CLONING HUMAN BEINGS

The Science of Animal Cloning

Commissioned Paper
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WHAT IS CLONING?

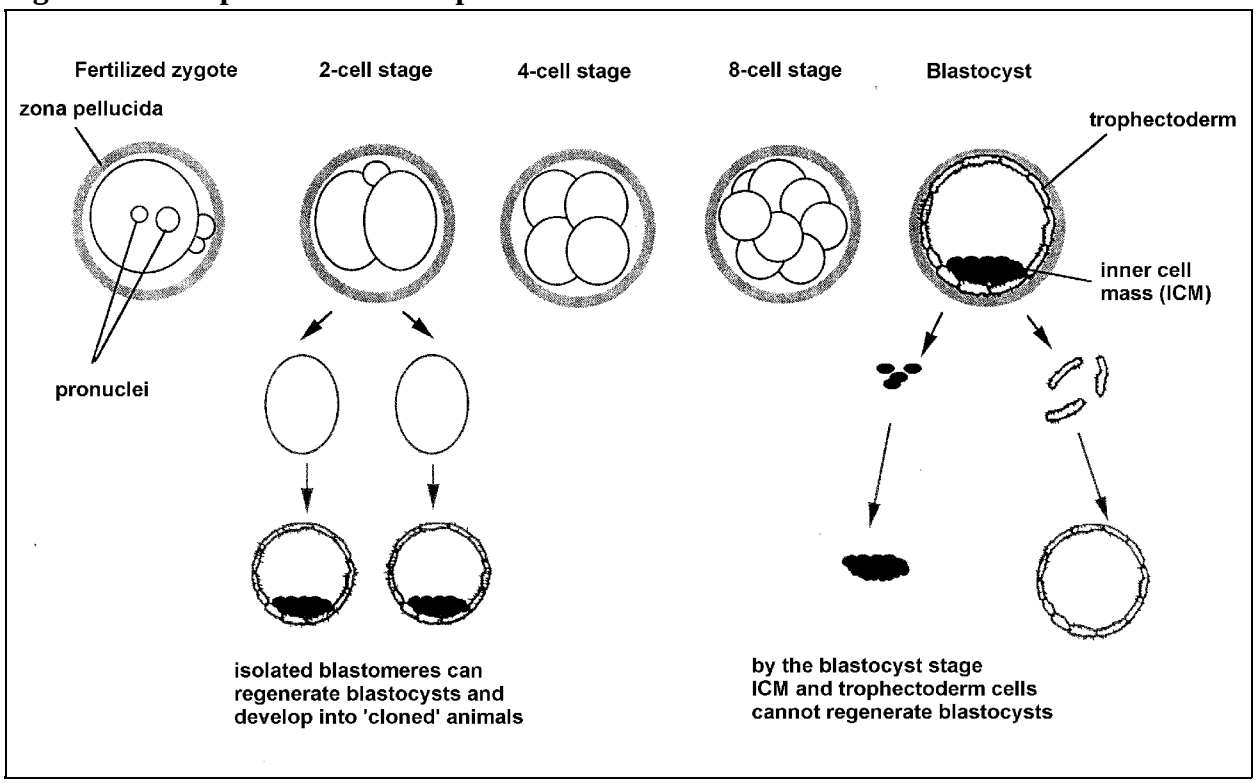
The word "clone" is used in many different contexts in biological research, but in simple terms it means a set of genetically identical individuals. Scientists talk about cloning DNA—the process of making and propagating a set of identical copies of a particular piece of genetic material, or about cloning cells—taking a single cell in culture and allowing it to multiply into a cell line. These techniques are some of the basic tools of the trade of modern biomedical research and are not currently a source of much public concern. But when we talk about cloning whole animals, especially mammals, the public rightly wants to know what is going on and why.

Genetically identical copies of whole organisms—clones—are commonplace in the plant breeding world. Many valuable horticultural or agricultural strains are maintained solely by vegetative propagation from an original plant, and never by sexual reproduction. This reflects the ease with which it is possible to regenerate a complete plant from a small cutting. The ability to propagate a valuable animal strain in the same way would revolutionize the agricultural business. However, in the animal kingdom, development is much less flexible than in plants. Many simpler invertebrate species have the ability to regenerate a whole organism from a small piece, although this is not necessarily their usual mode of reproduction. Vertebrates have lost this ability entirely, although regeneration of missing limbs, organs, or tissues can occur to varying degrees.

Although an adult vertebrate cannot make another adult, natural cloning does occur, in a limited way, with the formation of identical twins. These arise in humans and other mammals by chance separation of a single embryo into halves at an early stage of development. The resulting offspring will be genetically identical, deriving from one zygote—the result of the fusion of one egg and one sperm. A clone of two is not very remarkable, but it is a clone nonetheless. Experimental separation of cells from the early embryos of several mammalian species has shown that it is possible in some cases to get larger clones from one egg (Figure 1). In mice, only separated two-cell blastomeres are capable of generating entire mice (Rossant 1976), but in some domestic species, like sheep, it is possible to get separated eight-cell blastomeres to develop into viable offspring (Willadsen 1981).

At best, efficiency of this technique is never 100 percent, so the number of clones is small. However, the experiments are scientifically important, because they demonstrate that the cells of the early embryo are totipotent; that is, they retain the full potential to form an entire animal. As development proceeds, cells begin to differentiate into specialized cell types and can no longer revert back to the beginning of development (Figure 1). If this stability of the differentiated state could be reverted in some way, then producing animals from later differentiated cells or even adult cells would become feasible. Nuclear transfer experiments, first performed in amphibians in the 1960s, demonstrated how this could be done.

Figure 1: Preimplantation development in mammals



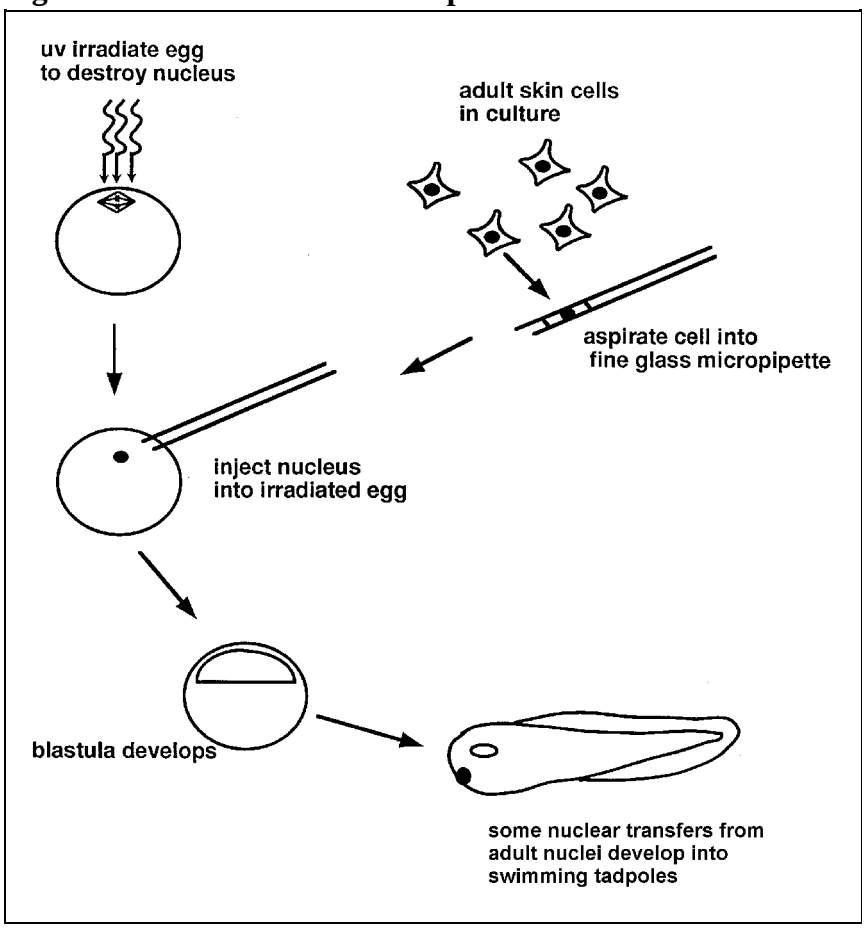
THE SCIENTIFIC QUESTION: DOES DIFFERENTIATION INVOLVE IRREVERSIBLE CHANGES IN GENETIC CONTENT?

The information for all the proteins produced in all the specialized cell types of the body is encoded in the DNA of the zygote and must be passed on intact into the next generation via the germ cells that form the eggs and sperm. However, there is no absolute requirement that the somatic cells—those cells not destined to give rise to the germ cells—retain the full genetic content in an unmodified form. A differentiated cell like a neuron must keep a set of neural-specific genes active and silence those genes specifically required to make muscle, liver, and other tissues. How does it do this? Is it an active process, in which genes are still present but repressed in some way, or is the DNA for the inactive genes lost or irreversibly inactivated in some way? In the early 1960s our understanding of the mechanisms of gene regulation was still rudimentary and this general question was extremely important.

Elegant experiments in *Xenopus laevis* by John Gurdon, following earlier experiments in *Rana temporaria* by Briggs and King (1952), provided strong evidence that the genetic content of differentiated somatic cells is essentially unchanged from that of the early embryo. Nuclei from donor differentiated cells were injected into recipient eggs from which the nucleus, containing the DNA, had been inactivated (Figure 2). If the donor nucleus could direct normal development of the recipient egg, this would strongly suggest that differentiation cannot involve permanent

changes in the genetic material. The first series of experiments used intestinal epithelial cells from swimming tadpoles (Gurdon 1962), and adult frogs were produced, albeit at a very low efficiency. The intestinal cells used were highly specialized brush-border gut cells, but were not derived from the final adult frog and so might not be terminally differentiated. Gurdon and colleagues (1975) performed another carefully controlled series of experiments in which they used nuclei from adult skin cells for transfer. Over 99 percent of the cultured cells expressed keratin, a differentiated marker of skin cells, and 4 percent of the nuclei transferred eventually gave rise to fully developed tadpoles. These experiments provided the strongest evidence to date that the nuclei of terminal differentiated cells could be reactivated by the cytoplasm of the egg and redirect normal development.

Figure 2: Nuclear transfer in amphibians



However, no viable adult frog was ever produced from an adult differentiated nucleus and there was a strong decline in the rate of recovery of feeding tadpoles with progressive age of nuclei transferred. This left open the theoretical possibility that complete reactivation of the adult

nucleus was prevented by some kind of irreversible change in the genetic material, and that there was, indeed, a progressive decline in nuclear potential with age. However, careful analysis at the time suggested that the major reason for developmental failure of transplant embryos was chromosomal abnormalities acquired as a consequence of the process of nuclear transplantation itself. The cell cycle of adult cells is much slower than the rapid pace of cell division in the early frog embryo. Expecting a transplanted nucleus to reprogram its gene expression, replicate its DNA, and enter normal embryonic cell cycles within an hour of nuclear transfer is unrealistic. The remarkable thing is that some nuclei manage to do so, rather than that so many do not.

The general conclusion from the amphibian nuclear transfer experiments of Gurdon and others was that the differentiated state did not involve major irreversible changes in the DNA. This conclusion was reached in the 1960s and early 1970s and has not been challenged in the intervening years (Gurdon 1974).

THE STABILITY OF THE DIFFERENTIATED STATE: OUR UNDERSTANDING TODAY

As our understanding of the regulation of gene expression has grown, we have learned that most patterns of differentiated gene expression are maintained by active control mechanisms (Blau 1992), in which combinations of regulatory proteins bind to control sequences adjacent to genes and turn them on or off. The particular differentiated state of a cell depends on its particular combination of regulatory proteins. This is not the only mechanism of gene control. There are some cases in which actual rearrangements and deletions of DNA occur, as in the expression of the immunoglobulin and T-cell receptor genes in lymphocytes. Heritable modification of the DNA by methylation can also affect gene expression. However, the overwhelming evidence suggests that given the right environment, it should be possible to activate or inactivate almost any gene in a cell.

This environment need not be the cytoplasm of the egg. Cell fusion experiments, in which different cell types are fused into one multinucleate cell called a heterokaryon, have demonstrated that extensive reprogramming of differentiated nuclei can occur. For example, when muscle cells are fused with non-muscle cells of various sorts, muscle-specific genes are activated in the non-muscle cells (Blau et al. 1985). Similarly, globin genes can be activated in many cell types after fusion with erythroid cells (Baron and Maniati 1986). These and other kinds of experiments have led to the isolation of specific protein factors that regulate cell differentiation, such as the myogenic factors that regulate the formation of the muscle cell lineages (Weintraub 1993).

All of this information has shown that the stability of the differentiated state is not absolute and, therefore, it should be theoretically possible to reprogram adult cells to reinitiate earlier programs of differentiation. Nuclear transfer experiments pointed the way and molecular biology is continuing to define the components of the regulation of cellular differentiation.

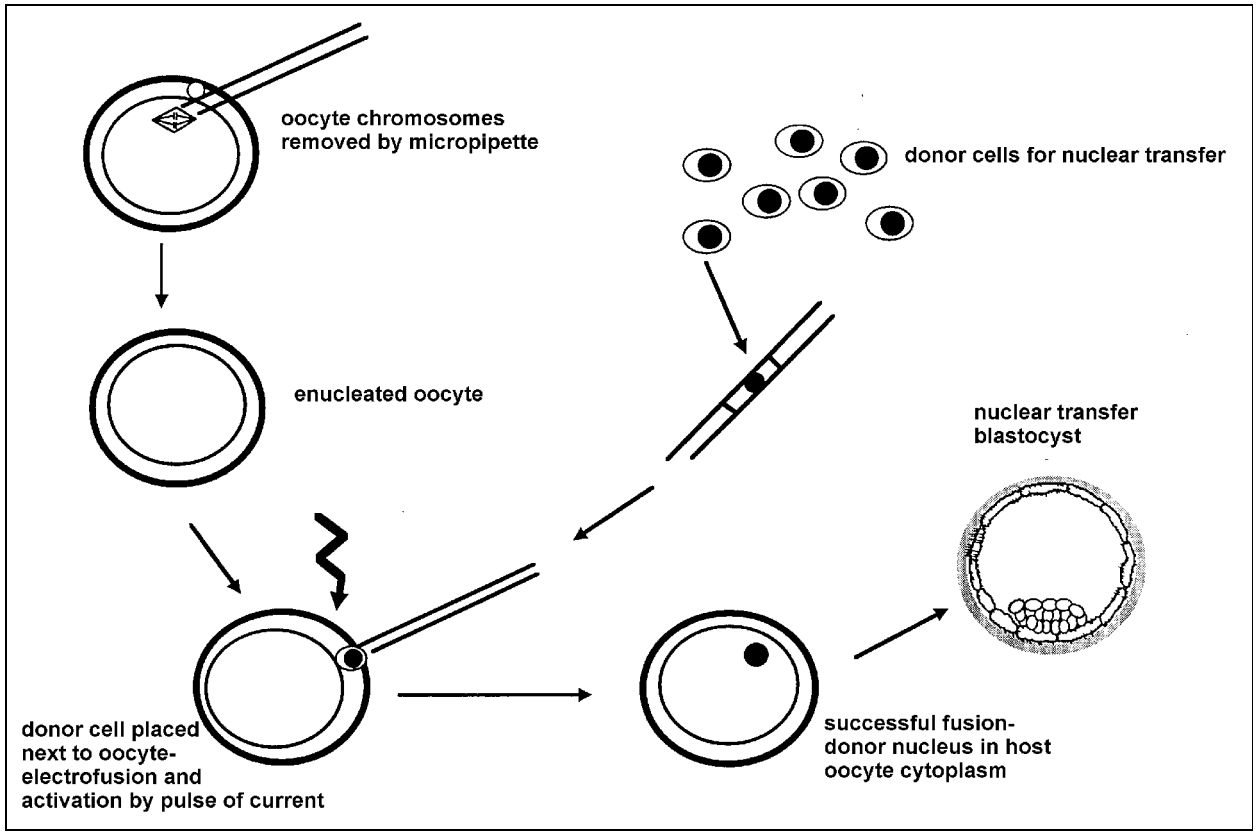
NUCLEAR TRANSFER IN MAMMALS: THE EARLY EXPERIMENTS

Following success in nuclear transfer experiments in frogs, there were some attempts in the 1970s to repeat the experiments in mice, the mammal of choice for experimental manipulation. It was known that early development occurs at a considerably slower rate in mammals than in amphibians, giving hope that reprogramming of the donor nucleus would occur more efficiently. In mice it takes about a day from fertilization to the first cleavage, giving ample time, it was thought, for the reprogramming of gene expression and adjustment of the cell cycle. This proved not to be the case. Early experiments showed that nuclei of adult cells fused with fertilized eggs did not undergo nuclear swelling or nuclear division (Graham 1969).

A careful series of experiments by McGrath and Solter in the mid 1980s showed that nuclei could be successfully exchanged between zygotes, with 90 percent reaching the blastocyst stage and beyond (McGrath and Solter 1984). Nuclei from 2-cell embryos could direct development to the blastocyst stage, but nuclei from later cleavage stages could not successfully recapitulate development after nuclear transfer. In fact, in mice, nuclei show less totipotency than whole cells—many experiments have shown that blastomeres from as late as the early blastocyst stage are still totipotent when combined with other embryonic cells (Rossant and Pedersen, 1986). This means that the failure of nuclear reprogramming has to be the result of something other than irreversible changes to the genetic material of the cells. In 1986, Willadsen showed that, unlike the situation in mice, enucleated unfertilized eggs from sheep could be fused with 8-cell stage blastomeres and viable offspring produced (Willadsen 1986).

Most recent experiments have used nuclear transfer into enucleated unfertilized oocytes, a procedure that prolongs the period of possible reprogramming before the donor nucleus has to undergo the first cleavage division. Oocytes arrested at metaphase II of meiosis, prior to fertilization, are enucleated by aspiration of the metaphase chromosomes into a fine glass micropipette (Figure 3). The nuclear donor cell is introduced under the egg membrane, or zona pellucida, and fused to the enucleated oocyte. The major technical advance in the last few years has been the use of electrofusion for both fusion of cells and activation of the oocyte. When the enucleated oocyte and the nuclear donor cell are subject to short electrical pulses in culture, membrane breakage and fusion occurs between the two cells and the electrical pulse also begins the processes of egg activation that would normally be triggered by fertilization. Using this approach, viable offspring have been obtained after nuclear transfer from 8-cell blastomeres in the mouse (Cheong et al. 1993) and from later stages of development in several other species, as will be discussed below.

Figure 3: **Nuclear transfer in mammals**



REPROGRAMMING IN THE OOCYTE ENVIRONMENT

There has been some study of the events that occur once an embryonic nucleus is exposed to the oocyte cytoplasm, and some, but not all, of the parameters that affect success of nuclear transfer are known (Fulka et al. 1996). Oocytes used for fusion are arrested in metaphase II of meiosis and only proceed to complete division, with extrusion of the second polar body, after fertilization or activation by some artificial signal, such as electrical current. In this arrested state, levels of maturation-promoting factor (MPF) are high. This cell-cycle regulatory complex promotes mitosis. When transplanted nuclei are introduced into the high MPF-containing oocyte environment, they usually undergo DNA replication, nuclear envelope breakdown, and premature chromosome condensation. Activation of the oocyte causes a decline in MPF activity and the nuclear envelope is reformed around the donor nucleus. The nucleus now takes on the appearance of the pronucleus of the egg, which is large and swollen. It is assumed that this process begins the reprogramming of the transferred nucleus, by exposing the chromatin to the oocyte cytoplasm and beginning the exchange of donor nuclear proteins for oocyte-derived proteins (Prather and First 1990).

Whether exposure to MPF and/or nuclear swelling is an absolute prerequisite for later development seems to be still unclear. Experiments in a number of species have shown that when nuclei are fused with oocytes that have been activated some hours prior to fusion, no DNA replication, chromosome condensation, or nuclear swelling occurs, but normal development can occur (Campbell et al. 1993, Campbell et al. 1994, Stice et al. 1994). Prefusion of blastomere and enucleated oocyte, with activation being induced after a few hours in culture, has also been attempted with success (Campbell et al. 1996). In all cases, the numbers of surviving progeny are too small to determine whether the differences in the success rates of the various treatments are statistically significant.

What is clear, however, is that the cell cycle stage of the donor nucleus does affect success. In rabbits, cows, sheep, and mice (Campbell et al. 1993, Cheong et al. 1993, Collas et al. 1992), experiments have shown that nuclei from cells in the early phases of the cell cycle do better than cells in S-phase or beyond. In the first phase of the cell cycle, G1, cells are diploid and relatively quiescent. They then enter a period of DNA replication, called S-phase, followed by another rest phase, called G2, where they have twice the diploid amount of DNA in preparation for mitosis. Because DNA replication is induced after nuclear transfer in the usual protocol, where fusion and activation are simultaneous, any nucleus that has more than the diploid DNA value upon transfer will end up with too much DNA, which will likely result in chromosome anomalies. Thus, the need to transfer G1 nuclei is paramount if chromosome damage is to be avoided. It seems likely that the failure to use carefully synchronized donor nuclei underlies some of the difficulties that have been reported in achieving successful nuclear transfer development in different species.

