, and the biological progenitors of the persons who provide the genetic material. Which of these many potential candidates should be identified as the “parents” of the child? This is an issue that needs statutory resolution since it is already the subject of case law in surrogacy and embryo donation cases. If a cloned child is actually a delayed genetic twin, is the genetic donor the child’s sibling or parent? This depends on how this society wants to define these terms. And are the parents of the genetic donor the child’s parents or grandparents? If a woman, for her second child, clones her mother, is the first born child the clone’s sibling or grandchild? Opponents of human reproductive cloning point out that these fundamental questions highlight the ways in which human reproductive cloning may confuse the structure of the family and blur generational boundaries.

On the other hand, proponents argue that human cultures accept many forms of familial relationship. *In vitro* fertilization and other assisted reproductive technologies have already raised many of the kinds of generational issues that cloning raises. The family has already been the subject of much change. The census shows two-parent families in the minority. While proponents contend that human reproductive cloning introduces concerns similar to concerns already present and tolerated by the law and society, opponents respond that the potential for confusion of roles is greater when a child may be a genetic twin of a parent.

b. Encouraging Genetic Enhancement

Some are concerned that human reproductive cloning might open the door to eugenics and to the systematic selection of genetic traits in offspring. Reproductive cloning itself functions as a form of genetic selection by making it possible to create a child with a known genetic identity. With the mapping and sequencing of the human genome, it may ultimately become possible to isolate and select the genes responsible for a given trait. If functioning genes could be inserted into the sperm, ovum, embryo,

somatic cell or clone, the genetic makeup could be altered. Rather than taking their risks with the genetic lottery that is sexual reproduction, prospective parents might choose to clone in order to control the genotype of their child and perhaps of subsequent generations.

Opponents of human reproductive cloning have also worried that parents would not choose wisely. Selection of certain physically attractive characteristics attaches a value to physical appearance that might devalue or disadvantage alternative phenotypes as persons or as societal models. Cloning not only offers the power to select a desired genetic phenotype, but also the power to produce multiple copies of such persons. If cloning is combined with such forms of genetic selection, some fear that science fiction images of the mass production of individuals with particularly desirable genetic traits could one day become a reality.

Proponents counter that speculative application of eugenics after human reproductive cloning does not in itself justify legal prohibition. All that would be necessary, they assert, is regulation of introduction of genes during or after the process. Genetic enhancement can be accomplished with or without human reproductive cloning and reproductive cloning can be done with or without enhancement.

c. Distributive Justice: Cloning only for the Rich

Because human reproductive cloning affords the ability to control a child's genotype, unequal access to such technology could exacerbate existing inequalities in our society. Reproductive cloning would probably be quite expensive and it is not likely to be covered by health insurance. But if human reproductive cloning is confined to those who can afford such a technology, only the wealthy will be able to pass on their 'genetic endowment' to their progeny in perpetuity. If this genetic inheritance did, in fact, correlate strongly with success in society, opponents of reproductive cloning fear that it would pose the risk of a society with entrenched, virtually permanent caste hierarchies. Judge Richard Posner, for example, projects that reproductive cloning might tend to crowd out sexual reproduction and, in so doing, aggravate inequalities in genetic endowment and wealth, thus creating pressures for eugenic regulation.

In *Plyler v. Doe*, the Supreme Court expressed concern about the denial of public education to illegal alien children because this might "promote the creation and perpetuation of a subclass of illiterates within our boundaries." If educational inequalities are troubling because they could perpetuate a caste system, then what about genetic inequalities? Thus widespread use of reproductive cloning could result in a 'DNA-divide,' a society of genetic haves and have-nots.

This argument depends on genetic inheritance correlating strongly with success and on the widespread use, by the wealthy, of human reproductive cloning. Societies already tolerate many inequities, perhaps most easily seen in the United States in large disparities in wealth or in access to health care. These also affect children. For example, most people believe that a "good education" correlates strongly with success and wealthy parents often try to buy such an education for their children. Is reproductive cloning different? In any event, proponents of human reproductive cloning could argue that the

potential for maldistribution of a safe and effective technique is not a reason to ban the technique. There is nothing in the nature of cloning technology that dictates it must be available only to the rich; it could be allowed only if it were made widely available.

d. Commodifying Persons and Commercializing the Family

Some opponents argue that by placing a price tag on the cloned child, human reproductive cloning threatens to commodify all children. The danger these opponents see is that children will be regarded as fungible goods that are manufactured according to precise specifications and traded on the market, rather than as unique beings who are priceless. Opponents urge that, in so doing, reproductive cloning also threatens to commercialize children and the family, a realm which many believe should be shielded from the economic values that govern the market. They contend that this kind of commodification is already present in other assisted reproductive technologies, particularly when third party gametes (eggs or sperm) are sold based in part on the seller's attributes. Offers to pay \$50,000 or more to desirable egg donors have been widely reported. Reproductive cloning could present a strong form of this commodification as it holds out the promise of delivering a "precise product," a baby with a known genotype and not just an unpredictable mixture of parental genes.

Proponents of reproductive cloning can respond that commerce in clones could be banned. We do not forbid organ transplants because of fears of commercialization; instead, we ban the sale and purchase of most organs and regulate their distribution. A similar regulatory scheme could be implemented with respect to DNA for use in reproductive cloning. Proponents contend that the family is not shielded from economic values and commercialization by current law. They argue that reproductive cloning, like other things in society, can contribute in both positive and negative ways to broad social problems, such as rampant commercialism, but it is not so intrinsically unjust or commercialized that we need to criminalize it on this account.

e. Reducing Genetic Diversity

Reproductive cloning replicates an existing genome, preventing the random recombination of genes that is a byproduct of sexual reproduction. As a corollary, a few fear widespread use of reproductive cloning to create children could ultimately reduce genetic diversity in our society. A real reduction of genetic diversity could have terrible consequences for humanity's ability to survive changing environments, such as new diseases.

Proponents find this argument implausible. There are over 6 billion different human genomes in the world today. It seems very unlikely that most people will choose to reproduce by cloning when the alternative is so much easier and cheaper. But even if a large fraction of the population did reproduce by cloning, there is no reason to believe that they would all choose to clone the same few people. On balance it seems unlikely that reproductive cloning will substantially reduce our genetic diversity.

f. Increasing the Population

At the Committee's public hearings, at least two members of the public argued that the world's population is already too big. Reproductive cloning would only increase it, causing substantial negative environmental effects. This argument seems weak. Reproductive cloning still requires women to carry pregnancies to term. Reproductive cloning would only increase the population if women decided to have more cloned babies than they would otherwise have had sexually-produced babies. The expense, difficulties, and risks of reproductive cloning compared with sexual procreation make this unlikely.

g. Threatening Socially Important Values

Some argue that reproductive cloning threatens socially important values such as individuality, privacy, and autonomy, values that are crucial to a democratic society. By making more predictable humans, opponents say, reproductive cloning undercuts our ideas of free will. Seeing human clones, people will have less ability to feel free and to act autonomously. This will in turn weaken political and social institutions that seek to protect the rights of autonomous individuals.

Proponents of reproductive cloning try to dismiss this argument as based on an extreme view of genetic determinism. Clones, they argue, would not be so much more predictable than other people as to shake society's faith in free will and the importance of the individual.