NUCLEAR TRANSFER IN MAMMALS: THE CURRENT STATE OF PLAY

Over the past ten years or so, there have been several reports of successful nuclear transfer experiments in mammals, nearly all of them using cells taken directly from early embryos. Surveying the literature on embryonic nuclear transfer, we find that the oldest embryonic nucleus that can successfully support development differs among species. In mice, no nucleus older than the 8-cell stage has been used successfully (Cheong et al. 1993). Four-cell blastomere nuclei have been successfully used in pigs (Prather et al. 1989), while in rabbits, 32- to 64-cell morulae can be used as nuclear donors (Yang et al. 1992). In cows and sheep, inner cell mass (ICM) cells from the 120-cell blastocyst stage have been used successfully (Collas and Barnes 1994, Smith and Wilmut 1989). Indeed, in both cows and sheep, cell lines have been made from ICMs and nuclei from these cells have been able to reprogram development after nuclear transfer. In the first experiments of this sort by Sims and First (1994), bovine ICM cells were grown in low-density cell suspensions for up to 28 days and then used as nuclear donors, without any attempt at synchronization of the cell cycle of the donor cells. Of those successfully fused, 24 percent developed to the blastocyst stage, and 4 out of 34 (12 percent) blastocysts transferred to recipient cows developed into normal calves. This success rate compares favorably with those using earlier

blastomeres, and suggests that it might be possible to achieve nuclear transfer success from permanent cell lines established from early embryos.

Wilmut and colleagues established permanent epithelial cell lines from sheep embryos and used these as nuclear donors after as many as 13 passages in culture (Campbell et al. 1996). In an attempt to avoid the problems of nuclear transfer of non-G1 nuclei into activated oocytes, they subjected their donor cell line to serum starvation prior to nuclear transfer. Under these conditions, where the cells are starved of essential nutrients, the cells exit the cell cycle and enter the so-called G0 state. Fusion of G0 nuclei to oocyte cytoplasm means that all nuclei can be activated to reenter the cell cycle together and problems of cell cycle asynchrony between donor and host are avoided. It was also suggested that the G0 state might actually be beneficial in terms of increasing the capacity of the nucleus to be reprogrammed by the oocyte cytoplasm. However, there is currently no direct evidence to support this, nor to conclude that nuclei synchronized in G0 are any better than nuclei synchronized in G1. Approximately 14 percent of fusions resulted in development of blastocysts, and 4 out of 34 (12 percent) embryos transferred developed into live lambs. The success rate in sheep and bovine experiments was almost identical, and suggested that long-term passage of early embryo cells need not inhibit their ability to be reprogrammed by the oocyte environment. Would the same be true of adult cells?

AND THEN CAME DOLLY

All of this background work led up to the famous Dolly, the first mammal to develop from the nucleus of an adult somatic cell (Wilmut et al. 1997). Wilmut and colleagues took fetal fibroblast cells and cells derived from the mammary gland of an adult sheep and applied the same approach of synchronizing cells in G0 prior to nuclear transfer. They reported successful production of live offspring from both cell types. Twenty-nine out of 247 (12 percent) of successful fusions between adult mammary gland nuclei and enucleated oocytes developed to the blastocyst stage, and 1 out of 29 (3 percent) blastocysts transferred developed into a live lamb—Dolly. This experiment was, in fact, the first time any adult animal had been derived from nuclear transfer of an adult nucleus, since the frog experiments generated only swimming tadpoles. However, the amount of new information about the stability of the differentiated state derived from this experiment was small, since no attempt was made to use only fully differentiated cells expressing specialized mammary gland proteins for the transfer, as was done for the skin cell experiments in frogs. The successful nuclear transfer animal could have derived from a less-differentiated, stem-cell-like cell in the population. The excitement generated by Dolly was more related to the realization that there may be no theoretical barrier to nuclear transfer into the oocyte from any cell of the body in any mammalian species. Hence, the science fiction scenario of copying or “cloning” an adult mammal, including humans, became science fact.

Several important questions remain unanswered about how feasible cloning from adult cells really will be, especially since only one successful adult nuclear transfer animal has been produced to date.

1. ***Are there true species differences in the ability to achieve successful nuclear transfer?*** We have seen that the published data suggest that nuclear transfer in mice is much less successful than in larger domestic animals. Part of this difference may reflect the intensity of research in this area in the last ten years, where agricultural interests have meant that more nuclear transfer work has been performed in domestic animals than in mice. But part of it may be real and reflect another critical component for the successful reprogramming of the donor nucleus—namely, the time between nuclear transfer and the activation of the embryonic genome. In order for a differentiated nucleus to redirect development in the environment of the egg, its particular constellation of regulatory proteins must be replaced by those of the egg in time for the embryo to be able to use the genome of the donor nucleus to transcribe the genes it needs for normal development. In mammals, unlike many other species, the early embryo rapidly needs to use the embryonic genome and cannot survive on the proteins and messenger RNA inherited from the mother in the egg. The time at which embryonic gene activation occurs varies among species—the late 2-cell stage in mice (Schultz 1993), the 4- to 8-cell stage in humans (Braude et al. 1988) and the 8- to 16-cell stage in sheep. The later onset of embryonic gene transcription in sheep provides an additional round or two of cell divisions in which nuclear reprogramming can occur, unlike the rapid genome activation in the mouse. Donor nuclei do turn on some of the 2-cell stage-specific genes after nuclear transfer in the mouse, but protein synthesis patterns are not identical between nuclear transfer and normal embryos (Latham et al. 1994). Further cross-species comparisons are needed to assess the importance of this difference in the time of genome activation for the success of nuclear transfer experiments.

2. ***Will imprinting affect the ability of nuclei from later stages to reprogram development?*** In mammals, the phenomenon of genomic imprinting means that the paternally and maternally inherited genomes are not equivalent (Solter 1988). Some heritable imprint is established on the chromosomes during gametogenesis, such that certain genes are expressed from only one of either the maternally or paternally inherited copies later in development. Imprinting explains why parthenogenetic embryos, with only maternally inherited genes, and androgenetic embryos, with only paternally inherited genes, fail to complete development (Fundele and Surani 1994). Nuclei transferred from a diploid organism, whether from the embryo or the adult, should contain both maternal and paternal copies of the genome and so not suffer the problems of parthenogenesis. However, an adult nucleus, if it is to be successful in reprogramming development, should retain intact the chromosomal imprints that normally determine whether maternal or paternal gene copies will be active. The successful generation of an adult sheep from an adult cell nucleus suggests that the imprint can be stable, but it is possible that some instability of the imprint, particularly in cells in culture, could limit the efficiency of nuclear transfer from adult cells. It is interesting that nuclear transfer embryos produced from established bovine embryonic cell lines died in mid-gestation, with specific deficiencies in placental development (Stice et al. 1996). Placental development has been found to be particularly sensitive to imprinting effects in mice (Moore and Haig 1991).

3. ***Will processes of cellular aging affect the ability of adult nuclei to program development?*** As somatic cells divide, they progressively age and there is normally a defined number of cell divisions that they can undergo before senescence. Part of this aging process involves the progressive shortening of the ends of the chromosomes, the telomeres. Germ cells and cancer cells evade this chromosome aging by possessing a telomerase activity that can keep telomeres full length (Chiu and Harley 1997). It seems likely that returning an adult mammalian nucleus to the oocyte will expose it to sufficient telomerase activity to reset telomere length, since oocytes have been found to be potent sources of telomerase activity (Mantell and Greider 1994).

4. ***Will the mutation load accumulated by adult cells affect nuclear transfer efficiency and predispose to cancer and other diseases?*** As cells divide and organisms age, mistakes and alterations in the DNA will inevitably occur and will accumulate with age. If these mistakes occur in germ cells, a heritable mutation occurs, but mutations in somatic cells are not necessarily harmless. Sporadic somatic mutations in a variety of genes can predispose a cell to become tumorigenic. Transfer of a nucleus from a somatic cell carrying such a mutation into an egg would transform a sporadic somatic mutation into a germline-equivalent mutation in all cells of the body, with presumably severe consequences on the likelihood of that mutation leading to malignant transformation. The risks of such events occurring following nuclear transfer is difficult to estimate.

WHY PURSUE ANIMAL CLONING RESEARCH?

The continued pursuit of nuclear transfer as a means of producing genetically identical copies of embryonic or adult organisms largely has been driven by technological needs rather than by the pursuit of basic knowledge of cellular differentiation. The goals are:

1. to generate groups of genetically identical individuals for research purposes,
2. to rapidly propagate “elite” animal stocks,
3. to improve the efficiency of generation and propagation of transgenic livestock, and
4. to generate targeted genetic alterations in domestic animals.

1. Making Clones for Research Purposes

Inbred strains of mice have been a major mainstay of biological research for years. These mice have been bred by brother-sister mating for many generations until they are essentially all genetically identical and homozygous (i.e., they carry two identical copies of all genes). Experimental analysis is then simplified, because variations in response to experimental treatment due to variations in genetic background can be eliminated. Clearly, generating homozygous inbred lines in larger animals with long generation times and small numbers of offspring is not readily achieved. The concept of generating small groups of identical animals by nuclear transfer has been proposed as an alternative strategy and apparently underlies the recent report from Oregon on successful nuclear transfer from early embryonic nuclei in monkeys. Repeated cycles of nuclear

transfer can expand the number of individuals derived from one donor nucleus, a trick first used in *Xenopus* experiments. Thus, the first nuclear transfer embryo is allowed to divide to early blastomere stages, and then those cells are used as donor nuclei for another series of transfers. This process can be carried on indefinitely, in theory, although practice suggests that fusion rates decline with each cycle of transfers. One experiment in cows, for example, produced a clone of 54 early embryos from nuclear transfer of a single blastomere nucleus from one parent embryo after three cycles of transfer (Stice and Keefer 1993). Viable calves were produced from all three cycles.

This approach is likely to be limited in its usefulness as a research tool, however. It must be remembered that a clone of animals derived from nuclear transfer from one individual is self-limited. Cloned animals do not breed true unless they are derived from an inbred stock, and each clone will differ genetically from a clone derived from another individual. Thus each member of a clone has to be made by the difficult procedure of nuclear transfer, and generation of large enough clones to be useful as experimental groups is likely to be prohibitively expensive in most animals.

2. Propagating Desirable Stocks

In animal breeding strategies, rapid spread of desirable traits within stocks of domestic animals is of obvious commercial importance. Artificial insemination and embryo transfer can increase the effective reproductive output of individual elite male and female animals, respectively, and are widely used in the livestock business. Nuclear transfer cloning, especially from adult nuclei, could provide an additional means of increasing the average "genetic merit" of a given generation of animals. The ability to make identical copies of adult prize cows, sheep, and pigs is a feature unique to nuclear transfer technologies and may well be used in livestock production if the efficiencies of adult nuclear transfer can be improved. The net effect of multiplying genetically favorable individuals by cloning will be to reduce the overall genetic diversity in a given livestock line, with possible adverse long-term consequences. Efforts will have to be made to ensure maintenance of a pool of genetic diversity for the future.

3. Improved Generation and Propagation of Transgenic Livestock

There is considerable interest in being able to genetically alter farm animals by introduction and expression of foreign DNA sequences in their genome. So-called transgenic animals were first made in mice by microinjection of DNA into the pronucleus of the egg. In a proportion of cases, the injected DNA integrates into a host chromosome and is then passed into all cells of the mouse and into the next generation as though it were a host gene. With the right DNA sequences attached, the foreign gene can be expressed and function in the transgenic environment. This ability to add genes to the genome has been a major research tool for understanding gene regulation and for making mouse models of certain human diseases. It has also been applied to other species, including livestock species. Proposed applications of this technology to livestock improvement include the possible introduction of growth-enhancing genes, genes that affect milk

quality or wool fibers, and disease-resistance genes (Ward and Nancarrow 1995). Progress has been slow. Initial results of attempting to manipulate meat production by overexpression of growth hormone in pigs led to undesirable side effects (Pursel et al. 1989). In light of the likely resistance of consumers to genetically manipulated meat, it seems probable that the use of transgenesis for livestock improvement will be limited.

The major activity in livestock transgenesis is focused on pharmaceutical and medical applications. The milk of livestock animals—sheep, goats, and cows—can be modified to contain large amounts of pharmaceutically important proteins by expression of human genes under the control of mammary gland-specific sequences (Houdebine 1994). In sheep, greater than 50 percent of the proteins in milk can be the product of a human transgene (Colman 1996). Even the milk of transgenic mice can yield milligram quantities of recombinant proteins. Since many such proteins are pharmaceutically active at very low concentrations, it is estimated that production of human drugs from transgenic animals could be a multimillion-dollar industry in the coming years. Regulatory approval for drugs prepared from milk is not yet in place.

The other major area of commercial interest is the use of transgenic animals for human organ transplantation. Pig organs in many cases are similar enough to human organs to be potentially useful in organ transplants if problems of rejection of the so-called xenograft could be overcome. Prevention of acute phase rejection of the xenografts has already been achieved by expression of human complement regulatory proteins in transgenic pigs. Further transgenic manipulation may lead to improved graft survival. Several companies are exploring the possibility of pig organ transplants despite possible risks of cross-species transfer of pathogenic viruses and the likely public resistance to xenografts.

How does nuclear transfer come into all this transgenic animal work? Transgenesis by zygote injection is inefficient. Not all injected eggs will develop into transgenic animals, and then not all transgenic animals will express the transgene in the desired manner. Characterizing a transgenic line of livestock is a slow and expensive business. Nuclear transfer would speed up the expansion of a successful transgenic line, but, perhaps more important, it would allow more efficient generation of transgenic animals in the first place. Foreign DNA could be introduced into cell lines in culture, and cells containing the transgene in the right configuration could be grown up and used as a source of nuclei for transfer, ensuring that all offspring are transgenic.

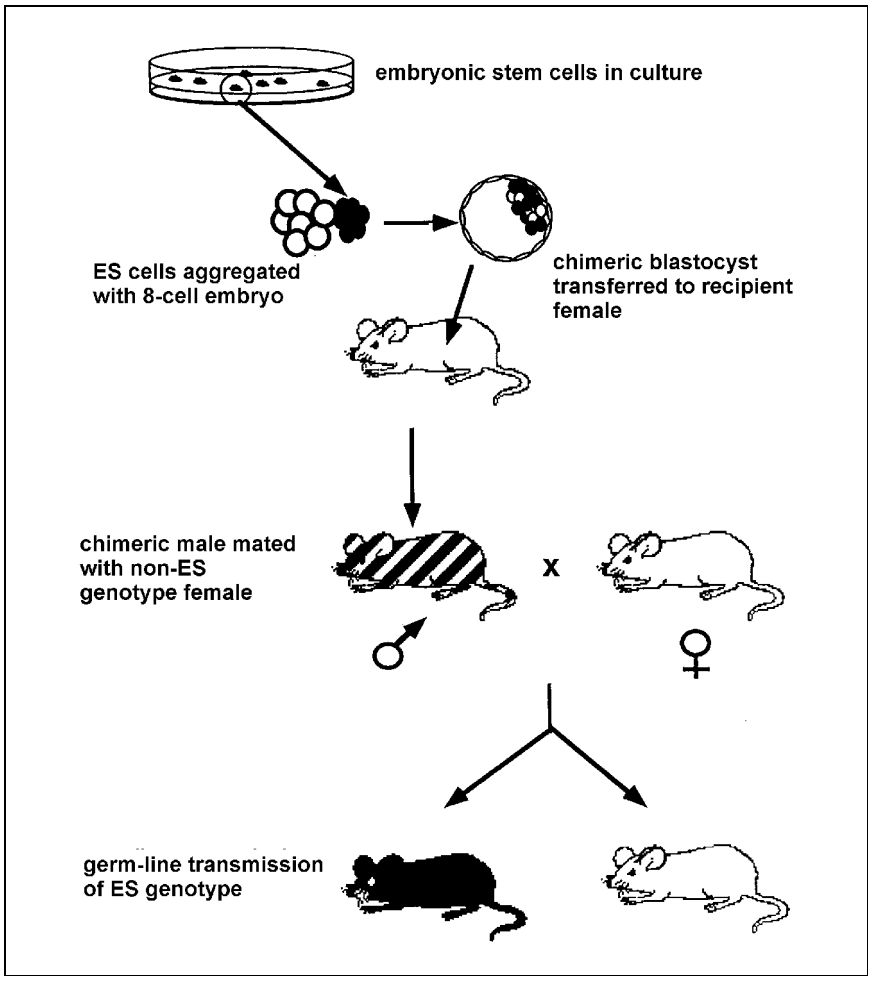
4. Generating Targeted Gene Alterations

The most powerful technology for genetic manipulation in mammals—gene targeting—was developed in mice, and depends on the ability of mammalian DNA, when added to cells in culture, to recombine homologously with identical DNA sequences in the genome and replace them. Thus, mutations or other desired alterations can be introduced into the genome in a directed and controlled manner and their effects studied (Capecchi 1989). This technology would have been of limited use, however, without some means of taking those changes generated in culture and reintroducing them into animals. In mice, this can be achieved by the use of embryonic stem (ES)

cells. These are cell lines derived from the ICM of the blastocyst, which can be cultured indefinitely in the undifferentiated state but which retain the potential to form all cells of the animal, including the germ cells, when returned to the environment of the early embryo (Figure 4). These "chimeric" animals can then be bred to transmit the ES genotype into the germ line. Thus, any genetic alteration made in the ES cells in culture can be introduced back into mice (Robertson 1986).

The combination of homologous recombination and ES cell technology has been responsible for the explosion of knock out mice, in which specific genes have been deleted from the genome. These mice enhance understanding of normal gene function and allow generation of accurate models of human genetic disease. Gene targeting approaches can also be used to ensure correct tissue-specific expression of foreign transgenes and to misexpress genes in inappropriate tissues. If applied to domestic animals, this technology could increase the efficiency of transgene expression by targeting transgenes to appropriate regions of the genome for expression. It could also be used to mutate endogenous genes so as to influence animal health and productivity or to

Figure 4: Generation of germline chimeras from embryonic stem cells

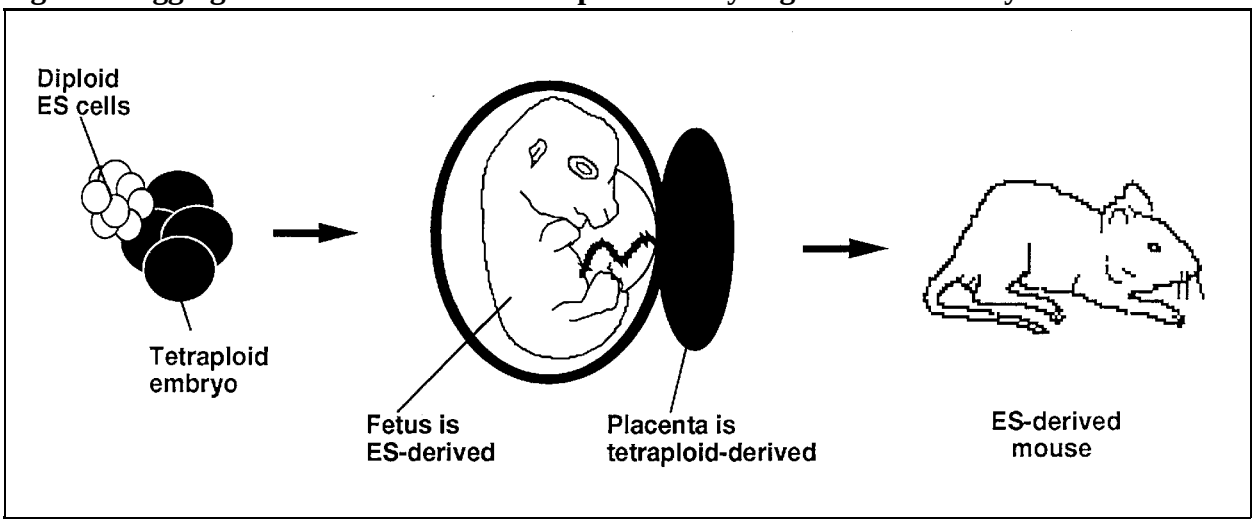


help prevent rejection of xenografts. However, to date, there are no fully validated ES cell lines in domestic animals. Nuclear transfer from non-pluripotent cell lines, as reported by Wilmut et al. 1997, provides a possible alternative to the ES cell route for introduction of targeted gene alterations into the germ line.

At this point it is unclear whether homologous recombination can occur efficiently in the kinds of cell lines used for sheep nuclear transfer. Experiments in mice have indicated that the ES cell environment is particularly conducive to homologous recombination, and efficiencies of targeted mutation tend to be much lower in non-ES lines. Attempts to generate ES cells from other species are continuing—primate (Thomson et al. 1995), rat (Iannaccone et al. 1994), and pig (Wheeler 1994) lines have been reported, and this may still be the best route to achieve precise gene alterations in domestic animals.

Apart from the fact that ES lines do not exist, the other argument for using nuclear transfer to introduce germ-line genetic alterations in farm animals is that it avoids one generation of breeding from chimeras, an important factor in farm animals with long generation times and small litter size. In fact, ES cells can also be used directly to generate cloned animals carrying the gene alteration of interest without the intermediate chimeric step. Clonal ES cell lines have been shown to be capable of forming entire mice when combined with developmentally compromised host embryos (Figure 5) (Nagy et al. 1993). Although this procedure is not yet very efficient, it illustrates the remarkable properties of these cells and suggests that similar approaches could be applied in other species.

Figure 5: Aggregation of ES cells with tetraploid embryos generates entirely ES-derived mice



HOW CAN WE USE INFORMATION FROM NUCLEAR TRANSFER EXPERIMENTS FOR HUMAN BENEFIT?

The biotechnology applications of nuclear transfer cloning in mammals are clear, but the underlying science does offer some opportunities for further understanding of the reversibility of the differentiation process. The demonstration that in mammals as in frogs, the nucleus of an adult cell can be reprogrammed by the environment of the early embryo, provides further impetus to studies on how to reactivate embryonic programs of development in adult cells—with exciting prospects for regeneration and repair of diseased or damaged human tissues and organs. Information on the mechanisms of reprogramming of the adult nucleus in the egg cytoplasm may provide clues as to how to reprogram adult differentiated cells directly without the need for oocyte fusion.

It may not be necessary to reprogram terminally differentiated cells, but rather to stimulate proliferation and differentiation of the quiescent stem cells, which are known to exist in many adult tissues—including the nervous system (Gage et al. 1995). Experiments in this area are likely to focus more on the conditions required for direct stimulation of the stem cells in specific tissues than on the actual use of nuclear transfer to activate novel developmental programs. These approaches to cellular repair using adult stem cells will be greatly aided by an understanding of how stem cells are established during embryogenesis. ES cells provide an interesting model for such studies, since they represent the precursors of all cell lineages in the body. They can be stimulated to differentiate in vitro into precursors of the hematopoietic, endothelial, neuronal, and muscle cell lineages, among others (Weiss and Orkin 1995), and they thus provide a potential source of stem cells for regeneration of all tissues of the body.

Once we have learned more about how to control the differentiation of mouse ES cells, one could envisage the generation of human ES-type cells as essentially endless sources of stem cells for tissue regeneration. Such cell lines could be generated from "spare" in vitro fertilized embryos or from fetal germ cells, as has proved possible in mice (Matsui et al. 1992). One could even envisage using nuclear transfer from an adult cell to generate an early embryo and therefore an ES line for each individual human, which would be ideally tissue-matched for later transplant purposes. This seems a rather expensive and far-fetched scenario; a more likely scenario would involve the generation of a few widely used and well-characterized human ES cell lines that had been genetically altered to prevent graft rejection in all possible recipients.

ETHICAL CONCERNS

As we move into the realms of direct human embryo manipulation, the ethical implications of this research become more apparent. It is outside the scope of this paper to discuss the various scenarios in which human nuclear transfer might be considered. Work with embryonic stem cells and genetic manipulation of early embryos in different species (including nuclear transfer) is already providing unparalleled insights into fundamental biological processes and promises to provide great practical benefit in terms of improved livestock, improved means of producing

pharmaceutical proteins, and prospects for regeneration and repair of human tissues. Great care should be taken in crafting any ethical or legal guidelines on human cloning to avoid inhibiting legitimate research in animals or humans that has the potential to provide immense benefits for the future.

References

Baron, M.H., T. Maniatis, Rapid reprogramming of globin gene expression in transient heterokaryons, *Cell,* 46:591-602, 1986.

Blau, H.M., Differentiation requires continuous active control, *Annu Rev Biochem,* 61:1213-1230, 1992.

Blau, H.M., G.K. Pavlath, E.C. Hardeman, C.P. Chiu, L. Silberstein, S.G. Webster, S.C. Miller, C. Webster, Plasticity of the differentiated state, *Science,* 230:758-766, 1985.

Braude, P., V. Bolton, S. Moore, Human gene expression first occurs between the four- and eight-cell stages of preimplantation development, *Nature,* 332:459-461, 1988.

Briggs, R., T.J. King, Transplantation of living nuclei from blastula cells into enucleated frogs' eggs, *Proc Natl Acad Sci U S A,* 38:455-463, 1952.

Campbell, K.H., P. Loi, P. Cappai, I. Wilmut, Improved development to blastocyst of ovine nuclear transfer embryos reconstructed during the presumptive S-phase of enucleated activated oocytes, *Biol Reprod,* 50:1385-1393, 1994.

Campbell, K.H., J. McWhir, W.A. Ritchie, I. Wilmut, Sheep cloned by nuclear transfer from a cultured cell line, *Nature,* 380:64-66, 1996.

Campbell, K.H., W.A. Ritchie, I. Wilmut, Nuclear-cytoplasmic interactions during the first cell cycle of nuclear transfer reconstructed bovine embryos: Implications for deoxyribonucleic acid replication and development, *Biol Reprod,* 49:933-942, 1993.

Capecchi, M.R., The new mouse genetics: Altering the genome by gene targeting, *Trends Genet,* 5:70-76, 1989.

Cheong, H.T., Y. Takahashi, H. Kanagawa, Birth of mice after transplantation of early cell-cycle-stage embryonic nuclei into enucleated oocytes, *Biol Reprod,* 48:958-963, 1993.

Chiu, C.P., C.B. Harley, Replicative senescence and cell immortality: The role of telomeres and telomerase, *Proc Soc Exp Biol Med,* 214:99-106, 1997.

Collas, P., J.J. Balise, J.M. Robl, Influence of cell cycle stage of the donor nucleus on development of nuclear transplant rabbit embryos, *Biol Reprod*, 46:492-500, 1992.

Collas, P., F.L. Barnes, Nuclear transplantation by microinjection of inner cell mass and granulosa cell nuclei, *Mol Reprod Dev*, 38:264-267, 1994.

Colman, A., Production of proteins in the milk of transgenic livestock: Problems, solutions, and successes, *Am J Clin Nutr*, 63:639S-645S, 1996.

Fulka, J., Jr., N.L. First, R.M. Moor, Nuclear transplantation in mammals: Remodeling of transplanted nuclei under the influence of maturation promoting factor, *Bioessays*, 18:835-840, 1996.

Fundele, R.H., M.A. Surani, Experimental embryological analysis of genetic imprinting in mouse development, *Dev Genet*, 15:515-522, 1994.

Gage, F.H., J. Ray, L.J. Fisher, Isolation, characterization, and use of stem cells from the CNS, *Annu Rev Neurosci*,18:159-192, 1995.

Graham, C. F., The fusion of cells with one- and two-cell mouse embryos, *Wistar Inst Symp Monogr*, 9:19-35, 1969.

Gurdon, J.B., *The Control of Gene Expression in Animal Development*, Oxford: Clarendon Press, 1974.

Gurdon, J.B., The developmental capacity of nuclei taken from intestinal epithelium cells of feeding tadpoles, *J Embryol Exp Morphol*, 10:622-640, 1962.

Gurdon, J.B., R.A. Laskey, O.R. Reeves, The developmental capacity of nuclei transplanted from keratinized skin cells of adult frogs, *J Embryol Exp Morphol*, 34:93-112, 1975.

Houdebine, L.M., Production of pharmaceutical proteins from transgenic animals, *J Biotechnol*, 34:269-287, 1994.

Iannaccone, P.M., G.U. Taborn, R.I. Garton, M.D. Caplice, D.R. Brenin, Pluripotent embryonic stem cells from the rat are capable of producing chimeras, *Dev Biol*, 163:288-292, 1994.

Latham, K.E., J.I. Garrels, D. Solter, Alterations in protein synthesis following transplantation of mouse 8-cell stage nuclei to enucleated 1-cell embryos, *Dev Biol*, 163:341-350, 1994.

Mantell, L.L., C.W. Greider, Telomerase activity in germline and embryonic cells of *Xenopus*, *EMBO J*, 13:3211-3217, 1994.

Matsui, Y., K. Zsebo, B.L.M. Hogan, Derivation of pluripotential embryonic stem cells from murine primordial germ cells in culture, *Cell*, 70:841-847, 1992.

McGrath, J., D. Solter, Inability of mouse blastomere nuclei transferred to enucleated zygotes to support development in vitro, *Science*, 226:1317-1319, 1984.

Moore, T., D. Haig, Genomic imprinting in mammalian development: A parental tug-of-war, *Trends Genet, 7*:45-49, 1991.

Nagy, A., J. Rossant, R. Nagy, W. Abramow-Newerley, J.C. Roder, Derivation of completely cell culture-derived mice from early passage embryonic stem cells, *Proc Natl Acad Sci U S A, 90*:8424-8428, 1993.

Prather, R.S., N.L. First, Cloning embryos by nuclear transfer, *J Reprod Fertil Suppl*, 41:125-134, 1990.

Prather, R.S., M.M. Sims, N.L. First, Nuclear transplantation in early pig embryos, *Biol Reprod*, 41:414-418, 1989.

Pursel, V.G., C.A. Pinkert, K.F. Miller, D.J. Bolt, R.G. Campbell, R.D. Palmiter, R.L. Brinster, and R.E. Hammer, Genetic engineering of livestock, *Science*, 244:1281-1288, 1989.

Robertson, E.J., Pluripotential stem cell lines as a route into the mouse germ line, *Trends Genet*, 2:9-13, 1986.

Rossant, J., Postimplantation development of blastomeres isolated from 4- and 8-cell eggs, *J Embryol Exp Morph*, 36:283-290, 1976.

Rossant, J., R.A. Pedersen, *Experimental Approaches to Mammalian Embryonic Development*, Cambridge: University Press, 1986.

Schultz, R.M., Regulation of zygotic gene activation in the mouse, *BioEssays*, 15:531-538, 1993.

Sims, M., N.L. First, Production of calves by transfer of nuclei from cultured inner cell mass cells, *Proc Natl Acad Sci U S A*, 91:6143-6147, 1994.

Smith, L.C., I. Wilmut, Influence of nuclear and cytoplasmic activity on the development in vivo of sheep embryos after nuclear transplantation, *Biol Reprod*, 40:1027-1035, 1989.

Solter, D., Differential imprinting and expression of maternal and paternal genomes, *Annu Rev Genet*, 22:127-146, 1988.

Stice, S.L., C.L. Keefer, Multiple generational bovine embryo cloning, *Biol Reprod,* 48:715-719, 1993.

Stice, S.L., C.L. Keefer, L. Matthews, Bovine nuclear transfer embryos: Oocyte activation prior to blastomere fusion, *Mol Reprod Dev,* 38:61-68, 1994.

Stice, S.L., N.S. Strelchenko, C.L. Keefer, L. Matthews, Pluripotent bovine embryonic cell lines direct embryonic development following nuclear transfer, *Biol Reprod,* 54:100-110, 1996.

Thomson, J.A., J. Kalishman, T.G. Golos, M. Durning, C.P. Harris, R.A. Becker, and J.P Hearn, Isolation of a primate embryonic stem cell line, *Proc Natl Acad Sci U S A,* 92:7844-7848, 1995.

Ward, K.A., C.D. Nancarrow, The commercial and agricultural applications of animal transgenesis, *Mol Biotechnol,* 4:167-178, 1995.

Weintraub, H., The MyoD family and myogenesis: Redundancy, networks, and thresholds, *Cell,* 75:1241-1244, 1993.

Weiss, M.J., S.H. Orkin, In vitro differentiation of murine embryonic stem cells: New approaches to old problems, *J Clin Invest,* 97:591-595, 1995.

Wheeler, M.B., Development and validation of swine embryonic stem cells: A review, *Reprod Fertil Dev,* 6:563-568, 1994.

Willadsen, S.M., Nuclear transplantation in sheep embryos, *Nature,* 320:63-65, 1986.

Willadsen, S.M., The development capacity of blastomeres from 4- and 8-cell sheep embryos, *J Embryol Exp Morphol,* 65:165-172, 1981.

Wilmut, I., A.E. Schnieke, J. McWhir, A.J. Kind, K.H. Campbell, Viable offspring derived from fetal and adult mammalian cells, *Nature,* 385:810-813, 1997.

Yang, X., S. Jiang, A. Kovacs, R.H. Foote, Nuclear totipotency of cultured rabbit morulae to support full-term development following nuclear transfer, *Biol Reprod,* 47:636-643, 1992.

CLONING HUMAN BEINGS

Views of Scientific Societies and Professional Associations on Human Nuclear Transfer Cloning Research

Commissioned Paper
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CONTENTS

PREFACE

In response to the news of the cloning of Dolly, a Scottish mountain sheep, President Clinton asked the National Bioethics Advisory Commission (NBAC) to report to him on the legal and ethical issues that cloning raises in regard to its potential use in human beings. To obtain the views of the scientific community, the NBAC asked a number of scientific societies and professional associations for their opinions on the use of nuclear transfer cloning using embryonic or adult human donor nuclei for three general areas of research: (1) basic developmental biology conducted in vitro on embryos up to day 14; (2) in vitro cell differentiation to generate specific human cell types for potential cell based therapies; and (3) the generation of cloned offspring for the treatment of infertility or related reproductive reasons.

This report summarizes the responses of the scientific organizations to the NBAC questions about human nuclear transfer research, as well as their general comments about the risks and benefits, possible restrictions, and the ethical and religious issues connected with human cloning research. It was prepared by RAND's Critical Technologies Institute (CTI) in response to a request from the Ad-hoc Cloning Science Working Group of the NBAC, and is intended for inclusion in the NBAC's report to the President on legal and ethical issues involved in the cloning of human beings. The author is an American Association for the Advancement of Science Fellow at CTI.

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> Improve understanding in both the public and private sectors of the ways in which technological efforts can better serve national objectives.

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SUMMARY

The cloning of Dolly, a Scottish mountain sheep, has brought into sharp focus the possibility of cloning human beings along with all its inherent moral, ethical and legal implications. On February 24, 1997, President Clinton asked the National Bioethics Advisory Commission (NBAC) to deliver a report to him within 90 days on the legal and ethical issues involved in the cloning of human beings and "possible federal actions to prevent its abuse." On March 4, 1997, President Clinton imposed a ban on the use of federal money for cloning human beings and asked for a voluntary moratorium by researchers working with private money until he receives the report from the NBAC.

As an aid to its deliberations, the NBAC requested that a number of scientific societies and professional associations provide their views about the use of nuclear transfer cloning, using either embryonic or adult human donor nuclei, for three general areas of research: (1) basic developmental biology conducted in vitro on embryos up to day 14; (2) in vitro cell differentiation to generate specific human cell types for potential cell-based therapies; and (3) the generation of cloned offspring for the treatment of infertility or related reproductive reasons. Thirty-two societies and associations responded to the Commission's request,[1] providing comments not only on the science of human nuclear transfer cloning, but on the associated risks and benefits, and ethical and policy issues as well.

The societies and associations made a clear distinction between the use of human nuclear transfer cloning for the purposes of research and for the cloning of an entire human being. The majority of respondents did not support cloning to produce a new individual. Although the societies and associations were asked to comment on the use of either embryonic or adult donor nuclei, the majority of respondents made no distinction between these two sources of donor nuclei.

The majority of societies and associations stated that research on basic developmental biology or new cell-based therapies should be allowed to proceed freely with proper peer review to ensure that established scientific and ethical principles are not violated. The overwhelming view was that the potential benefits of cell-based therapies far outweighed the risks of the research, and that the many possible contributions to science and medicine warranted this type of research. Prohibition or excessive regulation of this technology could limit our knowledge of the genetic

basis of diseases, such as certain birth defects, inherited disorders, and cancer, and impede the development of new therapies with the potential to help many people.

In contrast to their views on the use of nuclear transfer cloning for basic developmental biology and cell-based therapies, the majority of the societies and associations agreed that the generation of cloned offspring should be prohibited entirely at this time. Most of the objections centered on (1) ethical issues of personal and social well being, such as family relationships, identity, individuality, psychological impact, and expectations of sameness; and (2) scientific issues such as the low efficiency of nuclear transfer cloning and the high likelihood of abnormal offspring. The concerns of several respondents were nicely captured in statements made by the American Medical Association (AMA). The AMA, founded on the principle that physicians practice medicine within set standards of professional conduct and are bound by a code of ethics, stated, "Cloning as an approach to medical infertility has ethical hazards in the areas of confidentiality, consent, and discrimination. This and risks to personal and social well being would prevent professional endorsement at the present time." The AMA also stated, "Cloning as an approach to terminal illness or population enhancement is not acceptable medical practice." Finally, the AMA indicated that even if animal cloning technology ever met standards sufficient to permit clinical trials, it would still be necessary to establish that cloning offered an equal or better approach than existing therapy.

Several respondents were concerned that an ambiguous definition of "cloning" might interfere with valuable medical research. To avoid inadvertently prohibiting important genetic research, they argued that there needs to be a clear distinction between human cloning to produce a new human being, and cloning as a tool in biomedical research that in and of itself would not result in a new human being. Although most respondents indicated that cloning to produce a new human being was practically and morally unacceptable, they did not advocate legislation to prohibit research in this area. Instead, a voluntary moratorium was proposed. Because the prospect of cloning an entire human being is so preliminary at this stage, a voluntary moratorium would allow additional time to consider the scientific, ethical, social, and legal bases of such research. In contrast, most of the societies and associations indicated that there should be no new restrictions on nuclear transfer cloning for biomedical research beyond those already in place for similar types of research, which include (1) the obligation of researchers and physicians to observe self-restraint consistent with scientific, medical, and ethical codes of conduct; (2) oversight by the scientific community through such means as peer review and Institutional Review Boards; and (3) federal oversight, such as by a national bioethics authority, or regulation by the federal policy for the protection of human research subjects. Several respondents also stated that nuclear transfer cloning experiments should first be perfected in animal models, after which confirmatory experiments with human cells could be performed to address species variations.

It was notable that none of the societies or associations called for the enactment of federal or state legislation banning either the cloning of an entire human being, or cloning research to study basic developmental biology or to develop cell-based therapies. Several respondents specifically indicated that they opposed such legislation due to concerns that overly broad

regulations may inhibit or deter critical biomedical research. Many medicines, diagnostics, and vaccines to treat diseases such as heart attacks, cancer, diabetes, hemophilia, and hepatitis were developed with knowledge gained from the cloning of genes and cells. In addition, a legislative ban would have a force of permanence that may not be presently scientifically or ethically justified. The difference between a moratorium and legislation is that a moratorium can either be lifted in the future or made permanent when more information is available to assess the feasibility, desirability, and public acceptability of the cloning of human beings.

This summary of opinions came from a subset of the scientific and medical communities. However, it is by no means a complete account of all the scientific societies and professional associations that may have opinions on this complex issue. A more thorough investigation of the issues may provide many more important points of view and information critical to a decision on the allowability of human nuclear transfer cloning research.

ACKNOWLEDGMENTS

The author would like to thank the scientific societies and professional associations for their timely and informative response to the NBAC's request for input on the issue of human nuclear transfer cloning. The guidance, input, and review by Carol Greider, David Cox, Steven Holtzman, and Diane Scott-Jones from the NBAC Ad-hoc Cloning Science Working Group were invaluable for the preparation of this document. The author would also like to thank Rachel Levinson from the Office of Science and Technology Policy for the opportunity to work with the NBAC on this project. She would also like to thank the NBAC Staff—Henrietta Hyatt-Knorr, Patricia Norris, and Robin Dorsey—for their help in soliciting and compiling the society and association responses. The author is also very grateful to her colleagues at RAND—Richard A. Rettig, Katherine Webb, and David Adamson—for their quick and thorough review of this document.

LIST OF ABBREVIATIONS

CTI	Critical Technologies Institute
FDA	Food and Drug Administration
IRB	Institutional Review Board
NBAC	National Bioethics Advisory Commission
NIH	National Institutes of Health
RAC	Recombinant DNA Advisory Committee
Ref #	Reference number

INTRODUCTION

The first and only mammal to be cloned from an adult cell, the sheep named Dolly has brought into sharp focus the possibility of cloning human beings along with all its inherent moral, ethical, and legal implications. On February 24, 1997, President Clinton asked the National Bioethics Advisory Commission (NBAC) to deliver a report to him within 90 days on the legal and ethical

issues involved in the cloning of human beings and "possible federal actions to prevent its abuse." On March 4, 1997, President Clinton imposed a ban on the use of federal money for cloning human beings and asked for a voluntary moratorium by researchers working with private money until he receives the report from the NBAC.

The nuclear transfer technique that was used to clone Dolly from the udder of an adult sheep is not new technology. This technology has been used since the early 1960s to answer the question of whether the genetic material of differentiated cells from adult animals is irreversibly modified. Nuclear transfer experiments, first performed in amphibians in the 1960s, in mice in the 1970s, in sheep in the 1980s, and in monkeys in the 1990s have provided evidence that fully differentiated somatic cells retain all the genetic material of the early embryo, and that differentiation is almost entirely achieved by reversible changes in gene expression (Rossant 1997, Wilmut et al. 1997).

The nuclear transfer technology that produced Dolly is not new to Ian Wilmut and his group in Scotland, either. They have been studying the control of cell development for over ten years, and just last year published a report of the first mammal to be cloned from an established cell line (Campbell et al. 1996). Their major contributions to this area of research are (1) the complete genetic material from an adult mammalian cell has been used in the development of a new individual for the first time; and (2) donor cells, induced to exit the growth phase and become quiescent before being used for nuclear transfer, are more susceptible to reprogramming by the recipient egg cell and result in the normal development and birth of cloned offspring (Campbell et al. 1996, Wilmut et al. 1997).