4. Human Reproductive Cloning Is Impermissibly Unnatural or Inherently Immoral

During the March 28, 2001 congressional hearings on human cloning, Rep. Clifford Stears asserted that "[h]uman cloning is a form of playing God since it intervenes with the natural order of creation" and ". . . is an unethical use of technology." This brief quotation illustrates the two arguments that are perhaps most commonly expressed against cloning technology: that reproductive cloning is 'unnatural' and that it is an affront to divine power. Certainly, cloning could be considered 'unnatural' as it relies on human intervention in a 'natural process.'¹ It clearly runs counter to a normally functioning natural environment, at least for mammals. It does not provide for the random combination of genetic material from eggs and sperm that is the essence of sexual reproduction. In addition, it could theoretically render males reproductively obsolete. All that is needed to clone a human being are human eggs, somatic cell nuclei, and uteri; and a woman can supply all of these. A system of reproduction that renders males obsolete also renders the 'natural' method of human reproduction obsolete. Those opposed to human reproductive cloning on these grounds worry that the process will run counter to and even harm nature. On this view, the intent "to improve on nature" through reproductive cloning has been considered an overstepping of natural limits, human 'hubris of enormous magnitude.'²

Others note that humanity has been attempting to control nature from the very beginning—agriculture, motorized transportation, medicine all "interfere with nature." Over time, human intervention into nature has been met with both rejoicing and resistance as it is fraught with ambiguity—offering both remarkable good and ruinous

evil. American society has generally accepted that where science can intrude into “the natural order” for good – to improve human life and health, for example – it should do so. Many question the assumption that there is a strong connection between a thing being “natural” and it being “moral.”³ Intrusion into the “natural order of things” is a necessary component of human life. Although humans ought to take responsibility for the impact of their decisions and activity on “the natural order of things,” the fact that cloning technologies intervene in nature in and of itself seems an insufficient reason for prohibition of human reproductive cloning.

A similar argument against human reproductive cloning rests on the premise that the process and its outcome are contrary to God’s will. Reproduction, according to this argument, is solely God’s domain. When we take it upon ourselves to create humans through reproductive cloning, we are infringing on the divine domain, “playing God,” as it were. On this view, finite and fallible beings should not make decisions properly limited to the infinite and infallible. Many religious accounts give humans the responsibility for being caretakers of the rest of creation. The cloning of human beings oversteps the limits of this responsibility and runs counter to the responsibility itself. Furthermore, human beings produced through cloning lack the unique and essential quality of being conceived through love. “With cloning, human life does not arise from an act of love, but is manufactured in the laboratory to preset specifications determined by the desires of others.”⁴ Finally, many religious critics fear that human reproductive cloning will result in the use of cloned humans for personal gain. Respect for human dignity—resident in being created in the image of God—requires that a person be treated as an end in him/herself, not as a means to fulfill the desires or goals of another.

Proponents of reproductive cloning argue that the warning not to ‘play God’ is often invoked in the wake of a scientific development so powerful that it threatens comfortable boundaries of human action.⁵ As NBAC noted,^{6, 7} this slogan is usually called upon as a “moral stop sign” on the basis that: (1) humans ought not be probing the mysteries of life; (2) decisions regarding life’s beginning and ending belong to God; (3) humans are fallible and self-interested; (4) humans have inadequate knowledge of outcomes which God alone possesses; and (5) humans do not have the power to control processes governed by divine omnipotence. Theologian Ted Peters argues,⁸ “The phrase ‘playing God’ has very little cognitive value . . . from the perspective of a theologian.” Peters suggests that in common parlance it has come to mean “stop.” As such, it serves as a red light potentially thwarting not only science but also thoughtful deliberation about the direction and application of research. But it is precisely careful deliberation that is needed in considering potential uses and abuses of cloning technology. Peters and others^{9, 10, 11} would argue that ‘playing God,’ as it were, is precisely what God expects of humanity. Humans are partners—‘co-creators’—with God. As co-creators humans have influence on and take responsibility for the direction in which creation moves and changes—for better or worse. Although there are a wide range of theological positions, it is not necessarily wrong ‘to play God’ in a humble and accountable way. From this perspective, the admonition not to ‘play God’ does well to remind human beings of their fallibility and the importance of considered constraint, but it alone is not sufficient argument for prohibition of human reproductive cloning.

Finally, opponents of human reproductive cloning argue that the consistent polling data reflecting a strong popular will against or repugnance at human reproductive cloning can be viewed as a collective refusal to give substitute or proxy informed consent in behalf of cloned children to be subjected to such experimentation. Similarly, opponents may argue that such public will can be expressive of a widespread desire for societal control of certain aspects of the genetic revolution that "cross the line." Opponents urge that people may not always express their rationale for their revulsion with the same arguments, but that the people 'know it when they see it'. Under this view, human reproductive cloning is obscene technological replication, not protectable procreative liberty.

5. Pragmatic Difficulties with Permitting Some Human Reproductive Cloning Subject to Regulation

Selective regulation is another policy option regarding cloning for reproductive purposes. On its face, regulation may seem more attractive than the alternatives of unrestricted use of reproductive cloning or statutory prohibition. Regulation offers the promise of curbing abuses while allowing the technology to be used in certain circumstances. In addition, those who find prohibition an inappropriate use of governmental power may find regulation more acceptable. To assess the option of regulation, we need to specify what goals regulations are intended to accomplish, what kinds of regulation are envisaged, and what the effects of proposed regulations are likely to be.

The goals of regulation should be to eliminate or reduce problematic cases of reproductive cloning. As discussed previously in this report, some possible uses of reproductive cloning raise more serious and widespread moral concerns than other uses. Many citizens might oppose reproductive cloning in certain situations, but accept it under other circumstances. First, reproductive cloning would be ethically problematic if the clinicians carrying out the procedure did not have appropriate training and skills. Poor quality of care would compromise the safety of the woman who bears the cloned child, as well as the well-being of children who may be born. Second, reproductive cloning would be morally objectionable if the individual who is cloned did not consent to the procedure. Lack of consent would violate the autonomy and liberty of the person to be cloned, undermining his or her right to decide not to have offspring under those circumstances. Third, reproductive cloning would be problematic if extremely large amounts of money were paid for persons with specific phenotypic characteristics to provide nuclear DNA for reproductive cloning. Such payments would commercialize reproduction to the extent that the child is regarded as a commodity to be specified and purchased. These concerns about the quality of care, informed consent, and commercialization might be termed procedural in the sense that they would apply without regard to the circumstances where reproductive cloning was sought.

Another group of moral objections focuses on the reasons motivating reproductive cloning. Examples are reproductive cloning in which the parents have very specific expectations for the phenotype of the child, are planning to exert their utmost parental power to have the child follow their plans, and would be deeply disappointed if the child did not meet their expectations. For instance, a person may desire to achieve so called

"immortality" by producing a child who is genetically identical and has the same personality and occupation. Such cases raise concerns about psychological harm to the particular child because of unrealistic and excessive parental pressures. Also such cases are troubling because they involve physicians in activities that are inconsistent with important societal values. Such values include allowing children to fulfill their individuality rather than cherishing them only to the extent that they conform to parental expectations. This latter set of objections might be termed substantive.