In order to fully evaluate the issues that nuclear transfer cloning raises, the NBAC requested input from a wide cross-section of the scientific community. Various scientific societies and professional associations (hereafter "societies") were asked for their views on the use of nuclear transfer cloning, using embryonic or adult human donor nuclei, for three general areas of research: (1) basic developmental biology conducted in vitro on embryos up to day 14; (2) in vitro cell differentiation to generate specific human cell types for potential cell-based therapies; and (3) the generation of cloned offspring for the treatment of infertility or related reproductive reasons.

This report summarizes the responses of the scientific organizations to the NBAC questions about human nuclear transfer research, and describes their general comments about the risks and benefits, possible restrictions, and the ethical and religious issues connected with human cloning research. The strategy for soliciting input from the societies on human nuclear transfer is also presented.

STRATEGY FOR SOLICITING INPUT FROM SOCIETIES ON HUMAN NUCLEAR TRANSFER CLONING

In an effort to form recommendations that best represent the scientific community, the NBAC sought input from scientific societies and professional associations on the human nuclear transfer

cloning issue. Because of time constraints, it was not possible to mount a systematic survey of the members of the societies. Instead, the NBAC requested help from society and association leaders to obtain an informal assessment of the views held by their members, with the knowledge that the responses may only reflect the views of the leadership, or may even be the personal opinion of the respondent. The societies were asked to provide feedback regarding the appropriateness of pursuing six types of research (Questions 1–6):

1. Nuclear transfer cloning using *adult* human donor nuclei for basic developmental biological research on early embryos up to 14 days post fertilization, but not for ultimate implantation, gestation, and birth.

2. Nuclear transfer cloning using *embryonic* human donor nuclei for basic developmental biological research using early embryos up to 14 days post fertilization, but not for ultimate implantation, gestation, and birth.

3. Nuclear transfer cloning using *adult* human donor nuclei for research purposes on in vitro cell-differentiation to generate specific human cell types for potential cell-based therapies.

4. Nuclear transfer cloning using *embryonic* human donor nuclei for research purposes on in vitro cell-differentiation to generate specific human cell types for potential cell-based therapies.

5. Nuclear transfer cloning using *embryonic* human nuclei for research toward generating cloned offspring in the treatment of infertility or related reproductive reasons.

6. Nuclear transfer cloning using *adult* human nuclei for research toward generating cloned offspring in the treatment of infertility or related reproductive reasons.

The societies and associations were asked to indicate whether each kind of research should be (1) prohibited entirely, (2) allowed in some limited circumstances, or (3) allowed freely. They were also asked for the reasoning behind their answers, what types of limited circumstances they envisioned, and their views on why nuclear transfer cloning experiments using either embryonic or adult donor cells should be allowed or prohibited.

SOCIETY RESPONSES TO QUESTIONS ABOUT THE USES OF NUCLEAR TRANSFER CLONING

Thirty-two societies responded to the NBAC's request.[2] Table 1 lists the societies that responded, the corresponding reference number (Ref #) used in this report, and notes whether the response provided was in an official or personal capacity. In addition, four societies stated that they could not respond in the time allotted. Twenty-five of the 32 responses presented the official views of the society, while 7 represented the personal views of the respondent. Some of the societies that responded in an official capacity qualified their responses: eight stated that their responses

represented the leadership and not necessarily that of the entire membership; one submitted the consensus view of the society's Public Policy Committee; and one gave an impression of the views of the society's members. Six respondents provided general comments about their views on cloning, but did not directly address the six research areas (Questions 1–6) defined by the NBAC. Seven societies had no official position on human cloning or on the six proposed research areas. Nineteen respondents specifically addressed Questions 1–6.

Table 2 summarizes the responses of the scientific societies and professional associations on the six areas of human nuclear transfer research described in Questions 1–6. It is interesting to note that even though the societies were asked to comment on the use of either embryonic or adult donor nuclei, the majority of respondents did not differentiate between these two sources of donor nuclei. Three respondents specifically stated that they drew no distinction between the use of adult or embryonic nuclei, when used for in vitro purposes, on the assumption that such use be subject to usual ethical approval constraints (13, 32, 34).

Of the 19 respondents commenting on Questions 1–6, four represented the personal views of the respondent, and 15 represented the official views of the society. The majority of respondents stated that nuclear transfer cloning should be allowed freely for in vitro research on basic developmental biology (Questions 1 and 2) or for the in vitro generation of specific cell types for potential cell-based therapies (Questions 3 and 4). In contrast, the majority of respondents stated that the use of nuclear transfer cloning for the generation of cloned offspring in the treatment of infertility or related reproductive reasons (Questions 5 and 6) should be prohibited entirely.

A few respondents recommended that nuclear transfer cloning should be allowed only in some limited circumstances for in vitro research (Questions 1–4) or for generating cloned offspring (Questions 5 and 6). The types of limitations cited included the requirements that nuclear transfer cloning experiments be conducted under strict regulations and safeguards, and first be perfected in animal models. Although the majority of societies distinguished the cloning of human beings from the use of cloning for the purposes of research, three respondents stated that all research with nuclear transfer cloning, including creating entire human beings, should be allowed freely (10, 15, 24). In contrast, two respondents stated that all research with nuclear transfer cloning, including research not intended for implantation, gestation, and birth, should be prohibited entirely by enforcing a moratorium (12, 21).

Table 1. Respondents to the NBAC's Request for Input on the Issue of Nuclear Transfer Cloning

Society/Association	Ref #	Official/Personal	Comments
Norman Abeles Department of Psychology Michigan State University	1	personal	
American Association for the Advancement of Science (AAAS)	2	official	
American Association of Colleges of Pharmacy	3	official	
American Association of State Colleges and Universities	4	official	
American Board of Medical Genetics	5	official	
American College of Medical Genetics	6	official	leaders
American College of Obstetricians & Gynecologists	7	n/a	could not respond in time
American Federation for Clinical Research	8	n/a	could not respond in time
American Medical Association	9	official	
American Psychological Association	10	official	leaders
American Psychological Association Norman, Abeles, President	10a	official	
American Public Health Association	11	n/a	could not respond in time
American Society for Cell Biology	12	official	consensus
American Society for Human Genetics	13	official	
American Society for Reproductive Medicne	14	official	leaders
American Society of Parasitologists	15	official	leaders
Association of American Universities	16	official	
O. W. Barnett North Carolina State University, College of Agriculture and Life Sciences	17	personal	
Biotechnology Industry Organization (BIO)	18	official	
Council of Scientific Society Presidents	19	official	
Entomological Society of America	20	personal	
Federation of American Societies for Experimental Biology (FASEB)	21	personal	colleagues

Table 1. Respondents to the NBAC's Request for Input on the Issue of Nuclear Transfer Cloning (cont.)

Society/Association	Ref #	Official/Personal	Comments
Genetics Society of America	22	official	Board of Directors
Tony E. Hugli, Ph.D. Scripps Research Institute	23	personal	
Brian W. J. Mahy, Ph.D. National Center for Infectious Diseases, Centers for Disease Control and Prevention	24	personal	
National Academy of Sciences	25	personal	
National Advisory Board on Ethics in Reproduction (NABER)	26	official	leaders
National Health Lawyers Association	27	official	
Pharmaceutical Research & Manufacturers of America (PHARMA)	28	official	
Public Responsibility in Medicine and Research (PRIM&R/ARENA)	29	official	impression
Society for Assisted Reproductive Technology	30	official	leaders
Society for Clinical Trials	31	official	impression
Society for Developmental Biology	32	official	leaders
Society for Neuroscience	33	official	
Society of Integrative and Comparative Biology	34	official	
Society of Research Administrators	35	official	
Society of Research in Child Development	36	n/a	could not respond in time

Key

n/a = not applicable
no position = respondent has no official position on the issue
Board of Directors = circulated to the Board of Directors
colleagues = prevailing opinions of colleagues at recent professional meetings
consensus = consensus view of Society=s Public Policy Committee
impression = represents responders impression of the views of Society members
leaders = view of society/association leadership and not necessarily entire membership

Table 2. Summary of Scientific Societies' and Professional Associations' Views on the Issue of Human Nuclear Transfer Cloning

	Response of Scientific Societies/Professional Associations (number responding)			
Questions	**Prohibited entirely**	**Allowed in some limited circumstances**	**Allowed freely**	**No Position**
(1) Nuclear transfer cloning using *adult* human donor nuclei for basic developmental biological research on early embryos up to 14 days post fertilization, but not for ultimate implantation, gestation, and birth.	3	2	14	7
(2) Nuclear transfer cloning using *embryonic* human donor nuclei for basic developmental biological research using early embryos up to 14 days post fertilization, but not for ultimate implantation, gestation, and birth.	3	2	14	7
(3) Nuclear transfer cloning using *adult* human donor nuclei for research purposes on in vitro cell differentiation to generate specific human cell types for potential cell-based therapies.	2	5	12	7
(4) Nuclear transfer cloning using *embryonic* human donor nuclei for research purposes on in vitro cell differentiation to generate specific human cell types for potential cell based therapies.	3	5	11	7
(5) Nuclear transfer cloning *embryonic* human nuclei for research toward generating cloned offspring in the treatment of infertility or related reproductive reasons.	13	1	4	8
(6) Nuclear transfer cloning using adult human nuclei for research toward generating cloned offspring in the treatment of infertility or related reproductive reasons.	14	1	3	8

* 4/19 responses to questions 1–6 were personal views
* 5 additional societies officially replied
* 15/19 responses to questions 1–6 were official views but did not directly answer questions 1–6
* all responses of no position were official views

Specific Comments on Questions 1 and 2

Question 1: *Nuclear transfer cloning using adult human nuclei for basic developmental biological research on early embryos up to 14 days post fertilization, but not for ultimate implantation, gestation, and birth.*

Question 2: *Nuclear transfer cloning using embryonic human nuclei for basic developmental biological research on early embryos up to 14 days post fertilization, but not for ultimate implantation, gestation, and birth.*

The majority of respondents stated that using either embryonic or adult human donor nuclei for nuclear transfer cloning for in vitro research to study basic developmental biology should be allowed freely (6, 9, 10, 13, 14, 15, 18, 19, 24, 25, 26, 28, 31, 34). Several respondents indicated that this research should be allowed to proceed since it is promising, may prove extremely beneficial to medicine, does no harm, and is intended to benefit people (13, 14, 19, 26, 31, 34). This type of research may be necessary for understanding the scientific basis of cellular differentiation (10). It may also provide new and needed information about the morphology, biochemical and biophysical properties, genetic expression, and similar biological characteristics of pre-gastrulation-stage human embryos (14). Such research could also help improve the understanding of the origin of certain birth defects, increase the knowledge about cancer and metastasis, and explore ways to circumvent disease and inherited disorders of defects (14). The needed advancement within this important field of biological science warrants the use of early-stage embryos (14). It was pointed out that the NBAC's questions raise ethical issues surrounding research on embryos, whether or not they will be implanted (18). It was also noted that the Human Embryo Research Panel in 1994 addressed this issue and declared that early developmental research on embryos was acceptable for federal funding until the primitive streak appeared on the embryo, at approximately 14 days (18, 28). Therefore, NIH has already concluded that basic developmental research on embryos that will not be implanted is acceptable.

Those who replied that in vitro research using human nuclear transfer cloning to study basic developmental biology should be allowed only in limited circumstances thought that this research should only be conducted under strict regulations and safeguards (30, 32). Another respondent indicated that most of the basic research in this area should take place in experimental animals, but that some limited confirmatory experiments will have to take place with human cells, since species differences may occur (32).

Three respondents thought that in vitro research using human nuclear transfer cloning to study basic developmental biology should be prohibited entirely (12, 20, 21). One respondent holds a "pro-life world view" and believes that any scientific research with human embryonic tissues is immoral and unethical since it involves the ultimate death of a potentially completely unique human being (20). The other respondents called for a moratorium on all six areas of human nuclear transfer research described in Questions 1–6 to allow time for appropriate consideration of the technology's scientific and ethical implications (12, 21).

Specific Comments on Questions 3 and 4

Question 3: *Nuclear transfer cloning using adult human nuclei for research purposes on in vitro cell differentiation to generate specific human cell types for potential cell-based therapies.*

Question 4: *Nuclear transfer cloning using embryonic human nuclei for research purposes on in vitro cell-differentiation to generate specific human cell types for potential cell-based therapies.*

The majority of respondents stated that using either embryonic or adult human donor nuclei for nuclear transfer cloning research for the purpose of developing potential cell-based therapies should be allowed freely (9, 10, 15, 18, 19, 24, 25, 26, 28, 32, 34). One respondent indicated that the use of adult donor nuclei should be allowed freely (Question 3), while the use of embryonic donor nuclei should only be allowed in limited circumstances (Question 4) (14).

Several respondents indicated that research for the purpose of developing potential cell-based therapies should be allowed freely, since this research holds therapeutic promise, does no harm, the payoffs far outweigh the risks, and is intended to benefit people (10, 14, 19, 26, 34). In addition, nuclear transfer cloning of adult or embryonic nuclei to generate specific human cell types for potential cell-based therapies is a technology fundamental to developing new, more effective medicines (28, 34). Prohibition or excessive regulation of this technology could profoundly limit our knowledge of the genetic bases of disease and significantly impede or preclude the development of new, breakthrough drugs with the potential to help many people (28). This area of research holds the most future potential when combined with other approaches to cell-based therapies, such as promoting the growth of stem cells from adult tissues and generating embryonic stem cell lines (28, 32). It may also circumvent the current problems of graft rejection and scarcity of donor material (32). An example of the utility of this type of research is the possibility to develop healthy nervous system tissue and brain cells for transplantation in degenerative diseases such as Alzheimer's disease (30). It was suggested that guidelines for research using human cells in the development of cellular and tissue-based products could be coordinated with the new regulations being developed by the Food and Drug Administration (FDA), which are dependent on the origin of the cellular material as well as the intended use (18).

Some respondents thought that research using either embryonic or adult human donor nuclei for the purpose of developing potential cell-based therapies should be allowed in limited circumstances (6, 13, 30, 31). One reason for granting limited approval was that the cell-based therapies were not specified, and while some might be acceptable, others would not (31). In addition, it was suggested that there should be strict supervision with guidelines on appropriate consent by couples donating embryos (30), and that the processes and controls currently used in human gene therapy may be appropriate starting points for evaluating such experiments (6).

Two respondents indicated that there should be more limitations on the use of embryonic donor nuclei than on adult donor nuclei for research aimed at developing potential cell-based

therapies (14, 20). The view of one respondent was that the use of adult tissue for this type of research does not involve the ultimate death of a potentially complete, unique human being (20). Since the goal of this type of research is to better understand a variety of health and developmentally related subjects, the use of adult human donor nuclei was allowable with limitations, but the use of embryonic human donor nuclei should be prohibited entirely (20). The other respondent indicated that the use of adult donor nuclei for the development of cell-based therapies should be allowed freely, but research using embryonic donor nuclei could not exceed the 14-day stage of development (14). It was felt that the potential therapeutic benefits of directing cell differentiation warrant the use of early-stage embryos that are not grown beyond the 14-day limit; however, research exceeding the 14-day stage would be problematic (13, 14). In addition, before this research takes place with human cells, animal models should be used to determine whether it is feasible, possible, and/or beneficial (14, 30).

Two of the respondents indicated that research using adult human donor nuclei for the purpose of developing potential cell-based therapies should be prohibited entirely (12, 21), while three respondents stated that the use of embryonic human donor nuclei should be prohibited for this type of research (12, 20, 21). One respondent held a "pro-life world view" and believed that any scientific research with human embryonic tissues is immoral and unethical since it involves the ultimate death of a potentially completely unique human being (20). The other respondents called for a moratorium on all six areas of human nuclear transfer research described in Questions 1–6 to allow time for appropriate consideration of the technology's scientific and ethical implications (12, 21).

Specific Comments on Questions 5 and 6

Question 5: *Nuclear transfer cloning using embryonic human nuclei for research purposes towards generating cloned offspring in the treatment of infertility or related reproductive reasons.*

Question 6: *Nuclear transfer cloning using adult human nuclei for research purposes towards generating cloned offspring in the treatment of infertility or related reproductive reasons.*

The majority of respondents stated that using either embryonic or adult human donor nuclei for nuclear transfer cloning research toward generating cloned offspring in the treatment of infertility or related reproductive reasons should be prohibited entirely (6, 9, 12, 13, 14, 18, 20, 21, 26, 30, 31, 32, 34). One respondent indicated that using embryonic donor nuclei should be allowed in limited circumstances, but the use of adult donor nuclei should be prohibited entirely because there is no therapeutic benefit in cloning an existing or previously existing person (14).

The reasons given for entirely prohibiting research aimed at generating cloned offspring in the treatment of infertility or related reproductive reasons were similar for the use of either embryonic or adult human donor nuclei. The objections to this type of research included the observation that it would be years before the scientific data existed to determine if such

experiments were even feasible (6, 25). It was also pointed out that the efficiency of nuclear transfer is so low and the chance of abnormal offspring so high that experimentation of this sort in humans is currently unthinkable (13, 18, 19, 25, 32). It was suggested that an imposed moratorium would allow time for the appropriate consideration of the technology's scientific and ethical implications (12, 13, 18).

The concerns of several of the societies were nicely captured by one respondent: "Cloning as an approach to medical infertility has ethical hazards in the areas of confidentiality, consent, and discrimination. This and risks to personal and social well-being would prevent professional endorsement at the present time" (9). The respondent also stated, "Cloning as an approach to terminal illness or population enhancement is not acceptable medical practice" (9). Finally, the respondent indicated that even if animal cloning technology ever met sufficient standards that clinical trials might be permissible, it would still be necessary to establish that cloning offered an equal or better approach than existing therapy (9).

Most of the objections to the generation of cloned offspring centered on ethical issues. Further discussion and consideration of the ethics of generating cloned offspring would be desirable due to the potential implications for society in general (31, 34). It was asserted that "the deliberate generation of human clones impinges on the dignity and integrity of the human as an individual," and even though the therapeutic objectives of such studies might be to help infertile couples, it would be achieved at great cost to the offspring (32). "Humans cherish their uniqueness and an attempt to deliberately clone another human being involves an inescapable element of coercion, since the perpetrator has chosen to transcend the normal means of reproduction in order to produce a genetic copy of himself" (32). Although most of the respondents indicated that research in this area was practically and/or morally unacceptable, they were reluctant to advocate legislative prohibition of research in this area. Instead, a voluntary moratorium was proposed on such research (12, 13, 18, 21, 32).

A few respondents stated that nuclear transfer cloning using embryonic (10, 15, 19, 24) or adult (10, 15, 24) human donor nuclei for research toward generating cloned offspring in the treatment of infertility or for related reproductive reasons should be allowed freely. It was felt that the payoff far outweighed the risks and that this research did no harm and was intended to benefit people (19).

One respondent stated that nuclear transfer cloning using embryonic human donor nuclei for research toward generating cloned offspring in the treatment of infertility or related reproductive reasons should be allowed with limitations (14). The use of embryonic nuclear transfer technology might be a viable option for an infertile couple as long as all other types of treatment had been exhausted (14). For example, age-related infertility may be treated by transferring the nuclei of a couple's early embryo, produced in vitro, into a younger woman's enucleated egg to overcome problems encountered by older women (e.g., the outer layer of an older woman's egg, the zona pellucida, can be tough and not allow for cell division to occur freely; the cytoplasm and mitochondria of an older woman's oocyte are more likely to be

dysfunctional; and an older woman is more likely to produce a small number of embryos appropriate for transfer, and through nuclear transfer cloning, the number of embryos for transfer could be increased, thereby improving the likelihood of successful implantation and delivery) (14). However, if this type of infertility treatment were allowed, careful limits would need to be set as to the number of nuclei that can be used from the early embryo and the timing of the transfer of cloned embryos (14). In addition, if any resulting cloned embryos are cryopreserved, they should only be used in the event of a prior unsuccessful pregnancy attempt (14).

Another respondent stated that because nuclear transfer cloning using adult human donor nuclei for research toward generating cloned offspring raises both scientific and emotional issues of concern, it should be allowed with limitations (19). Specifically, it would be necessary to perform animal experiments before any human experiments were done since it is not known if clones of adult cells will produce harmed offspring (19). In addition, there are several emotional issues connected with this technology, including religious and other beliefs that married sex should produce all offspring, and the fear that creating a clone will diminish the donor in some fashion (19). The respondent stated that this research should be not be subject to legislation, but to oversight by the leaders of the relevant parts of the scientific community, perhaps as formal as the Recombinant DNA Advisory Committee (RAC), but certainly with a sunset for such an oversight (19).

GENERAL COMMENTS ABOUT HUMAN NUCLEAR TRANSFER CLONING

The general comments made by the scientific societies and professional associations fall into six categories: (1) definition of cloning; (2) knowledge gained and potential uses; (3) potential risks and scientific constraints; (4) restrictions, regulations, or legislation; (5) ethical and religious issues; and (6) general comments.

Definition of Cloning

To avoid inadvertently prohibiting important genetic research, there needs to be a clear distinction between human cloning to produce a new human being and cloning as tool in biomedical research that in and of itself would not result in a new human being (9, 12, 13, 18, 22, 25, 28, 30). According to these respondents, it would be unfortunate if an ambiguous definition of “cloning” interfered with valuable medical research.