From a regulatory perspective, the challenge is to try to devise regulations that would discourage or reduce these situations that raise procedural or substantive concerns. What kinds of regulations might be proposed? To address the first set of procedural concerns, regulations might require licensing of facilities, certification of practitioners, reporting of outcomes, informed consent from of all parties involved in reproductive cloning (including the donor(s) of nuclear DNA material, the egg donor, and the gestational mother), and limits on excessive payments for eggs and nuclear DNA materials. Such regulations would help to ensure the quality of services and appropriate informed consent. These kinds of regulations are in place and are widely accepted for other medical procedures.

To address the second class of substantive concerns, regulations might require clinicians engaged in reproductive cloning to take some steps to discourage cases in which parents will prize the child only to the extent that it fulfills their specific expectations. At a minimum, practitioners might be required to educate and counsel patients seeking reproductive cloning about the concerns raised about this method of reproduction, particularly concerns about excessive parental expectations for the child. This requirement would help ensure that decisions for reproductive cloning are truly informed and would increase the likelihood that children born of this technology would have opportunities to shape their own futures. However, education and counseling leave it to the parents to decide whether to continue to seek cloning for these purposes. Such regulations for education and counseling would be similar to current mandates for physicians to counsel patients before obtaining genetic testing or prenatal testing for birth defects.

Other regulations might go even further, to require clinicians to discourage reproductive cloning if parents desire a child with predetermined phenotypic characteristics. Furthermore, regulations might explicitly allow clinicians to decline to participate in cases of reproductive cloning in which, in their judgment, parents will try strenuously to foreclose the child's options that are incompatible with their expectations. Under regulations to discourage instances of excessive parental expectations, practitioners would evaluate the intention and motive of those seeking reproductive cloning. There is some precedent for clinicians making recommendations regarding specific reproductive decisions in requirements for physicians to recommend or obtain prenatal testing for syphilis, rubella immunity, Rh incompatibility, and HIV infection. However, having third parties evaluate the motives for reproductive decisions raises its own set of ethical problems, as we next discuss.

Well-intentioned regulations may be problematic because they are inefficient or have unacceptable burdens and unintended consequences. Regulations to discourage

cases of excessive parental control may be inefficient in several ways. They may be overly broad to achieve their goal, because in many cases the feared harms will not occur. Parents who at the onset seek to produce a child with certain specified characteristics may change their minds and love the child as a unique individual as the child develops its own characteristics. As with children born through sexual reproduction, parents are likely to learn through experience that children usually develop their own interests and characteristics, despite parents' expectations and upbringing. At the same time, regulations to discourage cases of excessive parental control may also be too narrow to achieve their goal. It is possible that parents who at the onset say that they will cherish their child no matter how he or she turns out may react differently when they see a child who cannot be distinguished physically from an existing individual. Faced with this close resemblance, parents may develop strong expectations that they could not predict and therefore did not discuss during prenatal counseling. Moreover, if the goal is to moderate excessive parental control and expectations, regulations dealing with reproductive cloning will miss the far greater number of cases in which parents have excessive expectations for children conceived through sexual reproduction or other forms of assisted reproduction.

It is possible by regulation to try to restrict access to reproductive cloning solely to couples who are infertile or at some genetic risk. These would be parents whose reasons for seeking to clone would not revolve around seeking a genetic duplicate for a pre-existing person. At least two of the witnesses before the Committee, Professor John Robertson and Dr. Glenn McGee, argued for such systems. However, there is no guarantee that access would be so carefully controlled. Potential broad based use of reproductive cloning raises concern among many that market forces, genetic determinism, and undue emphasis on genetic relatedness could be unintended consequences.

In addition, regulations designed to discourage or prevent most morally troubling cases of reproductive cloning may have detrimental consequences. First, such regulations may be burdensome and invade privacy, whether implemented by physicians or in a legal setting. When physicians currently discuss with patients reproductive decisions, they are usually non-directive in the sense that the physician lays out options, points out issues for the patients to consider, but leaves the final decision to them. If clinicians seek to discourage certain types of reproductive cloning, discussions would be directive. However, it is troubling if physicians evaluate the motives and intentions of persons making reproductive decisions and seek to discourage certain decisions. Reproductive decisions are personal and private. Persons engaging in sexual reproduction are not asked to justify their intentions. Many would consider it disrespectful and intrusive - an invasion of privacy -- to ask people to justify their reasons for such personal decisions. Furthermore, there is the risk that because of the power imbalance in the doctor-patient relationship, physicians and counselors may impose their own personal values about parenting onto patients who do not share their view. Moreover, it is difficult to specify precisely every situation of unacceptable reproductive cloning. Such vagueness in classifying acceptable and unacceptable actions may give physicians so much discretion that their recommendations are arbitrary and unfair. Forced to determine the acceptability of unusual cases, with no precedents to turn to, physicians may fall back on their own personal values. These values may be

controversial to others. For instance, some clinicians may want to restrict reproductive cloning to parents who are married or whose general values correspond to their own. Limiting access to medical services solely on the basis of personal beliefs, however, is difficult to justify as good public policy or an acceptable component of professional standards.

The decision whether to allow reproductive cloning could be placed in the hands of a governmental body, something akin to a licensing board or a family court. (Dr. McGee argued that the process could be made akin to judicial adoption procedures.) Taking the decisive role away from the physician mitigates some concerns, but not all. The grounds on which a governmental body would decide who could or could not have children through cloning would likely remain both vague and subject to “gaming” by eager parents. And citizens may be particularly reluctant to set a precedent of having reproductive decisions made by the government or made under governmentally-sanctioned standards for “appropriate” reproductive decisions.

Another problem is that substantive regulations may be ineffective and have unintended adverse consequences. Knowing that certain “reasons” for reproductive cloning are considered unacceptable, patients who are eager to use it for these purposes may misrepresent their reasons in order to gain access to the technology. Since such misrepresentation would be extremely difficult to detect, the regulations may not have their intended goal of discouraging reproductive cloning for more morally troubling reasons. In the long run, then, regulations may not achieve their desired goals but may lead to cynicism as well as intrusion into private matters.

In light of these difficulties, people will disagree over the desirability of regulation of reproductive cloning. These disagreements need to be considered in the context of specific types of regulations that might be envisaged. Procedural regulations regarding quality of care and informed consent raise few objections. Some citizens will believe that such procedural regulations provide adequate protection with acceptable burdens and side effects. Others who are concerned about abuses of reproductive cloning might consider additional substantive regulations. While some may judge substantive regulations desirable, others may reject them because they are ineffective or have unacceptable side effects. Persons who reject substantive regulations face a dilemma: is it preferable to prohibit reproductive cloning altogether or to permit it with only procedural regulations. The decision hinges on whether it is considered better to allow reproductive cloning, accepting that some persons will seek it for morally troubling reasons, or to prohibit reproductive cloning, accepting that persons will not be able to obtain it for reasons that many would find acceptable. Faced with this dilemma, some persons might reasonably conclude that the abuses of reproductive cloning would be so frequent and egregious as to justify a ban on reproductive cloning. Others would argue that the harms of regulated reproductive cloning are acceptable and do not justify such a restriction on reproductive rights.

Given the depth and breadth of concerns expressed both locally and globally, it is important to exercise caution when considering regulation of reproductive uses of human cloning technology. Even if a compelling argument is made in a particular case, it does not necessarily follow that reproductive cloning is justified or desirable in general.