“Cloning” is the copying of biological material to produce identical genetic copies from a single entity, such as genes, cells, or organisms. Scientists use the word “cloning” in many different ways. The term “human cloning” is routinely used to describe accepted and approved research such as (1) “clones” of human genes placed into various cell types to study their function; (2) human genes “cloned” into bacteria to produce proteins for therapeutic purposes (e.g., the production of Factor VIII to treat hemophilia, and the production of interferon- for the treatment of cancer); and (3) “cloning” of human cells for the study of cancer or genetic diseases.

These types of cloning are integral tools in biotechnology, and have been used to produce breakthrough medicines, diagnostics, and vaccines to treat heart attacks, cancer, kidney disease, diabetes, hepatitis, multiple sclerosis, cystic fibrosis, and other diseases (18).

Knowledge Gained and Potential Uses

Human nuclear transfer research could possibly revolutionize and certainly advance our understanding of basic developmental biology by (1) addressing how cells become different from each other during the development of an organism from egg to adult (32); (2) confirming that the genetic material of adult cells is intact and potentially "totipotent" (i.e., totally capable of recreating an adult organism) (32); and (3) advancing our knowledge of fundamental processes such as how genes control human development and how an oocyte can reprogram the adult nucleus (12, 18, 32). A full understanding of how the oocyte can reprogram the adult nucleus holds great hope for research of cell-based therapies for human genetic and degenerative diseases, and for developing novel strategies for the repair and regeneration of human tissues (32). In the decades ahead, these fundamental insights will provide the basis for even greater biomedical advances in the service of humanity (18).

Any decision to clone or permit cloning of humans has enormous potential for impacting our basic understanding about human development, capabilities, relationships, and rights (10a). In addition, human nuclear transfer research may provide new insights into reproductive biology, create improved animal models for human disease, and generate farm animals for the production of rare and currently expensive protein therapeutics (12).

Potential Risks and Scientific Constraints

Human nuclear transfer cloning using either embryonic or adult human donor nuclei to produce a new human being poses several potential risks, which were cited as reasons to limit or prohibit this activity. The most commonly stated risk was that the efficiency of nuclear transfer is so low and the chance of abnormal offspring so high that experimentation of this sort in humans is premature and, therefore, currently unthinkable (13, 18, 19, 23, 25, 32).

Several respondents agreed that nuclear transfer cloning experiments must be perfected first in animal models, and that it would be inappropriate to "waste" human tissues, cells, and even embryos in attempts to perfect techniques that could first be perfected in other species (6, 13, 14, 18, 19, 23, 25, 32). It was also suggested that it may be possible to adequately investigate, advance, and perfect the technology—as it may apply to man—using non-human primates, which should not prevent, inhibit, or delay the research in cloning technology (13, 23). Risks associated with the technology that might be tolerated in the case of farm animals would never be tolerated were the technology to be applied to human beings (18).

Even if this technology is perfected in animals, there will eventually be a need for human experiments (6, 32). The human species will provide more than a few surprises, and techniques

that work wonderfully in animals may fail dismally in human experiments (6, 32). Since the embryology of each species is different and very little basic research in human embryology has been performed, much more preliminary data is necessary before appropriate scientific protocols could be developed (18). Even after all of the procedures were verified and optimized, there is a high probability that many human eggs, as well as surrogate mothers, would be necessary to establish this technique as a reliable method of developing new human beings (18). Therefore, the use of nuclear transfer technology for the generation of entire human beings is neither feasible nor ethically acceptable at this time (6, 13, 18, 23, 25, 32).

Restrictions, Regulations, or Legislation

The types of restrictions proposed for the cloning of an entire human being included oversight by leaders of the scientific community, such as an Institutional Review Board (IRB), federal oversight by a national bioethics authority, and a voluntary moratorium. However, none of the societies or associations called for federal or state legislation banning the cloning of an entire human being. As for cloning research using human donor nuclei to study basic developmental biology or to develop cell-based therapies, most of the societies indicated that there should be no new restrictions on nuclear transfer cloning for biomedical research beyond those already in place for similar types of research, which include (1) the obligation of researchers and physicians to observe self-restraint because of scientific, medical, and ethical codes of conduct; (2) oversight by the scientific community, such as through peer review and by IRBs; and (3) federal oversight, such as by a national bioethics authority, or regulation by the federal policy for the protection of human research subjects. There were also a few proposals for a voluntary moratorium. Again, no one called for legislation banning cloning research. Although most of the respondents drew no distinction between the use of adult or embryonic human donor nuclei, one thought that there should be more restrictions with adult nuclei than with embryonic ones (15).

One statement seemed to capture the general feelings of most of the respondents on the issue of restrictions, regulations, and legislation:

> "Ian Wilmut's group has clarified what a number of scientific questions should be [about embryology, development, biology and developmental genetics], and that is a very great service. It would be a shame if those questions, and others, were not to be addressed because of restrictions (6)."

Self-Restraint. The scientific and medical communities subscribe to ethical codes of conduct (9, 18). Physicians have an obligation to "do no harm" to patients under the Hippocratic oath (18). Furthermore, the medical profession has taken care to uphold standards, articulated in the Helsinki Declaration and the Belmont Report, that are "consistent with medical obligations to patients and the public's health" (9). In addition, universities and companies have ethical codes of conduct for their employees (18). Scientists and physicians could jeopardize their professional standings and careers by performing ethically questionable research (18).

Oversight. Several societies and associations stipulated a need for oversight, guidelines, and strict research protocols of the highest standards when dealing with this unique field of human subjects research (1, 10, 12, 13, 14, 18, 19, 29). The importance of informed consent was also emphasized (1, 13, 30). However, it was clear that all the respondents calling for restrictions agreed that this area of research should not be subject to legislation. A suggestion was made for oversight by the leaders of the relevant parts of the scientific community, perhaps as formal as the RAC, but with a sunset provision for such oversight of some minimum necessary number of years (19). Alternatively, it was suggested that all human cloning research should obtain approval of an IRB, which could ensure that subjects are not abused, and research results are not a danger to the community (14, 29). Another suggestion was that the NBAC could become, or could appoint, a standing body to monitor and periodically report on the progress of research in this field as well as other innovative advances in reproductive biology (12, 18). Finally, it was proposed that the highest level of national oversight would be achieved if federal funding of human cloning research were allowed (14).

Voluntary Moratorium. Several societies and associations supported the President's call for a voluntary moratorium on the cloning of human beings until the NBAC reviewed the scientific, legal, and ethical implications of the recent scientific advances brought to light by the birth of Dolly (2, 6, 12, 18, 22, 28). Furthermore, three respondents proposed a continuation of this voluntary moratorium on the cloning of an entire human being beyond the 90-day review period (13, 18, 32). One recommendation was that the moratorium on research on implanted embryos derived by nuclear transfer last for three years to permit time for the consideration of the scientific, ethical, social, and legal bases for such research (13). At the end of the three-year period, all research subjected to the moratorium should again be reconsidered by the NBAC or another responsible agency (13). Two respondents called for a moratorium on all human cloning research until there has been enough time to allow for appropriate consideration of the scientific and ethical implications of the technology (12, 21). One suggestion for enforcing the moratorium was to have the NBAC appoint an international panel of eminent scientists to reinforce the call for a moratorium and to develop global research guidelines relating to nuclear transfer cloning (12). The advantage of a moratorium over legislation is that it can either be lifted in the future or made permanent, when more information is available to assess the feasibility, desirability, and public acceptability of these procedures (32).

Legislation. At least ten bills dealing with the cloning of a human being have been filed at the state level and at least three at the federal level (18). Representative Ehlers has two bills before Congress, H.R. 922 and H.R. 923, that refer simply to "human cloning" (22). Poor communication between scientists and legislators may produce an ambiguous definition of what is to be prohibited, which could result in interference with valuable life-saving and life-enhancing medical research or even practice (22). The point was made that the enactment of any state law on the subject of human cloning should be opposed because issues raised by the cloning of entire human beings should be addressed nationally and comprehensively, not on a state-by-state basis (18). A continuation of the moratorium on cloning human beings may obviate the need for any state or federal legislative action (18).

There is a fear that hastily drafted rules or legislation could inadvertently result in a much broader ban on research than intended or needed to address the ethical concerns (12, 18, 22, 29, 32). Overly broad legislation may inhibit or deter critical biomedical research that uses the cloning of genes and cells to develop future drugs for many currently incurable diseases and conditions (18). Hasty responses to profound developments or new capabilities do not always promote sound policy (29). Instead, guidelines about the use of highly controversial technologies should only follow deep and lengthy dialogue among stakeholders and advisors (29).

An example cited of policy adopted in the absence of thorough exploration of the issues is the federal ban on fetal research and the accompanying state regulations that followed (29). Massachusetts expanded the federal ban on fetal research to include neonatal research. As a result, truly critical information on normal values and measurements in neonates was not obtainable in Massachusetts. As a result, neonatologists left to work elsewhere and the care of sick neonates declined. An example of an appropriate, measured response to new technology was the development of guidelines for performing recombinant DNA technology, which resulted in a useful, reasonable, and effective national policy for regulating such research (29). Relocation of research is a common response to overly rigid controls (29). Although relocation to other academic centers has local implications, relocation of banned research to the "underground" or to foreign countries where no ethical guidelines may be observed may be a dangerous and tragic result of superficial consideration of the implications of such measures (29).

Ethical and Religious Issues

Several respondents made remarks about the potential impact of nuclear transfer cloning using adult donor nuclei to generate new individuals on issues of personal and social well-being such as family relationships, identity and individuality, religious beliefs, and expectations of sameness (6, 9, 10, 18, 19, 30). Some of respondents made very poignant remarks about these issues, which are reflected in the following comments from various society and association responses.

Family Relationships. Some respondents thought that nuclear transfer cloning using adult donor nuclei to generate an entire human being would have negative impacts on family relationships, while others believed that it would not. Some of the comments follow.

> "These new prospects [of cloning human beings from the genetic material of an adult cell] challenge some of the most fundamental concepts we hold about ourselves as social and spiritual beings. These concepts include what it means to be a parent, a brother or sister, a family" (18).

> "Unprecedented relational circumstances would or could arise. For instance, birth cousins may be genetic siblings, and marital prohibitions might be called into question" (9).

> "An additional argument against cloning is its supposed destruction of the family unit. This argument has been made with every new development in the area of reproductive medicine. I do not believe cloning will have any negative impact on the concept of family" (30).

Identity and Individuality. It was also pointed out that is not just people's genetic background, but their unique experiences, that play an essential role in determining who they are (10, 18, 30). Therefore, predictions of armies of identical individuals are not realistic (10). Other responses included the following.

> "We are quite familiar with identical twins in our everyday lives. We know, for example, that such twins have very distinct personalities despite sharing the same genetic makeup.... While we may encounter identical twins of the same age today, we have never experienced identical twins substantially different in age; indeed, perhaps alive during entirely different periods in history" (18).

> "One can make the argument that cloned children may be psychologically harmed by their lack of individual identity. However, this does not appear to be the case with identical twins and triplets" (30).

Religious Beliefs. Citizens of all religious and moral persuasions must be allowed to contribute to the discussion of cloning entire human beings (6). Three major ethics systems under which society functions—which could be used to determine how society would deal with the issue of human nuclear transfer cloning—are (1) the greatest good for the greatest number; (2) sets of rules (e.g., thou shalt not commit murder); and (3) golden rules (do unto others [Jesus] or do not unto others [Hillel]) (19). It would be inappropriate for scientists to assert that one system of ethics is better than another for this issue (19).

Expectations of Sameness. Cloning of an existing or previously existing person may be attractive as an approach to overcome terminal illness, a way to replace a deceased loved one, or simply for reasons of vanity. However, this implies that the resulting child will be identical, in all ways, to the person being cloned. In addition, there may be preconceived notions about the child's character, level of intelligence, and talents.

> "The possibility of having one's life over again, or having the life of a dying child over again might be attractive to people facing death and dying. However, this reasoning does not withstand examination.... Because the cloned individual is—because of the different environment in which he or she creates his or her life story—not the same person; then the dying individual does indeed still die and a 'second chance' is not achieved. Cloning, therefore, does not appear to be a reasonable medical approach to terminal illness" (9).

> "The idea that cloning will lead to creation of cloned children for reasons of pure vanity needs to be viewed from the perspective of the reasons why children are created by any method. There is a wide spectrum of motivations for wanting a child. Sometimes it is for pure vanity even when non-cloning (natural) methods are used. Banning reproductive use of cloning will not assure that children are produced for the right reasons. And dictating the "proper reasons" for producing a child is not an activity a government ought to be involved in" (30).

> "In our everyday lives we may decide to procreate a child and wait in wonder and awe to see the unique individual he or she will turn out to be. We do not, on the other hand, have experience creating a child where part of that decision may include an evaluation of the life, health, character, and accomplishments of an adult from whom we will take the genetic material that will become the child's entire genetic makeup" (18).

Additional Comments

"Research has always had a history of upsetting the status quo and by its very nature will always be a provocative change agent. Biotechnology now saves lives and makes for a better future. Heart transplants and gene therapy were shocking in their time; they have both become routine. In vitro fertilization, now an industry, was considered adultery only two decades ago. Our society adjusts after it has time to learn and understand the benefits [of new technologies]" (19). This remark reflects the general attitude of several of the respondents. The public reaction to the cloning of Dolly parallels the fears evoked during the early days of recombinant DNA research, plant transformation, organ transplantation, in vitro fertilization, and protocols involving genetics and gene therapy (6, 17, 19, 23, 29). Once fear was replaced by a body of evidence that demonstrated the concerns for safety were greatly exaggerated, a rational policy was developed (6, 17, 23).

Several respondents expressed their concern that 90 days is not enough time to make this type of critical decision, and that by forcing this decision to be made in such a short time frame, there may be a rush to judgment and unanticipated issues may be overlooked (6, 13, 19, 21, 22, 23, 25, 30). It was clear that the many of the respondents felt that this matter deserves a much less rushed and more thorough study and review (6, 13, 19, 21, 22, 23, 25, 30).

Correspondingly, the need to educate and inform the public, legislators, and the scientific and medical communities was thought to be vital to the understanding of these very complex issues (2, 6, 17, 19, 23, 28, 29). A place to start would be to establish a basic understanding of the special language, technologies, and issues that typify molecular biology, cell biology, and cloning protocols (29). As the public and scientists learn more about what types of cloning experiments are proposed, they will be more accepting of the technology and will become aware of the good that can result and not so afraid of the potential negative side (17).

The need for a rational, well-informed, national debate was also identified (6, 22, 23). "After the public and legislators have been better informed, and have had time to digest the implications and debate the issues pertaining to human cloning, a more enlightened policy should emerge for regulating future human experimentation" (23).

Some respondents commented that the guiding principle in the NBAC's recommendations should be the optimization of human health within moral bounds (12). Human research should be allowed freely in all circumstances that offer the promise of increased knowledge and/or potential therapeutic benefits, providing that the research does not place the subjects at a risk that outweighs the potential benefits or violate established ethical principles, that the research is properly reviewed prior to initiation, and that appropriate informed consent is obtained (13).

CONCLUSION

Thirty-two scientific societies and professional associations responded to the NBAC's request for their views on the use of nuclear transfer cloning using embryonic or adult donor nuclei for three general areas of research: (1) basic developmental biology conducted in vitro on embryos up to day 14; (2) in vitro cell differentiation to generate specific human cell types for potential cell-based therapies; and (3) the generation of cloned offspring for the treatment of infertility or related reproductive reasons.

The majority of societies agreed that research aimed at gaining knowledge in basic developmental biology or developing new cell-based therapies (areas 1 and 2 described above) should be allowed to proceed freely. It was their view that the benefits of these types of research far outweighed the risks, and the many possible contributions to science and medicine warranted this type of research.

In contrast, the majority of societies agreed that the generation of cloned human offspring, even if only used for the treatment of infertility or related reproductive reasons, should be prohibited entirely at this time. Most of the objections centered on the ethical issues of personal and social well-being. Other objections focused on scientific issues, such as the low efficiency of nuclear transfer cloning and the high likelihood of abnormal offspring.

The general comments made by the responding scientific organizations focused on five main issues:

1. the need for a clear definition of cloning to avoid inadvertently prohibiting important genetic research

2. the knowledge that was gained and potential uses of this technology

3. the potential risks and scientific constraints of this technology

4. the need for certain restrictions and regulations in the form of either self-regulation by the scientific community itself, national oversight, or voluntary moratorium, but not in the form of legislation

5. the ethical and religious issues that are brought to light by the potential to clone an existing or previously existing person.

This report summarizes the views of a cross-section of the scientific and medical communities. However, it is by no means a complete account of all the scientific societies and professional associations that may have important input into this complex issue. A more extensive investigation may provide other points of view and information critical to a decision on the allowability of human nuclear transfer cloning research.

APPENDIX: ALPHABETICAL LISTING OF SCIENTIFIC SOCIETIES AND PROFESSIONAL ASSOCIATIONS

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4. American Association of State Colleges and Universities
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References

Campbell, K.H.S., J. McWhir, W.A. Ritchie, and I. Wilmut, Sheep cloned by nuclear transfer from a cultured cell line, *Nature*, 380:64-66, 1996.

Rossant, J. The Science of Animal Cloning, paper prepared for the National Bioethics Advisory Commission, 1997.

Wilmut, I., A.E. Schnieke, J. McWhir, A.J. Kind, K.H.S. Campbell. Viable offspring derived from fetal and adult mammalian cells, *Nature*, 385:380-385, 1997.

Notes

[1]This was an informal request, not a formal survey. Most of the societies and associations did not have time to poll their members in a systematic manner. Therefore, most of the views that were expressed by the societies and associations were not necessarily representative of their entire membership.

[2]The statements in this document are the views of the societies and associations that responded to the NBAC's request, and are not those of the author, RAND Critical Technologies Institute, or the NBAC.

CLONING HUMAN BEINGS

Religious Perspectives on Human Cloning

Commissioned Paper
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CONTENTS

INTRODUCTION

In response to the cloning of a sheep in Scotland, President Clinton requested that the National Bioethics Advisory Commission (NBAC) investigate and make recommendations on the prospects of human cloning by May 26, 1997. Citing matters of morality and spirituality, the President, on March 4, 1997, imposed a temporary moratorium on federal funding of human cloning research. This paper was prepared for NBAC to assist in its deliberations and policy recommendations.

The research methods used in preparation of this report included: (1) a comprehensive review of literature in theological biomedical ethics on human cloning since the mid-1960s; (2) attendance at and review of the testimony of religious thinkers submitted at public hearings before NBAC on March 13 and 14, 1997; (3) solicitation and review of ecclesiastical statements on genetic engineering and human cloning; (4) an ongoing Nexus search to identify religious thinkers with perspectives on human cloning discussed in print media; (5) personal or telephone interviews with many of these thinkers. A bibliography of these sources is provided in appendices A and B.

The report generated from this research is organized into five sections: (1) a brief historical overview of religious thought on the ethics of human cloning; (2) a discussion of selected themes among theological bioethicists that recur frequently in ethical evaluations of human cloning. These themes are derived primarily from the scholarly literature of the western faith traditions; (3) a summary of approaches to the theology, ethics, and policy of human cloning from ten major faith traditions; (4) an appendix containing an annotated bibliography of religious literature on human cloning in biomedical ethics; (5) an appendix containing a bibliography of materials used in preparation of this report.

The author wishes to extend appreciation to NBAC for the invitation to prepare this report; to Dr. James Childress, NBAC, for procedural and substantive suggestions; to Dr. Joan Woolfrey, Oregon State University, for compilation of research materials; to librarians at the National Reference Center for Bioethics Literature, Georgetown University, and at The Hastings Center for research assistance; to many religious thinkers who provided time for interviews and provided research materials; and to Lois Summers for assistance in manuscript preparation.

RELIGION AND HUMAN CLONING: AN HISTORICAL OVERVIEW

It is possible to identify four overlapping time frames in which theologians and religious thinkers have engaged the scientific prospects and ethics of human cloning. The first phase of consideration occurred in the mid-1960s. This early discussion was shaped by a context of expanded choices and control of reproduction (for example, availability of the birth control pill), the prospects of alternative, technologically assisted reproduction (for example, in vitro fertilization, or IVF), and advocacy by prominent biologists and geneticists of cloning “preferred”

genotypes to avoid overloading the human gene pool with deleterious genes and thereby placing the survival of the human species at risk.

Prominent theologians engaged in these initial discussions of genetic manipulation and human cloning included Charles Curran, Bernard Häring, Richard McCormick, and Karl Rahner within Roman Catholicism and Protestants Joseph Fletcher and Paul Ramsey. The latter two staked out diametrically opposed positions and envisioned a world of human cloning that is remarkably prescient given the state of current discussion.

Fletcher advocated expansion of human freedom (autonomy) and control over human reproduction. He portrayed human cloning as one among a variety of present and prospective reproductive options that could be ethically justified under circumstances of overriding societal benefit. Indeed, for Fletcher, human cloning was a preferable method of reproduction relative to the "genetic roulette" of sexual reproduction: Laboratory reproduction was "radically human" because it was deliberate, designed, chosen, and willed [9–12].