6. A Political Argument

One thing that is clear about human reproductive cloning is that most Americans, and most Californians, oppose it. The survey results vary according to how the question is asked, but they consistently show large majorities against human reproductive cloning. One could argue that the popular will, even if it did not have a compelling basis, may be sufficient for a law banning cloning. Some people might conclude, now or at some point after the physical safety of cloning had been demonstrated, that the arguments against cloning are not very strong. If no substantial rights are being infringed, a government might ban things solely because its citizens do not like them. This might be the case at the local level, for example, with some zoning regulations that dictate the aesthetic attributes of a neighborhood. California state law may provide another example. In 1998, California, by referendum, banned the sale of horse meat for human consumption. The arguments for banning horse meat seemed mainly to have been a popular prejudice in favor of horses, but the ‘right’ of people to eat horsemeat seemed weak. One might view human reproductive cloning similarly and so believe that, in light of weak arguments in favor of human reproductive cloning, the public’s preferences should be respected.

This position seems unlikely to be popular. Proponents of reproductive cloning will insist that reproduction, through cloning or otherwise, *does* involve important interests and should not be prohibited without good reason. Most opponents of reproductive cloning will be confident that there are good reasons for a ban. But for those without confidence in either side’s arguments, a decision to ban human reproductive cloning based purely on public preference may be justifiable.

C. OUR CONCLUSIONS

The Committee believes that California should ban human reproductive cloning. Every Committee member finds the safety concerns about human reproductive cloning compelling and would forbid the technology unless or until it were shown safe. We all also accept some of the other arguments against human reproductive cloning, though different members of the Committee find different arguments persuasive. We recognize that both the science of human reproductive cloning and the ethical discussions concerning it are likely to change in coming years. These considerations led some members to consider another moratorium, banning reproductive cloning for another period of years. Ultimately, we concluded that the Legislature should pass, and the Governor should sign, a flat ban with no expiration date. A subsequent Legislature and Governor could, of course, allow human reproductive cloning based on new information or changed views. We concluded that, with this technology, the burden of going forward should fall to those who seek to convince the State to make such a change.

III. CALIFORNIA SHOULD NOT PROHIBIT BUT SHOULD REASONABLY REGULATE HUMAN NON-REPRODUCTIVE CLONING

RECOMMENDATION

The Committee unanimously agrees that California should not prohibit but should reasonably regulate human non-reproductive cloning. We believe that use of this technology offers potential medical and scientific benefits while not raising many of the same concerns as human reproductive cloning. Such uses might include cloning technology as a source of human stem cells that would not be rejected by a patient's immune system. California should regulate all human non-reproductive cloning in the State, public or private. That regulation should do at least three things: a) prohibit the use of pre-embryos after development of the primitive streak, b) ensure that the persons providing cells for this purpose gave informed consent, and c) require that the research be permitted by an approved Institutional Review Board ("IRB").*

We define non-reproductive human cloning as the transfer of human cell nuclei into enucleated oocytes to produce human pre-embryos without implanting the pre-embryos to produce a human child. Such a process would likely be used to create early pre-embryos to be used as sources of embryonic stem cells. As set out below, we would limit the use of such pre-embryos to the period before the appearance in the pre-embryo of the so-called primitive streak, which occurs 14 to 18 days after the pre-embryo's creation. This developmental stage has also been termed the blastocyst or pre-embryo. 1, 2

Human embryonic development is a complicated process. 3 The current scientific description of this process defines its terms carefully. The term "pre-embryo" is used to refer to an entity in a stage of development that begins after fertilization and ends approximately 14 days later with the appearance of the primitive streak. 4 The primitive streak is a band of cells at the caudal, or "tail," end of the embryonic disc from which the embryo develops. Its appearance is a crucial step in the development of an organism out of the sphere that is the pre-embryo. At the time the primitive streak appears, the pre-embryo is about one millimeter in size, roughly the size of the dot on the letter "i" in this text. If inserted in a uterus, it would rarely result in a live birth.

Various committees, in the United States and elsewhere, that have studied embryo research have concluded that the appearance of the primitive streak marks an important step in the moral status of the pre-embryo, and hence, the ethical arguments concerning pre-embryo research. Only about 40 percent of fertilized eggs ever reach the primitive streak stage. 5 Before the appearance of the primitive streak, the pre-embryo is not necessarily one individual – it could lead to identical twins. The development of a nervous system and any possibility of feeling sensations comes much later than the appearance of the primitive streak. For these reasons, many such committees have suggested limiting embryonic research to about 14 days or the appearance of the

* One Committee member, Francis Pizzulli, would go further in stipulating the substance of IRB review. His views on this point are set out separately at page 49.

primitive streak. For example, in 1994, the Human Embryo Research Panel of the NIH recommended that federal funding of embryo research be allowed under three conditions: (1) that the pre-embryos were less than 14 days old; (2) that the information which was sought could not be obtained by studies performed with animal embryos or other experimental designs; and, (3) that scientists could demonstrate a compelling reason for performing the studies. 6 These conditions have to be demonstrated to a committee for the protection of human research subjects (Institutional Review Boards), meeting the requirements of federal regulations.

The remainder of this section of our report discusses arguments for human non-reproductive cloning, then arguments against it, before discussing the Committee's conclusions. The arguments are generally summarized with their counter-arguments.

A. ARGUMENTS IN FAVOR OF HUMAN NON-REPRODUCTIVE CLONING

1. General Benefits to Human Health and Medicine

The arguments in favor of human non-reproductive cloning are scientifically complicated but, as matters of policy, quite simple. Research using this technique holds substantial promise of preventing and alleviating human disease, disability, and premature death. Non-reproductive cloning technology might be able to create populations of functional new cells to replace those damaged through wear and tear or disease. Undifferentiated human pluripotent stem cells obtained from donated pre-embryos have been coaxed into becoming neurons, liver cells and heart muscle cells, all of which appear to function normally *in vitro*. In light of these potential benefits, NBAC recommended that research on embryonic stem cells continue and be eligible for federal funding.

The possible uses of cloning technology to produce stem cells are numerous and varied. Such non-reproductive cloning could be used for basic research into human embryology and reproductive biology. The following are examples of this kind of research:

- o Increasing knowledge about embryogenesis, i.e., embryo formation, and the development of birth defects
- o Developing a better understanding of the biology of human implantation
- o Understanding better the causes of spontaneous abortion
- o Developing more effective or simpler forms of contraception
- o Improving methods of in vitro fertilization (IVF) treatment for both male and female infertility
- o Developing pre-embryo biopsy and sampling techniques for pre-implantation diagnosis of genetic or chromosomal abnormalities

Improved understanding of these processes might have benefits in preventing birth defects and in aiding, or preventing, pregnancy.

2. Avoiding Immune Responses to Transplanted Tissue

A second and more discussed area of use of non-reproductive human cloning involves cloning in conjunction with the use of human embryonic stem cells. The science behind human embryonic stem cells was discussed briefly in the background section, above. Its promise is immense, although still speculative. But if (1) embryonic stem cells can produce cells and tissues useful in medical therapy, but (2) those cells or tissues trigger an immune response in the patient, then (3) the use of human non-reproductive cloning to produce stem cells with the patient's own DNA might avoid that immune response. Any or all of those steps may not occur. Alternatively, other cells, such as adult stem cells, or other processes, such as transferring the patient's DNA into an embryonic stem cell rather than into an enucleated egg, might avoid any need for human non-reproductive cloning. Nonetheless, at this point such cloning looks like it may be very important to the usefulness of potential stem cell therapies.