By contrast, Paul Ramsey portrayed cloning as a "borderline," or moral boundary, for medicine and society that could be crossed only at risk of compromise to humanity and to procreation. He identified three "horizontal" (person-person) and two "vertical" (person-God) border-crossings of cloning: (1) Clonal reproduction would require dictated or managed breeding to serve the scientific ends of a controlled gene pool. (2) Cloning would involve non-therapeutic experimentation on the unborn. (3) Cloning would assault the meaning of parenthood by transforming "procreation" into "reproduction" and by severing the unitive and the procreative ends of human sexual expression. Theologically, cloning represented (4) the sins of pride or hubris and (5) of self-creation in which human beings aspire to become a man-God [27, 28]. The legacy of Ramsey has been especially noticeable in post-Dolly theological reflection [36].

A second distinctive era began in 1978, which was notable for two events, the birth of the first IVF baby, Louise Brown, and the publication of David Rorvik's *In His Image*, an account alleging the creation of the first human clone [30]. While Christian theologians concentrated on the ethical issues raised by IVF, Jewish scholars such as Seymour Siegel and Fred Rosner directed attention to human cloning and were neither as supportive as Fletcher nor as indicting as Ramsey. They instead expressed a need for more extensive discussion of the topic within the Jewish community.

This period also witnessed the beginning of formal ecclesiastical involvement with questions of genetic manipulation. In 1977, the United Church of Christ produced a study booklet on "Genetic Manipulation" that appears to be the earliest reference among Protestant denominational literature to human cloning [19]. It provided a general overview of the science and ethics of human cloning, while stopping short of rendering any specific theological verdict. Protestant-organized bodies, such as the World Council of Churches (1975, 1982, 1989) and the National Council of Churches of Christ (1980, 1983, 1986), as well as some individual denominations, issued resolutions or position statements giving cautious endorsement to genetic

interventions for therapeutic purposes. In addition, concerns expressed in 1979 by Jewish, Protestant, and Roman Catholic leaders about genetic engineering led President Jimmy Carter to request an examination of the scientific, ethical, and social issues of gene splicing by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.

The blastomere separation of human embryos at George Washington University in 1993 initiated a third era of religious discussion. The Roman Catholic tradition expressed vigorous opposition, with a Vatican editorial denouncing the research as "intrinsically perverse." Catholic moral theologians invoked norms of individuality, dignity, and wholeness to assess the ethics of the study [20, 21, 24, 32]. Conservative Protestant scholars held the research contravened basic notions of personhood, such as freedom, the sanctity of life, and the image of God. Other Protestant scholars recognized potential medical benefits from the research and advocated regulation rather than prohibition.

The fourth and most recent stage of religious discussion has come in the wake of the successful cloning of "Dolly" by Scottish researchers. Roman Catholic and conservative Protestant discussion has reiterated past opposition and warnings. Writing in the *Christian Century*, for example, Protestant theologian Allen Verhey has drawn on the arguments against human cloning initially voiced by Paul Ramsey and concluded that an account of the good life in a family is "inhospitable" to cloning [36, 38].

However, some Protestant thinkers, reflecting on the meaning of human partnership with ongoing divine creative activity, have expressed qualified support for cloning research and human cloning. Jewish and Islamic thinkers have encouraged continuing laboratory research on animal and human cloning, while expressing deep moral reservations about transfer of a cloned human embryo to a womb for purposes of gestation and birth. The testimony presented to NBAC in public hearings on March 13 and 14, 1997, provides the most considered statements of theological examination in this renewed discussion of the ethics of cloning research and its implications for human cloning.

Several conclusions can be drawn from this brief historical overview:

> There is a sustained theological engagement with the issue of cloning that anticipates and illuminates much contemporary discussion.
>
> There is no monolithic religious perspective on human cloning. Theological and ecclesiastical positions exhibit the pluralism characteristic of American religiosity.
>
> Despite changes in scientific research and technical capability, the *values* that underlie religious concerns about human cloning have displayed durability and staying power and have informed public consciousness and debate.

The religious discussion no longer is limited to professional theologians. It has expanded to encompass other professionals, including scientists, and other faith traditions, as well as education of religious adherents. Religious traditions have gradually aspired to be informed communities of moral discourse on issues of reproductive and genetic technologies.

THEMES IN THEOLOGICAL BIOETHICS

Theological discourse about human cloning has adopted either of two methods (and often both) of practical reasoning [2]. A first approach relies on a form of moral *casuistry*: It examines the extent to which human cloning is relevantly continuous with already "familiar" ethical contexts and issues. For example, a theological discussion may draw attention to the occurrence of "natural" clones, i.e., identical twins, and proceed to inquire in what respects laboratory-created clones are morally or theologically similar to or different from this already accepted social context for raising children. Casuistical argumentation presupposes the validity of the formal principle of justice (treat similar cases similarly); the central question in an ethical assessment will be the interpretation of human cloning as similar or dissimilar to certain social structures or medical practices already valued or criticized by society and the faith tradition. Lacking direct revelation on human cloning in sacred texts, casuistical and analogical reasoning has been a characteristic part of religious argumentation. The significant point is that conclusions about human cloning are influenced in large measure by the framing ethical context.

A second, and often complementary, mode of practical reasoning involves application of the moral and anthropological *norms* of the faith tradition to generate an ethical assessment of human cloning. For example, perhaps the most common norm of western theological anthropology invoked in the discussion of human cloning is that human beings are created in the "image of God" (*imago Dei*). This concept, which is very rich in ethical content, is then applied by methods of religious reasoning to provide a perspective or conclusion on human cloning in general, or the theological and moral status of any given clone (the status, for example, of a clone as an ensouled entity with full claims as a person).

This section will examine the principal theological themes in the western faith traditions that emerge in both the casuistical and normative modes of practical reasoning and analysis. It will begin with the casuistical approach, which seeks to identify the ethical contexts deemed relevantly similar to human cloning so as to warrant methods of analogical reasoning.

Casuistical Analysis

Family and Procreation

The family has been invoked as the prime social institution, and in some traditions, a divinely ordained institution for the bearing and nurturing of children. Within Roman Catholic moral teaching, procreation *and* education of offspring is a principle of natural law. Paul

Ramsey's opposition to human cloning stemmed in part from a view that Christians perform their primary responsibility to future generations through procreation and care for children. Jewish and Islamic law each impose fundamental duties and responsibilities through spousal, parenting, and familial relationships and through intergenerational ties.

The question of human cloning is thus theologically approached not from the secular standpoint of personal rights and individual autonomy, but rather from a framing context of familial relationships and responsibilities that society already values. The casuistical concern is the extent to which this relational and moral context can accommodate such cloning possibilities as a "replacement" child, laboratory twinning in place of natural twinning, or children with a genetic grandfather but no genetic father.

Core moral criteria for faith traditions in addressing these prospects include the impact of human cloning on the integrity of the family, the nature of parenthood, the role of marital sexuality and procreation, and the identity of a child. As noted above, in the wake of the recent cloning of "Dolly," Allen Verhey has appealed to the concept of a "good life in a family" to reject the prospects of human cloning. Verhey maintains that the primary justifications for human cloning—appeals to the principle of freedom and the principle of utility—are necessary but insufficient guidelines for the moral life of a family. In particular, Verhey focuses his critique on the potential disruption of the parent-child relationship: Human cloning risks transforming children into "products" of technological achievement rather than "gifts" created in love [36].

The stability of family is not a sufficient moral perspective by which to evaluate human cloning, but it is a necessary consideration within a religious framework. Islamic thought, for example, affirms that, since the family is intrinsic to a well-functioning society, cloning procedures that separate the spiritual and moral relations of spouses, and those of parents and children, may undermine the foundation for human community in general [31]. It is not a compelling counterargument to contend that social realities of familial life and relationships do not match theological idealism, for the moral and policy question in part is whether society should deliberately support alternative modes of reproduction outside marital love and procreation.

Reproductive Technologies

A second casuistical context that shapes religious responses to human cloning is the increasing acceptability and availability of various forms of reproductive technology. The widespread use of such procedures indicates that even if conjugal relations are a preferred setting for human procreation, it can be ethically acceptable to have recourse to methods of donor insemination or in vitro fertilization within or outside of a marital relationship. Joseph Fletcher argued that human cloning should be viewed as simply another option in a spectrum of asexual reproduction tailored to an expanding menu of human reproductive rights and choice. Given that society has already accepted donor insemination, egg donations, in vitro fertilization, contract pregnancy, embryo transfers, and so forth, the question must be asked whether and how cloning is unique or distinctive from these other practices.

This question is relevant even if, as in the case of the Roman Catholic tradition, none of the above practices is considered morally licit. In her testimony to NBAC, Prof. Lisa Cahill suggested a radical discontinuity between current reproductive technologies and cloning, using the language of "genuine revolution" to refer to human cloning [1]. The revolutionary impact of human cloning needs explication, however, to warrant drawing a moral and policy line between current reproductive technologies and prospective cloning. By contrast, Rabbi Elliot Dorff and Rabbi Moshe Tendler assimilated cloning within current medical practices, suggesting that human cloning was morally "easier" for the Jewish tradition than donor insemination or egg donation, because it would not raise issues of consanguineous relationships or "non-therapeutic" reproductive techniques [6, 34]. Prof. Abdulaziz Sachedina's identification of a consensus in Islamic scholarship on therapeutic uses of cloning also presumes an important continuity between human cloning and such procedures as in vitro fertilization [31].

The question of the moral uniqueness of cloning inevitably imposes itself on religious traditions. Theologian Roger L. Shinn has put the religious dilemma this way: "I know of no way of drawing a line and saying: thus far, scientific direction and control are beneficial; beyond this line they become destructive manipulation" [33]. Absent a complete prohibition on reproductive technology, any moral or policy line-drawing will seem arbitrary unless a distinctive feature of human cloning can be identified.

Nonetheless, there are reasons why faith traditions would resist treating human cloning as continuous with reproductive technologies for *policy* purposes. The latter is unregulated and relies on good-faith compliance with professionally developed guidelines for ethical practice. There is, however, no current mechanism of public oversight or accountability. Secondly, the political language of reproductive technology is that of "choice" and "rights," whereas religious traditions more commonly invoke an ethic of "duty" or "responsibility" in the context of procreation and parenting.

Research and Therapy

A third moral context invoked by theological bioethics concerns a distinction between non-therapeutic and therapeutic research. A principal objection to human cloning articulated by Ramsey, and reiterated by many subsequent theologians, is that human cloning will inevitably involve non-therapeutic research on the unborn without valid consent. The current inefficiency of mammalian cloning technology (the production of Dolly was the only technical success in a research project involving 278 sheep embryos) has suggested to religious thinkers that cloning of human embryos for research or for transfer and gestation will result in morally significant loss of potential human life. This is of particular concern for the Roman Catholic tradition, given its teaching that the preimplantation human embryo is entitled to full moral respect and dignity. In arguing against blastomere separation, for example, Richard McCormick claims that less than full respect for the human pre-embryo as potential human life will lead to diminished respect for all pre-nascent life [20]. While Protestant theologians such as Ronald Cole-Turner see no theological

difference between a cloned and an uncloned human embryo, they express substantial reservations about the likelihood of embryo loss due to technical inefficiency [3].

A second research issue, presented to NBAC by Prof. Gilbert Meilaender [22], is that progress in biomedical research is an "option," not an obligation for society to pursue. This echoes positions formulated by Ramsey and philosopher Hans Jonas; such a claim in part is rooted in a view that non-infliction of harm (non-maleficence) has moral priority over promotion of benefits (beneficence) in human subjects research. On such an account, claims that human cloning research possesses therapeutic intent will be inadequate, for some faith traditions will understand the certain loss of life of human embryos as a real harm and not merely a symbolic or speculative harm. Thus, researchers will be required to make a case not only that their research may produce benefits (such as the development of medicinal products), and not only that these benefits will outweigh the harms, but that serious efforts have been undertaken to minimize the harms. The moral burden of proof on researchers will be even heavier for proposals to engage in research on human cloning with the objective of transfer of a clone for gestation and birth.

Jewish and Islamic traditions are more favorably disposed to cloning research with therapeutic objectives, such as alleviation of infertility. Jewish law does not attribute full moral status to the human embryo, while Islamic scholarship is divided on the timing of ensoulment. Thus, the loss of human embryonic life through cloning research does not carry the same status of "harm." Moreover, Jewish law permits almost any action (except for breaches of three commandments) to be performed for the purpose of saving life. In the case of cloning research, this may encompass new methods to remedy or avoid serious genetic disease, but would preclude research directed at reproducing a clone solely for organ harvesting.

On the question of human cloning research, the western religious traditions place the burden of proof on the side of biomedical research. Research may be permitted, but is not required, and the prospect of therapy must meet a standard of probability of specific benefit and assurance of minimization of harm, not a standard of possibility of speculative benefit, and dismissal of symbolic harm. Additional questions must be addressed regarding the justification of research on the preimplantation embryo and the distribution of the benefits and harms of cloning research; the latter concern has been forcefully expressed by minority religious communities (see section 3). If biomedical science were unable to meet the burden of moral proof, which is rooted in the basic principles of respect, beneficence, and justice, the proposed pharmacological and medical benefits of cloning research may have to be forgone, and it would be extremely difficult to justify support for research to transfer a human clone into a womb for birth.

Genetic Interventions

The prospect of human cloning as therapeutic research suggests a final moral context: Cloning research may be viewed as relevantly similar to other forms of genetic interventions already in place in medicine. This casuistical context not only provides justification for cloning research, but also important procedural and substantive limitations. Unlike reproductive

technology, for example, gene therapy is subject to stringent public regulation and oversight. There is moreover a general consensus that some defensible lines can be drawn with respect to genetic interventions, such as between somatic cell and germ-line therapy and between therapy and enhancement. Restrictions on human cloning research might then follow a model of prohibition on germ-line interventions, as recommended to NBAC by Rabbi Tendler [34]. A third limit is that benefits be directed toward individuals rather than society. That is, rather than using cloning procedures for the general improvement of the human species, as proposed by Fletcher and other early religious and scientific proponents, an ethical and regulatory model that followed the social precedent of accepted genetic manipulations would focus on therapeutic manipulations for an individual.

It is difficult, however, to subsume human cloning entirely under the moral casuistry of genetic therapy. Genetic screening for abnormalities may be performed on the early embryo through diagnosis of undifferentiated cells, but this cannot be considered therapeutic research on the embryo. Germ-line interventions affect the genetic characteristics of a person of a future generation. They do not directly determine whether that person will exist, as cloning of a person would.

Normative Analysis

Religious traditions and communities have articulated a variety of ethical norms to address the wide range of practical issues and problems that persons encounter in moral life. These norms may be derived from sacred writings and their interpretation, ongoing historical reflection within a religious tradition, and personal experience, among other sources, and can be applied to the wide array of moral choices persons confront from the beginnings to the endings of life. This section presents certain theological norms, themes, and values that may be applied through practical reasoning to the question of human cloning within religious communities, and that supplement the analogical and casuistical methods delineated above.

Personhood and the Image of God

It has been argued that the most significant issue forced upon society by genetic science is an understanding of normative humanity [15]. The same question is encountered in theological discourse on human cloning. Lutheran theologian Philip Hefner argues that cloning is a "revelation of the human situation.... In cloning, we are, in fact, addressing ourselves, and it is about ourselves that we have the greatest questions" [17].

The question of personhood (and human distinctiveness) is commonly described and explained in the western faith traditions with reference to the theological theme of the image of God (*imago Dei*). Normative humanity is theologically rooted in the creation of human beings in the image of God (*Genesis* 1:27-28). Interpretations of the moral meaning of the *imago Dei* depend in part on prior convictions about the nature of God and those characteristics of God human beings are

believed to image. Nevertheless, it is possible to identify several implications of significance to the questions of human cloning:

> Human beings are bestowed with the gift of freedom and moral agency. Moral agency is inherent in the human self and creates logical and correlative moral responsibilities. The logical correlation encompasses respect for the equal freedom and agency of other persons. The moral correlation of personal freedom is personal responsibility for actions before one's conscience, others, and ultimately before God.
>
> Human beings are created in God's image, but they are not God. They are finite and fallible, with limited capacities to predict and direct the course of actions they initiate, or to assess accurately the outcomes of these actions.
>
> A fundamental equality is inherent in the human person. This equality transcends differentiation between persons made on the basis of gender, race, class, ethnicity, etc.
>
> Human beings are relational and social creatures. They are created in and for relationship with God, for community with other persons, and with creation.
>
> The image of God is reflected in human diversity, involving but not limited to gender diversity. The differentiation of the sexes provides a divine warrant for procreation and the sacredness of sexuality.
>
> Human beings are embodied selves. The person is revealed and experienced through the body and not merely as an intellectual or spiritual essence, or a disembodied mind or will.
>
> Human beings bear the image of God through the exercise of their creative capacities and potential. This includes creative ways of exercising "dominion" over the natural world.

Each of these features of the *imago Dei* helps explain and define religious responses to cloning. Religious concerns about the disruption or confusion of relationships, diminished diversity, the primacy of procreation, and the significance of the body can be rooted in this theological concept. Moreover, reproductive technology and genetic interventions that culminate in cloning may be interpreted as a responsible exercise of human (and divine) creativity.

The divine commands given to humanity subsequent to their creation in God's image are also invoked in religious discourse on human cloning. Human beings are obligated to multiply through the earth. This provides a warrant not only for sexual love and procreation as good, but also, on some theological perspectives, for an intrinsic connection between the "unitive" and "procreative" purposes of sexuality.

How human dominion over nature should be carried out can be interpreted in at least three ways of significance for cloning. One notion is an ethic of stewardship in which human beings are

entrusted with administrative responsibility for creation. Human stewardship involves caring for and cultivating creation after the manner of a gardener. The stewardship ethic accepts the givenness of nature as a good to be maintained and preserved.

A second model, particularly significant in Jewish and Islamic discourse, suggests a "partnership" of human beings with God in caring for and improving upon creation. "...as participants in the act of creating with God, human beings can actively engage in furthering the overall well-being of humanity by intervening in the works of nature, including the early stages of embryonic development, to improve human health" [31]. The natural world in this view is inherently malleable, and can be shaped in several different forms in service of divine and human goals. This model holds the potential for seeing cloning research, and perhaps some forms of human cloning, as using human creative potential for good.

A third understanding is that of human beings as "created co-creators." This claim recognizes that human beings are created beings, dependent on God, and finite and fallible in their existence. Simultaneously, human beings assume a role of co-creator to envision and implement knowledge for the betterment of humanity and the world. Human beings are called to "play human" [26] through their freedom and responsibility in creating an essentially open human future. Reproductive and genetic technology, as well as human cloning, can be one particular expression of responsible created co-creatorship.

Finally, although creation is "good" and human beings are "very good," over the course of history, humans have displayed an irremediable propensity to use their divinely authorized dominion for unauthorized domination, to violate their covenant of partnership with God, and to create after their own image rather than the divine image. The person created in the image of God is nonetheless marked by sin. All human activities are pervasively imperfect. The prospect that humans can and do choose evil rather than good means caution is a moral necessity [14]. However, human imperfection is not necessarily a warrant for halting technological advances [17], although it should inform a posture of modesty regarding human aspirations.

This analysis contends that issues of human cloning inevitably beg the question about the nature of the person, and within the western religious traditions, the fundamental concept of theological anthropology put forward to describe and explain human personhood and distinctiveness is the image of God. The question is unavoidable even if the religious content is not shared.

Procreation and Parenthood

In the initial phase of theological assessments of cloning, Paul Ramsey argued that the covenant of marriage included the goods of sexual love and procreation. These were divinely ordained and intrinsically related: Human beings had no permission to sever what God had joined together. On this basis, Ramsey, Bernard Häring, Richard McCormick, and other theologians objected to cloning as part of a panoply of envisioned forms of reproductive technology. Their

arguments claimed that such technologies separate the unitive and procreative ends of human sexuality and transform "procreation" (which implicitly places humans in a role of co-creator) into "reproduction." The most authoritative statement of this position was issued by the Vatican in 1987 in its *Instruction on Respect for Human Life* (*Donum Vitae)*, which contained a prohibition on human cloning either as a scientific outcome or technical proposal: "Attempts or hypotheses for obtaining a human being without any connection with sexuality through 'twin fission,' cloning, or parthenogenesis are to be considered contrary to the moral law, since they are in opposition to the dignity both of human procreation and of the conjugal union" [5].

Protestant scholars have offered a similar critique through appeals to fundamental theological tenets that distinguish between "begetting" (procreating) and "making" (reproducing). The Nicene Creed of early Christianity affirmed that Jesus, as the authentic image of God and the normative exemplar of personhood, is "begotten, not made" of God. The theological interpretation of "begetting" emphasizes likeness, identity, equality, and of the parent's very being. By contrast, "making" refers to unlikeness, alienation, subordination, and of the parent's will as a project.

Oliver O'Donovan, an Anglican theologian, has drawn out the implications of this distinction for human cloning. O'Donovan portrays human cloning as the culmination of scientific or technical "making" in human reproduction: "...the development of cloning techniques...will be a demonstration, if it occurs, that mankind does have the awesome technical power to exchange the humanity which God has given him for something else, to treat natural humanity itself as a raw material for constructing a form of life that is *not* natural humanity but is an artificial development *out of* humanity" [25]. Thus, the use of scientific capacity comes at the cost of an artificial, diminished humanity. This ruptures the fundamental relational ties of likeness, identity, and equality.

This distinction further illuminates two meanings of "making" embedded in the title of Ramsey's *Fabricated Man*. A child born through cloning is designed and manufactured as a *product*, rather than welcomed as a gift. Moreover, the *process* is itself unauthentic, or "fabricated," with respect to what it means to be human.

The question is whether this position literally throws the baby out with the technology, either through current forms of reproductive technology or proposed methods of cloning. If no distinction is permitted between unitive and procreative sexuality, or between begetting and making, then it becomes difficult to justify contraception or technically assisted conception. Rev. Moraczewski has argued that, within the Roman Catholic context, the threshold of moral acceptability was violated with the birth of the first test-tube baby in 1978 [24], while from a conservative Protestant perspective, Prof. Meilaender offered a modified form of this view in his remarks before the NBAC, commenting that he "would have got off the train" of reproductive technology long before it arrived at the cloning station [22]. Put another way, if, as is the case with most Christian denominations, there is qualified acceptance of DI, IVF, etc., drawing a line

against cloning is likely to appear arbitrary with respect to the theological values underlying procreation and parenthood.

Science and Technology

Media reports have portrayed a classical confrontation between science and religion over the prospects of human cloning. This is misleading, insofar as not all arguments against cloning are religious, and not all religious arguments oppose cloning. Indeed, the issues instead offer the possibility for substantive and sustained dialogue between leading scientists and theologians. Probing the intersections of ethics, science, and theology can offer mutual enrichment: Scientists are informed as to how research in genetics and biology inevitably broaches theological questions, while theologians are critically challenged as to whether and how to accommodate religious convictions to new scientific knowledge [14].

The quest for scientific knowledge per se is not considered theologically threatening. Islamic scholars, for example, emphasize that all scientific discovery is ultimately a revelation of the divinely ordained creation. Scientific knowledge is thereby a symbol or sign of God's creation [16]. This perspective is embedded in the comments of the respected Shi'ite jurist (Sheikh Fadlallah) that recent cloning discoveries occurred "because God allowed it" [8], and those of Prof. Sachedina that cloning may be a divinely given opportunity for human moral training and maturity [31]. Similar assessments of the legitimacy of scientific inquiry appear in Catholic and Protestant traditions. Invoking a Calvinist claim that the world is a theater of God's glory, one ecclesiastical statement indicates that "in the sciences, the human does indeed receive glimpses of God's theater" [29].

These prospects for dialogue and theoretical convergence can dissipate when examining specific scientific applications. Scientific descriptions of the world do not supply theological or normative prescriptions for acting in the world. The faith traditions have insisted that two principal issues—who controls technological developments, and the ends or purposes of technology—are ethical rather than technical questions. This can support a sharp distinction between endorsement of the scientific quest for knowledge and critique of applications of scientific discoveries in the social, political, and clinical worlds. This theological critique may assume several forms in the context of cloning:

> The reduction of nature, animals, the human pre-embryo, or persons to merely an object for scientific manipulation. The concern behind objectification is a loss or diminished sense of awe and wonder at the mystery and meaning of life. Awe is a foundational religious sentiment. It has also been described by Einstein as the source of true science [7]. The loss of awe and wonder then can reflect a deformed scientific and religious sensibility. Moreover, theological concern has been raised about the difficulty of de-limiting diminished awe to the laboratory setting. Cloning may be perceived to assault the dignity of those involved in the process of human cloning as much as it does the person who results from cloning [23].

Theological criticism has also been directed toward the "technological imperative." Two variations of this imperative have been invoked: "If we have the technical capacity to clone, we *should* pursue this research"; "If we have the technical capacity, we *will* inevitably pursue this research." The theological sentiment expressed in both cases is a concern about loss of control, about either the ethical debate or about the scientific pursuit. It may in addition reflect theological suspicion not of science, but of scientists, particularly if research is conducted without adequate public monitoring and accountability. In the Protestant traditions particularly, this suspicion is supported or reinforced by a general claim about the impact of human sin from which scientists as persons are not immune. This concern can be met to some extent by establishing appropriate procedural review.

The theological context of cloning also elicits disputes over the relationship of knowledge and power. Joseph Fletcher used the language of "rational control" to warrant cloning, but this in essence meant harnessing the power of the modern sciences to transform nature and human nature. On more direct theological grounds, the Jewish tradition supports technological and medical interventions in response to the divine mandate to master the earth in service to humanity.

Other theologians have challenged Fletcher's unbridled optimism about beneficial applications of scientific knowledge by focusing on the ways that power can be a form of oppression rather than liberation. The comments of Anglican scholar C.S. Lewis have been reiterated by contemporary theologians in the context of both genetics and cloning: "If any one age really attains, by eugenics and scientific education, the power to make its descendants what it pleases, all men who live after it are the patients of that power. . . . Each new power won by man is a power over man as well" [18]. This claim does not suggest society has the luxury of choice between use or abuse of cloning. Rather, the abuse is itself embedded in and expressed by the use.

Playing God

Much of the preceding analysis reflects theological ambivalence and criticism about biomedicine that is often expressed in the slogan of "playing God." This slogan is invoked as a moral stop sign to scientific research and medical practice on the basis of some or all of the following attributes:

Human beings should not probe the secrets or mysteries of life. Continued scientific pursuit to reveal these secrets can create a "God of the gaps" theology, in which "God" is reduced to a symbol that simply fills in for those questions modern science has not yet answered [37].

Human beings do not have the knowledge, especially knowledge of outcomes, attributed to divine omniscience.

Human beings do not have the power to control the outcomes of actions or processes that is a mark of divine omnipotence.

Human beings have no authority to make decisions regarding the beginnings or endings of life, which is reserved to divine sovereignty.

Human beings are fallible and display a propensity to evaluate actions according to self-interest rather than by the self-giving quality of divine love.

In these respects, the appeal to "playing God" serves to remind human beings of their finitude and fallibility. By not recognizing personal limits and human constraints on scientific aspirations, persons enact the Promethean presumption of pride or hubris. In the initial theological discussions of human cloning, Ramsey summarized his objections by stating: "Men ought not to play God before they learn to be men, and after they have learned to be men, they will not play God" [27, p. 138].

Even within the theological communities, however, the prohibition against playing God may be disputed or not viewed as a sufficient sanction against cloning. Allen Verhey has argued that the prohibition is simply too indiscriminate in its judgments to be of ethical use, and neglects moral invitations to play God, particularly in the realm of genetics [37]. Protestant scholar Ted Peters agrees with Ramsey that human beings are not called to play God, but argues that this does not by itself define what is necessary for us to be human. Hence, we are responsible for using our creativity and freedom (features of the *imago Dei*) to forge a destiny more consonant with human dignity and beneficence. In "playing human," according to Peters, there is no theological reason to leave human nature unchanged, nor any theological principle that is necessarily violated by human cloning [26].

Arguments against cloning that invoke the language of "playing God" are not always theological, and they are seldom sound or sufficient. The slogan is often presented as the conclusion of an argument whose premises are either unexamined or unidentified. At the very least, the theological and moral concern behind the prohibition needs explication. The language of "playing God" cannot by itself carry the full weight of an ethical or policy prohibition on human cloning.

Human Destiny and Eschatology

Theological views of medicine and medical interventions grounded in themes of creation, such as those identified above, may tend to be more conservative with respect to reproductive or genetic technologies, not to mention cloning, because of the divine evaluation of creation and persons as *imago Dei*, as "good." The role of medicine is then conceived to be to restore disordered biological organisms to their initial goodness. By contrast, theological positions that focus on human destiny rather than human nature, on "eschatology" in theological language rather

than "creation," tend to be much more supportive of an array of reproductive and genetic interventions as means for improvement or enhancement of the human condition.

The question of human destiny has been an underlying theme of the cloning debate from its inception. Scientific proponents such as Muller and Lederberg affirmed a pessimism about the survival of the species due to genetic overload. Cloning represented a prospective intervention to avoid this "genetic apocalypse" and promised a future of unlimited possibility. Paul Ramsey's theology of cloning likewise assumed an apocalyptic prognosis of human destiny, though very different in content: "Religious people have never denied, indeed they affirm, that God means to kill us all in the end, and in the end he is going to succeed" [27, p. 136]. However, the end of species survival did not, for Ramsey, justify the means of cloning. Survival is meaningful only if values of human dignity and freedom are respected.

The use of cloning to save the endangered species of human beings is no longer part of the debate, although cloning techniques have received some support to rescue endangered animal species or even endangered indigenous cultures. However, the general question of the extent to which human beings are shapers and creators of their personal and collective futures continues to be important. Discourse on destiny can be especially important in a liberal pluralistic society that is agnostic about the substantive telos of human life and society.

Some theologians in the cloning debate therefore tend to stress an openness to human nature, rooted in a creative *imago Dei* and a dynamic view of history, rather than a more rigid and static formulation of human nature and destiny. The theological and ethical interpretation of cloning then turns on the nature of human responsibility in the face of uncertain (and perhaps unforeseen) consequences.

Some Jewish thinkers affirm that the divine mandate of mastery empowers human beings with responsibility for shaping a malleable world using innovation and discovery. Responsibility for deleterious outcomes from human self-creativity falls not to humans but to God. The Jewish tradition affirms an optimism in the face of uncertainty about unanticipated consequences rooted in divine control and care; indeed, to be overly cautious to the point of moral paralysis may invite trouble. As one Orthodox rabbi has expressed it: "Human beings do the best that they can. If our best cost/benefit analysis says go ahead, we go ahead. 'G-d protects the simple' is a Talmudic principle that allows us to assume that when we do our best, G-d will take care of what we could not foresee or anticipate. If things do not work out, the theological question is G-d's to answer; not ours" [13, p. 132]. On this view, cloning may express moral responsibility insofar as it is directed to the service of God and humanity.

What is clear within Jewish thought is the critical importance of moral education of progeny who will live in the generations to come. One form of immortality discussed in biblical and rabbinic sources comes through the influence of parents (and others) on their children. The transmission of knowledge, skills, and the teaching and emulation of moral dispositions is an ongoing obligation that binds the generations together. Rabbi Tendler has emphasized the

importance of moral education as the best form of human control over cloning technology: "Are we good enough to handle this good technology? Of course we are, if we can set limits on it. And when we can train a generation of children not to murder or steal, we can prepare them not to use this technology to the detriment of mankind" [35].

An Islamic interpretation also assumes a malleability to the human self that allows for creative shaping of destiny. Islamic tradition describes two forms of creative processes. *Bari* refers to creation out of nothing and is reserved to the domain of God. *Khaliq* concerns creation from material already in existence, and the human mind is empowered by Allah to participate in *khaliq* as a co-creator [16, 31]. The ethics of cloning is then addressed by a distinction between theoretical research in science and practical application in society.

The Protestant Christian variation may emphasize the idea of *creatio continua*—divine creative activity is an ongoing process—coupled with the theme that persons are co-creators called to participate with God in shaping a better future. Indeed, destiny is so open and indefinite that the Christian may be a "co-explorer" with God in revealing new and unlimited possibilities through innovative technology [4]. This perspective on human destiny offers qualified support to human cloning, insofar as it is technically feasible and publicly supported.

Lest these theological accounts of human destiny seem to bless and anoint scientific progress, they are balanced within each of these traditions by recurring warnings, often in narrative form, about not crossing certain lines. The archetypal figure is that of Prometheus in Greek mythology; each theological tradition has its own Promethean analogue. The theological caveat is that creative initiative may be a form of rebellion of the created against the creator. The consequences of such rebellion are catastrophic havoc and perhaps destruction of the human creator, or of that which has been created. This lesson is as fundamental to religious narrative and mythology as it is to modern science fiction. The hard questions for theologies of human destiny are identifying what lines may not be crossed, where they are located, and whether human cloning is one such line.

Communities of Moral Discourse

In the March NBAC hearings, members of the commission repeatedly challenged the religious thinkers to explicate the relevance of their testimony for purposes of formulating public policy in a pluralistic society. This section discusses some substantive and procedural approaches discussed by theologians and religious writers with respect to policy on human cloning.

It is first important to recognize that religion in American culture already embodies pluralism (see Section Three for further illustrations). The religious perspectives on cloning are diverse in conclusion, modes of reasoning, and fundamental premises. There is no monolithic "religious" view on cloning (or most ethical issues in biomedicine). However, this has not been seen as an impassible barrier by the faith traditions; discourse across religious traditions on many

contested ethical issues in biomedicine is common and expanding, and this can provide important models for public discourse between persons who share the common bond of citizenship.

It follows from this observation that religious discourse on the ethics and policy of cloning should not be marginalized because it may invoke values or assumptions that are not part of a social consensus or appeal to premises that are not generally shared. While public policy must invoke publicly accessible reasons to support its conclusions, it is not evident that scientific, professional, philosophical, economic, or legal reasons considered or proposed as grounds for policy are themselves independent of assumptions about the human good. Prof. Meilaender's testimony to NBAC emphasized that it is an "illusion" to understand any constructive policy recommendation as free of value presuppositions [22]. Those presuppositions themselves may not meet the standard of publicly "accessible," "shared," or "persuasive" reasons. Thus, religious values or reasons should not necessarily be held to a higher standard of public relevance than other forms of reasons.

Religious communities have a self-understanding as "communities of moral discourse." That is, they are a locus for moral and policy education for believers (and often nonbelievers) who are also citizens, and this education often addresses very contested issues in the society. Given general public ambivalence about biotechnology—and in particular trepidations about cloning research, its processes, and its products—religious communities can be critical venues for informing and eliciting public values on human cloning.

The traditions of religious reflection see in the question of human cloning an invitation to sustained and substantive public discourse about the common good. It would be a missed opportunity were public policy to default to an ethics of autonomy, the politics of procedure, or the crafting of compromise among special, vested interest groups. The principle of autonomy or self-determination is a necessary principle for the moral life of persons and the life of the polis. It needs to be supplemented, however, and situated within a richer moral context of human interdependency and solidarity, care for the vulnerable, and restraint on private interest.

As all the religious thinkers before NBAC testified, the prospect of human cloning strikes at very deep issues of human identity and community. Policy recommendations should not presume consensus on the meaning of human personhood. Instead, the policy process should seek to identify points of common ground and determine if conflicts of positions are rooted in disputes over scientific facts, or over philosophical or theological values. Factual disparities can presumably be resolved through the provision of more complete or reliable information. Value pluralism may not be beyond resolution. Some important values may not be absolute, core, or "bottom-line" values, but rather are presumptive values that can give way in the face of conflicting, weightier values, one of which may be the capacity to sustain public discourse in the face of reasoned disagreement. The policy process must be as cognizant of the fundamental questions asked by religious traditions as of the fundamental values invoked by these traditions in support of certain conclusions.

This is but a specific exemplification of a theme common in the testimony before NBAC of the religious thinkers, namely, that procedural models beg substantive ethical (and theological) questions. A policy of regulatory control and/or voluntary adoption of professional guidelines, e.g., would be necessary but still insufficient. It is also critical to examine the character, integrity, and virtues embodied by persons permitted to control the cloning process. This can be supplemented by the proposal of Rabbi Tendler of a curricular requirement for the teaching of the ethics of professional and scientific integrity to medical students and research scientists [34]. Rabbi Dorff, meanwhile, encouraged reliance on current regulatory mechanisms, such as institutional review boards and institutional animal care and use committees, regarding the protection of human and animal subjects [6]. The human capacity to use technology with justice and beneficence in the service of the common good makes public discourse on cloning possible, while the capacity to abuse cloning technology for self-interested purposes makes public oversight and accountability necessary.

RELIGIOUS TRADITIONS

This section contains more specific information on the views of distinctive religious traditions regarding ethical questions in human cloning research. With very few exceptions, the religious traditions discussed here have yet to develop specific theological or denominational positions on the moral or public policy aspects of human cloning. The theological literature examined and the religious thinkers interviewed for this section characteristically employ analogical reasoning in discussing cloning, invoking values or historical experience used to support positions on issues deemed relevantly similar to human cloning.

In considering the implications of these religious positions for public policy on human cloning, it may be useful to adopt the metaphor of a traffic semaphore. Under this metaphor, traditions may be analyzed and compared under several possibilities with respect to society's assessment of the process of cloning research and the product of cloning a human being:

> "Red" indicates a full stop to research and/or cloning. The policy analogue is a permanent moratorium or prohibition.
>
> "Flashing red" indicates the need to stop to evaluate risks before proceeding. The policy analogue is a temporary moratorium until important scientific and social questions are addressed.
>
> "Amber" indicates the need to proceed with caution and care, slowing the pace of or stopping research as necessary. The policy analogue is a regulatory model coupled with the adoption of guidelines by relevant professional bodies.
>
> "Green" indicates permission for cloning research and/or cloning on the assumption that other stakeholders in human cloning will conform to norms of professional and social

responsibility. The policy analogue is the adoption of guidelines by relevant professional bodies.

Given the diversity of American religiosity, an inherent risk of the following analysis is oversimplification for the sake of generalizations. The discussion nonetheless should indicate important questions raised by religious communities and thinkers about science, technology, and human cloning.

African American Churches

Faith traditions in the African American religious community comprise approximately 11% of religious adherents in the United States. The African American churches, stemming from Methodist and Baptist traditions, locate themselves within the "black Christian tradition." This tradition is united by commitment to a fundamental principle of human equality before God, often phrased as "the parenthood of God and the kinship of all peoples." The principle offers a theological basis for criticism of racism and sexism and necessitates social reform through non-violent measures and religious witness.

Social Context. The black Christian tradition understands the history of research abuses of African Americans at the hands of medicine, such as the Tuskegee experiments, as a violation of the fundamental principle of human equality. Moreover, due to ongoing racism in society and medicine, it maintains the prospects for further exploitation of African Americans through cloning research are substantial. "The history of scientific abuse and medical neglect carries with it a legacy that is permanently imprinted upon...the collective consciousness" of African Americans (Secundy).

Given this history of past abuses, society should assume a posture of greater vigilance for minority communities. Preston N. Williams, a participant in the 1970s discussion of cloning, argues both that public oversight is necessary with respect to cloning, and that it also must be "race conscious," lest the African American community experience further marginalization within biomedical science and society (Williams). This requires emendations to current codes of research ethics and institutional review policies, insofar as they do not address race relations and issues of power in the research setting. Present procedures of informed consent are not deemed morally sufficient for cloning research.

Accountability and Education. While technology is not morally objectionable per se, applications of technology within this social context can be morally indefensible. Of particular concern are entrepreneurial efforts in biomedicine that are motivated by private interest and supported by concerns for commercial profit and/or racism. At a minimum, strong regulations that build in public accountability must be developed by legislative bodies to protect vulnerable patients and families from coerced choices or economic inducements. In addition, the scientific research community should voluntarily adopt strict protocols and monitoring. Communal distrust of scientific and research institutions and suspicion of commercial endeavors also entails a more

comprehensive policy approach than oversight and accountability. Some African American writers stress that policymakers must learn a fundamental lesson from the community's distrust of organ procurement methods, and implement a major informational and educational campaign with respect to genetic, reproductive, and cloning technologies. While it is often difficult to enforce regulations or prohibitions, the lessons of the civil rights movement provide some confidence in an approach to human cloning that complements public accountability with public education.

Embryo Research and Therapy. African American churches affirm, along with elements of historical Christianity, that human life begins at conception. The use of human embryos for medical research is problematic, since it involves experimentation on living human embryos rather than embryonic material. In addition, the tradition is concerned about the procedures required for creating embryos and those used in discarding embryos. A minimal criterion of moral acceptability is therapeutic intent: Cloning of human cells, for example, should not be allowed to benefit any individual racial or ethnic group "outside of the context of a clearly identified, morally defensible, medically justifiable" condition that would benefit from such technology (Robinson).

Fairness. The tradition also raises questions about fairness and social priorities in resource allocation. The history of medical progress has often meant that African Americans assume the heaviest burdens and receive the least benefit for participation. Moreover, scientific energies and public monies used to support cloning could divert attention from diseases specific to the African American community or from poor health indices, such as high premature birth or infant mortality rates. The principle of human equality is violated when a new area of research investigation is opened up, while many within the African American community do not have access to basic health care.

African American churches do not have any objections to the use of reproductive technologies per se as a means of bringing children into the world. However, the churches' principle of equality is invoked to criticize selective access to reproductive technologies, particularly to the exclusion of African Americans. Rev. Geoffrey Ellis, president of the NAACP Interdenominational Coalition, contends that those with the technical capacity to clone "certainly will make more people like them. This certainly rules out more people like me" (Ellis). If financial resources dictate access to human cloning services, members of the black Christian tradition may experience further social marginalization. Human cloning may therefore perpetuate social stratification rather than affirm human equality.

Cloning Research: Flashing Red
Human Cloning: Red

Buddhism

The Buddhist Churches in America claim approximately 100,000 adherents. There are, in addition, numerous non-affiliated Buddhist temples, monasteries, and organizations. There is as yet no systematic consideration of cloning by Buddhist scholars, nor is there is any formal

teaching authority. This manifests the Buddha's warning to his followers that speculation about metaphysical issues was futile because the human problems of birth, old age, death, and sorrow remain regardless. However, basic Buddhist teachings present an ethic of responsibility, centered on the values of non-injury and the relief of suffering of sentient beings, compassion, the "no-self," the moral authority of intuition, and reincarnation. These values offer some elements of a Buddhist response to reproductive and genetic technologies, including cloning.