As important as it is to consider questions of the extent of moral respect due to the human pre-embryo, proponents of non-reproductive cloning claim that the potential benefits of stem cell technologies make it equally important to consider the cost of not using embryonic cells. If someone suffers a life threatening illness and dies because nothing can be done, there is no moral culpability. If, however, the development of life sustaining therapy and treatment is restricted, then proponents of human non-reproductive cloning might argue that those members of the public who support such constraints bear some responsibility for those patients they have determined not to help.

Opponents of human non-reproductive cloning do not deny its potential scientific and medical benefits, although they do point out, quite accurately, that many of those benefits are speculative and, if they emerge at all, will not appear soon. Instead, they generally urge that the same or similar benefits could be obtained from using cells that do not require the destruction of pre-embryos, such as adult multi-potent stem cells. The value of those cells, however, is at least as uncertain as the value of cells created by human non-reproductive cloning. 1, 2

B. ARGUMENTS AGAINST HUMAN NON-REPRODUCTIVE CLONING

At least four arguments can be made against human non-reproductive cloning. Most of them are the same as more general arguments against the creation or use of human pre-embryos and embryos in research. To the extent human non-reproductive cloning is used in such research, it is necessarily subject to those arguments. One argument, however, applies only to non-reproductive human cloning and not to other research with created pre-embryos. We discuss that argument first.

1. Human Non-Reproductive Cloning Will Lead to Human Reproductive Cloning

Many people are concerned not so much with the beneficent use of pluripotent stem cells to treat and cure disease but of the potential abuses of this technology. Such an argument was expressed by Judy Norsigian, Executive Director of the Boston Women's Health Book Collective, in her testimony to the House Committee on energy and

Commerce regarding the Human Cloning Prohibition Act of 2001 on June 20, 2001. ‘While we do not oppose the use of human embryos for valid medical research, including their use to generate embryonic stem cells, we do oppose the creation of clonal human embryos. To allow this procedure would make it all but impossible to enforce the ban on the creation of fully formed human clones. Further, it would open the door to other, more profound forms of human genetic manipulation.’”

This is a form of slippery slope argument that suggests that taking the initial step (in this case, allowing the creation of pre-embryos for research including the development of cells and tissues for transplant) necessarily results in an action determined to be wrong (in this case, the use of human cloning to produce a child). Because a possible outcome or application is wrong, the argument goes, the first step ought not to be taken. One could argue that human non-reproductive cloning could lead to reproductive cloning in two quite different ways; it is not clear that either path is plausible.

One argument is that the presence of cloned human pre-embryos in research laboratories will make it substantially easier for someone to attempt reproductive cloning – the cloned pre-embryos will already have been created. If viable human pre-embryos can be created by nuclear transfer cloning – an as-yet unanswered question – that process seems unlikely to prove difficult. The ability to ‘harvest’ eggs exists at hundreds of IVF clinics around the country; the nuclear transfer step, though not efficient, seems unlikely to be difficult to learn. In any event, those who seek to have a cloned baby are likely to want a clone of a particular person and not any cloned pre-embryo found in a laboratory.

In addition, reproductive cloning requires that cloned pre-embryos be implanted into willing gestational mothers. The difficult steps are likely to be finding those willing gestational mothers and performing the implantation successfully. Research on pre-embryos before the primitive streak forms would provide little guidance to would-be reproductive cloners on whether such cloned pre-embryos would develop to term and how best to implant. Regulation of reproductive cloning arguably could focus more easily on recruitment of gestational mothers and implantation rather than on creation of cloned pre-embryos.

The slippery slope argument has a second variation. One could argue that human non-reproductive cloning would make reproductive cloning more likely by making the public accustomed to, and accepting of, the idea of human cloning. For this argument to be true, people would need not to distinguish strongly between the creation of pre-embryos and the creation of babies. Although some people, notably those who believe the strong form of the moral status of pre-embryos, do equate the two, it seems unlikely that most people will. Public acceptance of non-reproductive cloning used to make liver or heart cells seems to us unlikely to breed public acceptance of cloned babies.

2. The Moral Status of the Pre-Embryo

The developments in nuclear transfer and stem cell technologies outlined above have sparked hope that new effective therapies will become available to treat human disease and relieve suffering. However, they have also raised deep ethical and religious

concerns inherent in research with human pre-embryos and cadaveric fetal tissue. 1. 2 These concerns center on the moral status of the persons, or objects, created by human non-reproductive cloning. The arguments come in both a strong form, which considers the pre-embryo itself entitled to full human rights and hence cannot be created for the purposes of research, and a weaker form, which holds that it is entitled to some more limited respect.

Edmund Pellegrino, in testimony to NBAC regarding the derivation and use of human embryonic stem cells, nicely summarized the core claims of the strong argument from the pre-embryo's moral status.

. . . [H]uman life is a continuum from the one-cell stage to death. At every stage, human life has dignity and merits protection.

. . . [T]he embryo would be treated as a means to an end. Its inherent moral status is violated because it must be killed in order to obtain stem cells. There is no moral or legal basis for subjecting any member of the human species to harm or death in non-therapeutic research based on prediction that it will die anyway, no matter how certain that prediction might be. 3

This perspective is based on the acceptance of the status of the human pre-embryo as a fully human person. On this view, which grants the pre-embryo moral status equivalent to that of an infant or adult, the full moral rights and protections of personhood are bestowed at the moment of conception. Therefore, any procedure which results in direct harm to the pre-embryo may not be undertaken even in pursuit of a good end for someone else. This concern has two parts. First, using the pre-embryo as a means to benefit others is wrong in itself; second, the pre-embryo's informed consent is not, and cannot be, obtained. Both violate human dignity. Nonetheless, many who hold this view seemingly recognize the promise of stem cell research as Pellegrino indicates:

The Commission should instead [of legitimizing embryonic stem cell research] strongly encourage the funding and development of alternative sources of stem cells—those that do not depend on the destruction of living human embryos or make use of cells from induced abortions. In light of the rapid developments in this field, the possibility and probability of the development of morally acceptable sources of stem cells is a reality. 4

The argument from the weaker moral status of the pre-embryo differs from the full personhood view just described. This developmental view of moral status posits that an individual acquires interests, rights, and roles incrementally as his or her development of sentience, consciousness and relationships justifies these safeguards. Based on the developmental continuum from pre-embryo to adult and the “symbolic” value of pre-embryos as human “beginnings,” the human pre-embryo deserves “profound respect” but not the protections associated with full personhood. This position could also lead to arguments against human non-reproductive cloning, but has more often been used to support such research. 5

Arguing that human pre-embryos are alive and are valued, Meyer and Nelson 6 have suggested that while the human pre-embryo commands “minimal but real” respect and cannot, for example, be considered property, its destruction need not display disrespect. Their account grants that human pre-embryos deserve respect in all circumstances, even when destroyed for good reasons. Examples of restrictions on the treatment of pre-embryos that would demonstrate such respect include the use of pre-embryos only if the research goals cannot otherwise be obtained and only if the pre-embryo is less than 14 days old.

Discerning the moral status of human pre-embryos is a matter of profound perplexity and debate. David H. Smith 7 opines that, "The fact is we really don't know what they are, and our obligations are indeterminate. We are in a new territory, collectively feeling our way." In such an atmosphere of ambiguity and potential benefit, it appears appropriate to try to work out incrementally and with great care the kinds of pluripotent stem cell research that are morally justified. 8

3. Protection of Egg Donors

If donated human eggs are needed to create cloned pre-embryos, research and clinical success of human non-reproductive cloning will necessarily increase demand for such eggs – and increase the pressures on women to provide them. Egg donation is not an entirely benign process. It requires the use of ovulation producing drugs and entails specific rates of super-ovulation. The egg retrieval procedure bears a significant set of risks. In return, the donors would receive no personal health or monetary benefits from a potentially harmful procedure used to benefit others. 1

The donor’s informed consent is also a concern. Some women are vulnerable to pressures to participate in research or to help the infertile. There is reason to believe that egg donation has already been subject to abuse by the assisted reproduction industry. 2 Payments have been made that exceed compensation for the costs of participation and actually amount to payment for the egg itself. This commercialization does not respect the participants in the process. As Cynthia Cohen 3 notes: "It takes little imagination to foresee the primary means for getting women to provide eggs for the purposes of [non-reproductive cloning] will have to involve coercion of those in the process of attempting to have children by means of the new reproductive technologies." To avoid economic and other forms of coercion, there should be safeguards for the well-being and freedom of choice of the women providing eggs.

4. Distributive Justice

The last argument revolves around access to the fruits of human non-reproductive cloning. It can be argued that justice requires society to ensure that the benefits of medical science be distributed fairly with particular attention paid to those consistently marginalized by the health care system. The benefits of the regenerative medicine that non-reproductive cloning makes possible should not further polarize health status and access to care. In her testimony to this Committee, Patricia Baird spoke of the "seventh generation rule" which is applicable here—decisions are to be made not solely based on

immediate gratification but with concern for the costs and benefits accrued for children and seven generations to come. 1

C. OUR CONCLUSIONS

We believe that the enormous medical promise of stem cells to relieve human suffering makes a compelling ethical case for the pursuit of many lines of research. Human non-reproductive cloning, which might prove essential to effective stem cell therapy, is one such line of research. The moral scale weighing harms to a limited number of pre-embryos on one side against potentially hundreds of thousands of affected and clearly morally significant humans, on the other hand, can, it seems to us, justify the use of pre-embryos in this work. To ban such research would, to many of us, be itself unethical.

On the other hand, there are appropriate concerns about this kind of research. We believe, therefore, that California should regulate the use of human non-reproductive cloning. In particular, it should take steps to ensure that all such research done in California, whether publicly or privately funded, be approved by appropriate Institutional Review Boards or their equivalents. It should require that the egg donors, and the donors of the cells whose nuclei are transplanted, give real and appropriate informed consent. And, from a sense of caution about the moral status of the pre-embryo, we join other groups in recommending that such research be limited to pre-embryos in which the primitive streak, an essential early sign of development, is not yet present.

IV. IMPLEMENTATION ISSUES

RECOMMENDATIONS

In banning or regulating human cloning, California may be affected by actions of the federal government. Federal regulation needs to be watched carefully to ensure that California's actions are both necessary and appropriate. . The actions of other states, which might provide experience useful to the California regulatory plan, should also be watched.

Regulating a scientific field undergoing rapid change is difficult for a legislature. The California Legislature should define the terms of its prohibition on human reproductive cloning carefully and its regulation of human non-reproductive cloning carefully but broadly. It should delegate the implementation, including further definition, of that regulation to a state agency.

The Committee strongly believes that California will increasingly face complex challenges arising from genetic and reproductive technologies. "Cloning" by embryo-splitting is one of many such technologies. We recommend that California establish an on-going mechanism to advise the Governor and the Legislature on this and related issues of human biotechnology.

The Committee's discussions raised several questions concerning how California should implement a policy about human cloning. These questions have led to three recommendations.

A. ISSUES OF FEDERALISM

The federal government has not yet acted to prohibit human reproductive cloning, although the FDA has asserted jurisdiction over it. Federal actions might make legislation by California unnecessary or even, under the Supremacy Clause of the Constitution, invalid. California should watch federal legislation and regulation carefully and take it into account in its own actions.

If the federal government were to ban reproductive cloning, a similar action by California would probably be unnecessary. Such legislation could still have some benefits. It is possible that federal legislation prohibiting reproductive cloning might be held invalid as beyond the powers granted Congress by the Constitution's Commerce Clause. In that event California legislation could be effective when federal legislation was not. It is conceivable, though very unlikely, that federal legislation could be invalidated on the grounds that it violates a federal constitutional right to clone. In that case, similar legislation by California would almost certainly be similarly invalid.

If the FDA's jurisdiction over human reproductive cloning under its existing authorizing statutes were upheld, or if Congress expressly gave the FDA that authority, the need for California to act would be diminished. It might not, however, disappear. The FDA would regulate human reproductive cloning with respect to safety. If

California believed that even safe reproductive cloning should be banned, it might want to enact restrictive legislation since the FDA in such a scenario, would legally have to allow reproductive cloning if proven safe.

If the Congress bans human non-reproductive cloning, California would not be able to permit that procedure. If Congress merely regulates such cloning, California might be able to add further regulatory requirements, depending on whether the federal statute preempted state law. It might be, of course, that such federal regulation would cover all the issues of concern to the State, in which case California legislation might be unnecessary.

B. ISSUES OF DEFINITION AND ADMINISTRATION

All regulation of human cloning requires a definition of the procedure to be regulated. Existing statutes and proposed legislation have used differing, and in ways inadequate, definitions of human cloning. Some have even argued that the definition in the existing California statute, the best of those in current use, is ambiguous. Advocates for assisted reproduction have argued that it prohibits the transplantation of the nucleus of a human oocyte that would later be fertilized by sperm, thus giving rise to an embryo with the conventional two parents. It can be argued that the definition does not include this procedure. In any event, as the sanctions in the existing statute are imposed almost exclusively by the State Department of Health Services, concerned researchers or assisted reproduction clinicians could have, but did not, seek an interpretation of the language from that Department. In spite of the weaknesses of their arguments, they illustrate the challenges of clear definition.

There are two main problems in defining human cloning. First, legislatures often lack the scientific expertise needed to write an accurate definition. A number of bills introduced in American states used definitions that were scientifically inaccurate or meaningless. Second, the technology may change more rapidly than the definition. For example, 1990 British legislation banned “human cloning” but defined it in a way that did not include the Dolly procedure. As another example, existing definitions, including California’s, talk about the transplantation of a donor cell’s nucleus into a human oocyte. It might be possible, however, to clone a human through transplantation of a nucleus into a human embryonic cell or even a non-human oocyte. Neither would be covered by existing legislation.

Instead of seeking to write an exact definition into the statute, the Legislature should write a broad definition and invest a state agency with the duty of writing, and, when necessary, revising, specific definitions. For example, a legislative definition might read as follows:

Human reproductive cloning is defined as the creation of a human fetus that is substantially genetically identical to a previously-born human being. The use in humans of somatic cell nuclear transfer with a donor cell from an adult, as used in the creation of Dolly, is an example of such cloning. The Department of Health Services shall have the power to write and interpret regulations defining more

precisely the procedures that consist human reproductive cloning for the purposes of this statute.

With this kind of a definition the administrative agency could have, or acquire, scientific advice on a proper definition. It could also change or interpret the definition to keep pace with changing technology much more rapidly and easily than the Legislature.

C. CONFRONTING NEW ISSUES ARISING FROM BIOTECHNOLOGY

The Committee was given a relatively narrow mandate – to make recommendations about state policy on human cloning. Even that mandate, however, led to some difficult new issues. The most troublesome for the Committee was “cloning” by embryo-splitting (also known as “blastomere-separation”).

Embryos can split at an early stage to produce two (or, rarely, more) people who are genetically identical. This is the source of human identical twins, who make up about one birth in every 240. Although there has been very little research into artificial embryo-splitting in humans, there seems to be no substantial barrier to splitting embryos that are created through *in vitro* fertilization. In essence, this process would create additional identical twins. In the normal course of events, none of the twins would be identical to anyone who had been alive before; each would have a copy of a new genome. This mitigates substantially many of the arguments against human reproductive cloning.

Embryo splitting is not addressed by the existing California legislation on cloning, nor did the Committee believe that it was clearly within our mandate. Embryo splitting, however, can raise issues similar to those arising from human reproductive cloning by nuclear transfer and addressed above. The first important issues are those of physical safety. A review of the results of research on this process with other mammalian species would be important.

A second cluster of issues arises from the potential use of embryo-splitting to have a “delayed” twin. One or more embryos created by this splitting could be frozen for a period of time, later to be removed from cryopreservation and implanted into a woman. This might occur weeks or years after the first embryo is implanted and brought to term. The latter twin would have a genotype that has already come into existence. The parents (or others) could wait and see whether they wanted another copy of the first child, producing many of the concerns of nuclear transfer cloning.

On the other hand, this is only a concern if some of the split embryos are frozen for a significant period of time. Embryo splitting and implantations only a short time apart (*e.g.*, months) would look more like the case of naturally-occurring identical twins. Whether, for example, 5 or 10 year birth separations are sufficient to trigger the same kinds of psychological risks as reproductive cloning from a mature adult requires a more discriminating analysis. Similarly, the use of embryo-splitting to have a delayed twin as a source of replacement tissue or nonessential organs for the first child also implicates the commodification of children and abuse arguments addressed above.

The Committee was not charged with making recommendations on embryo-splitting, and thus did not solicit witnesses on the topic. Nevertheless, in light of the overlapping issues and arguments, the Committee believes further evaluation of these issues, by someone, is appropriate. This appears to the Committee to be a perfect example of the kinds of complicated issues that human biotechnology will raise for state governments. Currently, the Legislature and the Governor have few ways to get expert advice on such issues. This Committee is an exception, not the rule.

We strongly recommend that California establish some kind of mechanism to provide expert advice to the government on such issues. Such a group would require some modest funding and staff. It should, however, prove invaluable in helping the State come to grips with the new dilemmas posed by rapid advances in our understanding of human biology. Not only would this enable California to play its historic role as a leading state “laboratory of democracy,” in the words of Justice Louis Brandeis, but, more importantly, it would increase its ability to protect its citizens from dangerous or unwise applications of our new scientific knowledge of human biology.

SEPARATE STATEMENT OF FRANCIS C. PIZZULLI

I believe Recommendations Nos. 2 and 4 should go significantly further. They should (1) suggest the scope of an enforcement agency, particularly for non-federally funded entities that are not deterred by IRB disapproval and consequent loss of federal funding; (2) recommend directing the agency having jurisdiction over public and private research to promulgate regulations for the approved IRBs: (a) to identify possible risk/benefit criteria supplemental to federal IRB regulations (which do not address human non-reproductive cloning), especially as there is more than minimal risk to women donating eggs, *e.g.*, (i) the progress of work to derive stem cells from nuclear transfer in primates and other species; (ii) the status of alternative approaches to solving the immune response issue in cell replacement therapy (*e.g.*, via adult stem cells or histocompatibility reprogramming techniques on embryonic stem cells); (iii) the criteria proposed by the 1994 NIH Human Embryo Research Panel (discussed above) (*e.g.*, the information sought could not be obtained by other means and the proponent demonstrates a compelling reason for the research of outstanding scientific value); (iv) security controls; and (b) to implement centralized oversight as appropriate, such as is found in NIH's Recombinant DNA Advisory Committee (RAC) and Human Pluripotent Stem Cell Review Group (both of which provide for some public access). Reasonable regulation under the above criteria neither mandates immediate approval nor precludes the possibility that technological developments will obviate the demand for this technique for cell replacement therapy.

The bipartisan approach to the public oversight of cloning – as exemplified by the overwhelming passage of S.B. 1344 led by genetics policy expert Patrick Johnston (D-Sacramento) and Jim Battin (R-La Quinta) -- teaches that what Leon Kass and Daniel Callahan refer to as the opening act of a long debate over a genetics “revolution” need not be based on traditional divides. As Lori Andrews points out, both new and old analytical concepts and values may be invoked in the debate, ranging from child abuse and incest laws, to genetic bondage and constitutional antipathy to caste systems and titles of nobility, as well as questions of who merits “merit” in a world of genetic enhancements.

Public trust in an effective oversight system, state or federal, will redound to the benefit of the regulated sector in addressing the citizenry's fears of a brave new world being fabricated without its informed consent.

APPENDIX TWO THE CALIFORNIA STATUTE

California's statute concerning human cloning was enacted in 1997 by legislation known as Senate Bill 1344, found in Stats. 1997 chapter 688. That legislation has been codified into six sections of the California Codes, plus an introductory note. The codified version of the statute follows.

HEALTH AND SAFETY CODE DIVISION 20. Miscellaneous Health and Safety Provisions CHAPTER 1.4. Human Cloning

Codified as a note before § 24185

Stats 1997 ch 688 provides:

SECTION 1. It is the intent of the Legislature to place a five-year moratorium on the cloning of an entire human being in order to evaluate the profound medical, ethical, and social implications that such a possibility raises. It is not the intent of the Legislature that this moratorium apply to the cloning of human cells, human tissue, or human organs that would not result in the replication of an entire human being. During this moratorium period, the State Director of Health Services should be called upon to establish a panel of representatives from the fields of medicine, religion, biotechnology, genetics, law, bioethics, and the general public to evaluate those implications, review public policy, and advise the Legislature and the Governor in this area.

§ 24185. (Operative until January 1, 2003)

Cloning proscribed

- (a) No person shall clone a human being.
- (b) No person shall purchase or sell an ovum, zygote, embryo, or fetus for the purpose of cloning a human being.
- (c) For purposes of this section, "clone" means the practice of creating or attempting to create a human being by transferring the nucleus from a human cell from whatever source into a human egg cell from which the nucleus has been removed for the purpose of, or to implant, the resulting product to initiate a pregnancy that could result in the birth of a human being.

§ 24187. (Operative until January 1, 2003)

Administrative penalties

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

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

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

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

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

§ 24189. (Operative until January 1, 2003)

Repeal

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

BUSINESS & PROFESSIONS CODE

DIVISION 2. Healing Arts

CHAPTER 5. Medicine

ARTICLE 12. Enforcement

§ 2260.5. (Operative until January 1, 2003)

Cloning violation

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

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

§ 16004. (Operative until January 1, 2003)

Cloning violation

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

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

§ 16105. (Operative until January 1, 2003)

Cloning violation

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

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

APPENDIX ONE
MEMBERS OF THE ADVISORY COMMITTEE ON HUMAN CLONING

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Appendix Three
Advisory Committee on Human Cloning
Agenda of Meetings

DEPARTMENT OF HEALTH SERVICES
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ADVISORY COMMITTEE ON HUMAN CLONING
AUGUST 20, 1999 MEETING

1350 Front Street, Auditorium
San Diego, CA

The topic to be addressed at this meeting is the ethical and societal implications of human cloning.

AGENDA

- 10:00 am Introductions and Procedural Items
- 10:20 am James Walters, Ph.D., Professor of Christian Ethics, Loma Linda University
- 10:40 am Committee Questions
- 11:00 am Karen Lebacqz, Ph.D., Robert Gordon Sproul Professor of Theological Ethics, Pacific School of Religion
- 11:40 am Committee Questions
- Noon LUNCH
- 1:30 pm Paul Billings, M.D., Ph.D., Geneticist, Chief Medical Officer, Texas Department of Veterans Affairs
- 1:50 pm Committee Questions
- 2:10 pm Public Presentations
- 3:20 pm Committee - Discussion - Next meeting agenda
- 4:00 pm Adjourn

Present: M. McLean, B. Lo, H. Greely, T. Trotter, L. Shapiro, D. Gollaher, B. Lubin, R. Hoag, T. Friedmann, F. Pizzulli, G. Cunningham
Absent: R. Rao, F. Coeytaux

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ADVISORY COMMITTEE ON HUMAN CLONING
MEETING, AUGUST 20, 1999
1350 FRONT STREET, AUDITORIUM
SAN DIEGO, CALIFORNIA

The topic to be addressed at this meeting is the ethical and societal implications of human cloning.

AGENDA

- 10:00 am Introductions and Procedural Items
- 10:20 am James Walters, Ph.D., Professor of Christian Ethics, Loma Linda University
- 10:40 am Committee Questions
- 11:00 am Karen Lebacqz, Ph.D., Robert Gordon Sproul Professor of Theological Ethics, Pacific School of Religion
- 11:40 am Committee Questions
- Noon LUNCH
- 1:30 pm Paul Billings, M.D., Ph.D., Geneticist, Chief Medical Officer, Texas Department of Veterans Affairs
- 1:50 pm Committee Questions
- 2:10 pm Public Presentations
- 3:20 pm Committee - Discussion - Next meeting agenda
- 4:00 pm Adjourn

Present: M. McLean, B. Lo, H. Greely, T. Trotter, L. Shapiro, D. Gollaher, B. Lubin, R. Hoag, T. Friedmann, F. Pizzulli, G. Cunningham

Absent: R. Rao, F. Coeytaux

DEPARTMENT OF HEALTH SERVICES

GENETIC DISEASE BRANCH
2151 BERKELEY WAY, ANNEX4
BERKELEY, CA 94704
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**ADVISORY COMMITTEE ON HUMAN CLONING
JANUARY 27, 2000 MEETING**

**Children's Hospital of Northern California
5700 Martin Luther King Jr. Way
Oakland, CA**

MINUTES

The primary topic to be addressed at this meeting is the legal implications of cloning.

9:00 am	Introductions and Announcements
9:30 am	Patricia A. Baird, MD, University of British Columbia, Medical Genetics
10:30 am	John A. Robertson, JD School of Law, University of Texas
11:30 am	R. Alta Charo, JD, University of Wisconsin, School of Law
12:30 pm	Lunch
1:30 pm	James W. Walters, PhD, Professor of Ethical Studies, Loma Linda University
2:30 pm	Public comments and Discussion
4:00 pm	Adjourn

Present: M. McLean, R. Rao, L. Shapiro, B. Lubin, F. Coyteaux, F. Pizzulli, H. Greely, R. Hoag, T. Trotter, T. Friedmann, B. Lo

Absent: D. Gollaher

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ADVISORY COMMITTEE ON HUMAN CLONING
MEETING, MAY 15, 2000

Hiram Johnson Building Auditorium
455 Golden Gate Avenue
San Francisco, Ca

The primary topic to be addressed at this meeting is the use of cloning in infertility treatment.

Agenda

9:00	Introductions and Announcements
9:15	Ronald Harkey, California Department of Health Services
9:45	Discussion and Questions
10:00	Mark Eibert, Attorney
10:45	Discussion and Questions
11:15	Richard Chetkowski, M.D., Fertility Specialist
11:45	Discussion and Questions
Noon	LUNCH
1:00	Bonnie Steinbock, Bioethicist
1:45	Questions and Discussion
2:15	Public Comment Period
4:00	Adjourn

NOTE: This meeting is open to the public and there is no charge for attendance. Reasonable accommodation will be provided if requested by May 10, 2000. Please contact George Cunningham, MD, 2151 Berkeley Way, Annex 4, Berkeley, CA 94704, telephone 510/540-2552, fax 510/849-5102, e-mail gcunning@dhs.ca.gov.



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ADVISORY COMMITTEE ON HUMAN CLONING
MEETING SEPTEMBER 22, 2000

Junipero Serra Building
324 West 4th Street, Carmel Room
Los Angeles, CA

MINUTES

The primary topic to be addressed at this meeting is the therapeutic applications of cloning.

9:00 am	Introductions and Announcements
9:30	Stem Cell Technology and Cloning Lawrence Goldstein, University of California, San Diego
10:15	Questions and Discussion
10:30	Ethical and Legal issues for Non-reproductive Cloning Glenn McGee, Ph.D., University of Pennsylvania
11:15	Questions and Discussion
Noon	Lunch
1:30 pm	FDA (not yet responded)
2:30	Public comment period
3:30	Closed meeting of the committee
4:00	Adjourn

Present: M. McLean, R. Rao, L. Shapiro, F. Coyteaux,, H. Greely, R. Hoag, T. Trotter,

Absent: D. Gollaher, T. Friedmann, F. Pizzulli, B. Lo and B. Lubin

DEPARTMENT OF HEALTH SERVICES

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**Advisory Committee on Human Cloning**

May 8, 1999

10:00 AM- 3:00 PM

UCSF Laurel Heights Conference Center
3333 California Street
San Francisco, CA 94188

AGENDA

1. Introductions and Orientations
2. Discussion of how meetings will be structured and conducted.
3. Henry Greely, JD
Historical summary of the development of cloning as public policy issue.
4. Bernard Lo, MD
Summary of the operation and recommendation of President's Bioethics Committee.
5. Theodore Friedman, MD
Summary of technological advances in cloning research since Dolly. State of the art today.
6. Committee
Discussion of definitions of terms. How are we to define "cloning" for purposes of our review?
7. Committee
Discussion of agenda and time of meetings.

Present: George Cunningham, Ted Friedmann, Roger Hoag, Larry Shapiro, Bert Lubin, Tracy Trotter, Radhika Rao, Francine Coyteaux, Margaret McLean, Francis Piuulli, and Hank Greely

Absent: D. Gollaher and B. Lo

APPENDIX FOUR

Partial Reading List

We provide this list of publications on human cloning for readers of this report who would like further information on the issues we discuss. The list contains references largely on the social and ethical issues raised by the possibilities of human cloning; few if any of the readings listed require significant scientific background. This list is by no means exhaustive, but it should provide a useful starting place.

Books

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APPENDIX FIVE REFERENCES

I. BACKGROUND

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II. CALIFORNIA SHOULD PROHIBIT REPRODUCTIVE CLONING

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III. CALIFORNIA SHOULD NOT PROHIBIT BUT SHOULD REASONABLY REGULATE HUMAN NON REPRODUCTIVE CLONING

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