Buddhist teachings indicate that the Buddha (560-477 BCE) provided a four-fold decision-making method for his followers should they encounter unanticipated questions. The four steps involve recourse to (1) original Buddhist texts; (2) derivation of rules in "consonance" with the original texts; (3) the views of respected teachers; (4) the exercise of personal judgement, discretion, and opinion. Buddhist scholars have cited this method as a resource for Buddhists in addressing the issues of cloning, with a particular emphasis on the authoritative nature of personal intuition and opinion (Nakasone). By its nature, then, there is a notable diversity of views by Buddhists on cloning, rather than a Buddhist view.

Procreation and Reproduction. Buddhist scholars generally agree that the process by which children are born into the world makes no difference. "Individuals can begin their lives in many ways," including but not limited to human sexual generation. Cloning is thereby understood as an alternative method of generating new human life, in principle continuous with other methods (Keown). One Buddhist ethicist has supported use of reproductive technology, so long as it benefits the couple who wish to have a child and does not bring pain or suffering. However, some Buddhist scholars find in human cloning an impoverished approach to procreation. It marks a diminished creativity and diversity, analogous to the difference between the creativity, initiative, and investment that is required for an original painting and the mechanistic process required to reproduce the painting (Nolan).

Human Status and Enlightenment. The status of human being is critical within Buddhist thought, because it is the only ontological condition by which an entity can achieve "enlightenment" and liberation from a world marked by suffering. Buddhist scholars throughout history have reiterated that, due to *karma*, the chances of being born as a human being are rare and remote. Human life is a precious opportunity to escape from perpetual rebirth (*karma-samsara*) by following the teachings (*dharma*) of the Buddha.

In this respect, any form of human reproduction, sexual or asexual, that allows for the birth of a human being may be especially valuable. Buddhist tradition contains stories of "spontaneous generation." Buddhist scholar Damien Keown states that cloning, if it "is ever perfected in human beings, would show only that there are a variety of ways in which life can be generated. It would not cast doubt on whether the host from which the clone was taken, or the clone itself, were ontological individuals" (Keown, 90).

Some forms of Buddhism may endorse cloning because of the chance human life gives to achieve enlightenment. The Dalai Lama, the exiled leader of Tibetan Buddhism, was questioned

about his attitude towards the following hypothetical scenario: "[What] if at some future time...you could make by genetic engineering, with proteins and amino acids, or by engineering with chips and copper wires, an organism that had all of our good qualities and none of our bad ones,...?" The Dalai Lama indicated he would welcome such a technological development, because it would facilitate the process of rebirth and liberation.

Moral Development and Spiritual Priorities. Buddhist understandings that change is the nature of reality suggest that, in considering technological developments, the central questions concern how persons can accommodate change and how they can use change to expand their self-understanding and their understanding of humanity. Cloning may be an occasion for self-knowledge, which is a central feature to the experience of enlightenment. Nonetheless, the end of enlightenment as an end in itself may not, for some Buddhists, justify the use of any means of reproduction.

A different position on cloning can be supported by claims and stories in Buddhist texts. It is important in Buddhism for children to express generosity to their parents, especially the mother, for the risks of birth and nurture they assume in bringing a child into the world. Human cloning offers a way of reproduction that, if efficient, would diminish risk, and thus diminish the generosity and gratitude of the child.

Moreover, while cloning may preserve genetic identity, it cannot assist in what for Buddhists is most critical—the cultivation of spiritual identity. The problem of distorted priorities is illustrated in a famous narrative, the "Parable of the Mustard Seed." In the parable, a distraught woman sought out the Buddha, requesting that he restore life to her dead child. The Buddha indicated that a cure was simple: The woman needed to prepare tea from five or six grains of mustard seed. The Buddha stipulated, however, that the grains needed to come from a house not visited by death. The woman was unable to obtain a single grain, thus learning about the universal truth of death. This narrative supports Buddhist concerns with cloning research or human cloning due to the attention focused on bodily, material life to the neglect of cultivating discovery or the inner life of a person. This misguided priority is reflected in the statement of Gen Kelsang Tubpa, a Buddhist monk: "Cloning is just another example of man's belief that by manipulating the external environment he will create happiness for himself and freedom from suffering."

Some Buddhist scholars have raised objections to applications of cloning, particularly commercial or social agendas that may support cloning for reasons contrary to the interest of the clone. These agendas may include pressures on scientists for continual progress and discovery or for commercial gain from pharmaceuticals or organ harvesting. In this respect, there would be greater suspicion within Buddhism about private-sponsored cloning research without public oversight.

Sentience and Cloning Research. While cloning might be permissible under some understandings of Buddhism, the scientific research necessary to build up to cloning encounters difficulties. Part of the "Noble Eightfold Path" promulgated by the Buddha prohibits infliction of violence or harm

on *sentient* beings. This would seem to permit research on human pre-embryos, but the primacy Buddhism places on birth as a human being as a necessary condition of enlightenment can restrict such research. Buddhism does hold that a new being comes into existence shortly after fertilization. Moreover, especially where the research process is very inefficient and causes loss of life, both embryo research and animal research would be especially problematic. Any Buddhist account would ask of cloning research or human cloning: "How does this serve all sentient beings?"

Cloning Research: Flashing Red
Human Cloning: Amber

Hinduism

"Hinduism" is a western term for a family of philosophies and religious practices that have their origins in the Aryan period of Indian history and the Vedic scriptures (1200 BCE). There is no formal teaching authority for the world's one billion Hindus (Hindu population in the United States is estimated at two million). However, classical texts and commentary have offered four principal values: Dharma (virtue, morality); Artha (wealth, power); Kama (aesthetics, sexuality); Moksa (liberation) to guide Hindu life. Liberation from the cycles of rebirth is the ultimate goal within Hinduism, while Dharma regulates the pursuit of Artha and Kama. Using these values, scholars of Hinduism and Hindu practitioners have begun to initiate ethical discourse on a wide array of social practices in India and North America, including those of cloning.

The most current and summational statement of Hindu thought on human cloning has been developed by the editors of *Hinduism Today*, an international journal published in ten languages, and was formulated in response to an inquiry regarding the preparation of this report. Entitled "For the President, Mr. Bill Clinton," the statement of 1 April 1997 reads in part:

"Hindu leaders applaud President Clinton's call for a spiritual view on the human cloning predicament, noting that it shows his deep understanding of complex issues which cannot be resolved by science or politics alone. Hindu swamis appeal to the U.S. President, and indeed to all heads of state who will face this issue, for laws to restrain cloning of humans and emphatically urge him to engage spiritually minded people to guide and control the process. Good people are the best promise of a good outcome. It is our wish to inform the President that Hinduism neither condones nor condemns the march of science. If done with divine intent and consciousness, it may benefit; if done in the service of selfishness, greed, and power, it may bring severe negative karmic consequences. The simple rule is this: Cause no injury to others and let dharma—the law of good conduct and harmony with the universe and its many forces and creatures—be the guide for all such explorations" (*Hinduism Today*).

Self. Classical Hinduism does not accept distinctions found in western thought between God, human beings, and other creatures, or between the supernatural, human nature, and nature.

Rather, the self (*atman*) is part of the creative force (*Brahman*) and life energy residing in all creation. Hinduism affirms a oneness of self with divinity rather than separation. A person cannot "play God," because in an ultimate sense the self *is* God. Hindu texts describe the *atman* as pure spirit. It is "eternal, free from disease, free from old age, deathless, free from decay; it cannot be pierced, cut or agitated" (Lipner). Two concepts of relevance for issues of cloning may be inferred from this religious anthropology. First, if the real self or true consciousness is radically distinct from the body, it is beyond the reach of material science and hence cannot be harmed by genetic manipulations or cloning. A second correlative principle is that scientific processes and methods (though not their practical application) manifest the workings of divine consciousness.

Creation by Cloning. Values embedded in Hindu narrative tradition may offer the community analogues to human cloning. Hindu creation narratives are replete with references to the creation of a person, a deity, or social groups through cells of skin or drops of blood. However, in a classic narrative, the *Ramayana*, only demonic persons *(asuras*) come from divine blood. This suggests to some Hindu spiritual leaders that society has little control over ensuring only good outcomes of cloning.

Cloning Research. The animating spirit is present from fertilization in classical Hindu thought. Biological development does not shape moral development, however, for the embryo is given the status of person throughout pregnancy. Hindu thought is thus concerned with moral attitudes toward research on the pre-embryo; in particular, such concerns would focus on exploitation of the vulnerable, and whether the underlying dispositions could be limited to the research setting or would influence how human beings treat each other and treat animals.

The *Dharma* gives great authority to *ahimsa*, or the non-injury of sentient beings. This inclusive scope of beings within the moral community renders much contemporary animal research without justification. Animal research for the benefits of animals can be justified, but it is more difficult to justify when such research is conducted solely to advance human interests.

Human Cloning. Some Hindu scholars may permit human cloning under very circumscribed or exceptional circumstances. The primacy of generational continuity, especially the establishment of father-son lineage, is underscored in the *Mahabharata* (an Indian epic analogous to the *Odyssey*). The continuation of generational lineage may take place through several different methods of having a son as offspring, including a "son by artifice, a son who comes by himself, ...[and] the son of unknown seed." The epic also indicates that when a lineage is threatened by extinction, a different law—*appaddharma*—applies and permits production of offspring through relationships outside of marriage (Desai, 246, 247). Other scholars maintain that the four values of Hinduism would support human cloning when it is conducive to material or spiritual well-being, such as to alleviate infertility or for saving life through providing compatible bone marrow (Sharma).

Life Priorities. Within any Hindu discussion of cloning, there is concern that scientific attention on cloning will divert attention from the true purpose of life, which is to become conscious of and actualize one's self in union with the divine. Sri Easwaran has suggested that the question we

need to ask in light of significant scientific discoveries such as the splitting of atoms or of cloning is: "Will this help me in my search for realizing God, who is enshrined in the depths of my consciousness?"

Other Hindu spiritual leaders have posed the same question about what cloning reveals about human priorities: "Will [cloning] help us to draw nearer to God if we have such bodies? Will the soul's evolution toward the goal of spiritual liberation be advanced one millimeter?...Will mankind's inner consciousness be enhanced?" (*Hinduism Today*).P

The cultivation of spiritual self-awareness, rather than manipulation of the external environment, or one's biological self, which is no less an external organic environment, is the overriding concern of the Hindu tradition. While Hindu thought would not recognize any ontological distinction between the in-dwelling spirit of naturally born persons and of cloned persons, the latter is likely to experience discrimination because of embedded social bias. Human cloning thereby suggests that the wrong questions about life's meaning and about social priorities are being asked.

Cloning Research: Flashing Red
Human Cloning: Flashing Red

Islam

Islam ("submission") is the youngest of the Abrahamic family of religions (Judaism, Christianity, Islam). Islam presents continuity with Judaism and Christianity—Abraham and Jesus are "prophets" in Islamic tradition—as well as distinctiveness, which stems from the revelation of the Qur'an to the Prophet Muhammad (610 CE). The two main sub-traditions of Islam are Sunni (about 80%) and Shi'ite (about 20%). Within the United States, the Muslim population is estimated to comprise between three and six million persons.

Islam does not recognize a separation of religion, ethics, law, and politics; rather, Islamic law or Shari'a *regulates belief, worship, the family, and personal and social morality. Islamic scholars have recently begun to apply the tradition's authoritative sources—Qur'anic teachings, stories attributed to the Prophet (*hadith*), and* Shari'a*—to developments in modern biomedicine.*

Science and Technology. The pursuit of knowledge, including scientific inquiry, receives a divine warrant in Islamic thought. Indeed, the Islamic Code of Medical Ethics portrays the pursuit of knowledge as worship of God. Scientific discoveries do not threaten God as much as they reveal the intricacies of God's creation and will to humanity. Scientific research and investigation in most circumstances should not be curbed, and human interventions in nature are permissible to promote health.

However, Islam does not view technology as morally neutral. Instead, Islam believes careful consideration must be given to potential abuse. Islamic traditions thereby express

significant moral concern regarding the potential for discrimination in a sinful world, especially stemming from political and economic systems that do not give primacy to the promotion of human dignity. Islamic discussions of human cloning have also emphasized the possibilities for evil present in the commodification of knowledge and of persons through motivations of profit.

Therapeutic Research. The Qur'an describes persons who reject God and follow Satan as persons who "will change God's creation" (4:119). This has led leading Sunni authorities in Saudi Arabia and Egypt to condemn cloning as "the work of the devil" and advocate punishment for scientific researchers. However, Islamic jurists in general have not interpreted this Qur'anic passage to preclude forms of genetic intervention, such as somatic cell therapy, provided that such interventions are done for therapeutic purposes and are life-promoting in intent. The question Islam poses to proposals for human cloning is this: In what sense can such research legitimately be described as therapeutic?

Schools of Islamic thought have not provided a consensus on the moral status of the human embryo. Some traditions affirm that ensoulment occurs at fertilization, whereas other traditions indicate ensoulment occurs at the end of the fourth month (120 days) following fertilization. Within these latter traditions, it becomes possible to argue for research on the human pre-embryo for purposes of human health. Moreover, if the embryo is not accorded personhood, then destruction of the embryo is permissible.

Relationships. While Islam warrants biomedical research and clinical application for therapeutic purposes, issues of the integrity of relationships have raised questions about the legitimacy of reproductive technologies. The tradition gives special attention to preserving spousal, procreative, and parenting relationships because of designated role-responsibilities within the *Shari'a*. Use of third-party gametes for reproduction violates precepts concerning legitimacy, lineage, and inheritance. Transformed relationships can confuse relationships and their correlative responsibilities. These values, and objections to third-party assisted reproduction, would extend to cloning of human beings. Nonetheless, use of cloning research as an aid to fertility within the bounds of marriage would likely be substantially supported by Islamic scholars and traditions (Sachedina).

The *Shari'a* also places moral priority on refraining from harm over the production of benefits. The formation of public policy on a medical technology then must place the burden of proof on those who advocate technological innovation to establish clear benefits and to weigh immediate and prospective long-term harms.

Cloning Research: Amber
Human Cloning: Flashing Red

Judaism

Judaism is the oldest of the western monotheistic faith traditions. Its primary source of authority is the Torah, the revealed will of God in the Hebrew Bible, and rabbinic commentaries on the Torah contained in the Talmud and Mishnah. Within the United States, there are four main Jewish traditions—Conservative, Orthodox, Reform, and Reconstructionist—that collectively claim approximately 3% of the U.S. religious population. Jewish scholars have drawn on their authoritative sources and casuistical reasoning to make substantial contributions to biomedical ethics since its inception. Indeed, discussion of human cloning by Jewish scholars begins to appear in the late 1970s.

The Divine Mandate and the Self. Human beings have a command and challenge from God to use their rational, imaginative, and exploratory capacities for the benefit and health of humanity. Judaism affirms that human beings have inherent worth as creatures created in the image of God, and the Talmud understands human beings as partners with God in the ongoing act of creation. In their unique role, persons receive a divine mandate for stewardship and mastery, which encompasses a very strong emphasis on use of medical knowledge and skills to promote health, cure, and heal.

Nonetheless, the divine mandate of mastery generates moral ambivalence in the tradition with respect to cloning. Cloning is troubling because of the prospect that the mandate to master nature will be transformed into mastery over humans. The Jewish understanding of the self entails that persons are more than their genotypes. Rabbi Jakobovits has highlighted the transcendent character of the person within Jewish thought: "...man, as the delicately balanced fusion of body, mind, and soul, can never be the mere product of laboratory conditions and scientific ingenuity." Jewish perspectives on cloning are also profoundly influenced by the eugenics programs carried out on European Jewry under Nazi Germany.

An Ethic of Responsibility. Judaism is committed to an ethic of responsibility or duty, rather than an ethic of rights. The overriding duty (with three exceptions), derived from the Torah and rabbinic commentary, is the preservation of human life. Given this presumptive duty, it is possible to support cloning when it is presented as a therapeutic remedy for a genetic disease or condition, such as infertility, that besets an individual or couple. However, many proposals for human cloning do not meet these conditions of underlying disease, therapy, and individual benefit.

One exception to the command to preserve life, the prohibition of idolatry, is relevant to an assessment of cloning. Human cloning raises a danger of self-idolization. Through sexual intercourse and the raising of children, human beings are confronted with the inescapable "otherness" of persons. This otherness enables the development of humility and the authenticity of "I-Thou" relationships. These characteristics curb human hubris and self-idolization (Dorff).

The ethic of responsibility is also expressed in Jewish norms of parenthood and the responsibilities of lineage. The more the processes by which one becomes a parent—conjugal relations, conferral of genetic identity, fetal gestation in a mother's womb, birth, and raising a child—are separated from the actual creation of life, reservations and objections in Jewish thought

increase. In the context of human cloning (or other reproductive technologies), the ethic of responsibility would be diminished because of changed roles (father, mother, child) and relationships (spousal, parental, filial). It would be unclear who has responsibilities to whom between and among the generations. According to Rabbi Tendler, "we do not live well with generational inversion" that might be induced by cloning.

Status of a Clone. One source invoked by some Jewish scholars to inform community reflection are the "Golem" narratives in Jewish mysticism. The Golem narratives describe the creation of artificial, human-like life by a mystic; the Golem is subsequently destroyed without occasioning regret, because, lacking the capacity to speak, it is not considered to have human status. The narratives are deemed to present parallels to human cloning insofar as they implicitly address the status of human life without direct human parentage. However, were a human clone to be actually produced from biomedical research, there is rabbinic consensus that the clone would have human status, and the imperative to protect life would require protection and care for the clone.

Cloning Research. Jewish scholars are wary of a public policy prohibiting cloning research, which would violate the command of mastery, interfere with valuable scientific research, and compromise public oversight and accountability. It is considered important to pursue scientific research that precedes cloning for transfer because of its potential benefits. Since Jewish law does not grant full moral status to the human embryo, cloning research conducted on the early human embryo can be warranted; however, a high incidence of embryo deaths, attributable to the inefficiency of research, would violate the maxim of do no harm.

Human Cloning. The prospects of human cloning elicit ambivalence but seldom explicit condemnation in Jewish scholarship; the ambivalence is expressed in a Talmudic maxim that, at some point, human beings must ask whether they are prepared to forgo the honey from a bee in order to avoid the sting (Tendler). Jewish scholars support extensive consideration by the Jewish community of the ethical and social issues pertaining to human cloning. Rabbinic discussion does express fundamental concerns about the potential commodification of human life through cloning. Insofar as cloning, coupled with capitalistic motivations, transforms the person into a product or fungible commodity, it would violate the sacred character of human life.

Cloning Research: Amber
Human Cloning: Amber

Native American

It is worth recalling that the source of philosophical critique in Huxley's Brave New World *was Native American culture. Native Americans do not partition religion from other life domains; rather, religion is a "way of life." Good health requires living in conformity with the ways of life Native Americans received at the time of creation. The whole of creation is good within Native American narratives and all creation is animated, interrelated, and responsible for harmonious interaction to sustain the order of life in the world.*

Within this world view, Native Americans give primacy to the good of the whole, or the group, rather than to alleged needs of individuals. Individual actions must be placed within a holistic perspective; as with a pebble that causes a ripple effect in an entire body of water, so there are no isolated actions that do not have repercussions on the greater whole (Cordova).

Life Balance. Illness is a result of disorder or imbalance between persons, or between persons and nature, or within a person. The aim of traditional healing practices is to restore balance and order to the person. Ritual, ceremony, and language are no less important to maintaining or restoring health. A study of the Navajo found that thought and language were potent forces for the shaping of reality, for better or ill. Native culture would express substantial concerns with how biomedical technology shapes our language (for example, AIH, AID, GIFT, IVF, and SET to describe ART) and thus transforms reality in a manner out of harmony with the given ways of life.

Cloning Research. Animal cloning, and the potential for human cloning, risks substantial disruption of the created order and balance. Animal research erodes the reverence and kinship between humans and other created beings. Cloning research on human embryos symbolizes the western, non-Native pursuit of technical solutions to what are ultimately metaphysical problems; moreover, these technological skills are not accompanied by necessary practical wisdom about the ways of life. Sakim, a traditional elder from the Muskogee tribe observes of cloning: "We are becoming more like Creator with every day that goes by. However, it is only our abilities that are growing that way. We are not blessed with nor in any manner fraught with the judgment of Creator. That is the fundamental problem."

Resource Priorities. Fertility drugs, other methods of reproductive technology, and cloning can disrupt the balance of communal co-existence. This communal balance relies on an acceptance that human beings and groups exist in a bounded space that may not be expanded. The human species as a whole has nonetheless expanded beyond its given bounds through overpopulation; cloning simply will perpetuate a problem of human growth and increasing scarcity of those resources needed to live a decent human existence. In this context, "the application of the knowledge to clone a human being is unjustified" (Cordova). In particular, a focus on scientific technology such as cloning will divert needed attention and resources away from basic care for Native Americans, whose life expectancy is the shortest of any demographic group. The needs of a few cannot be prior to the good of the whole.

While interrelationship is cherished, it is not mutually exclusive with personal identity. A Sioux creation narrative reflects the importance of individuality as a necessary condition for diversity and interrelationship: "The reason Wakan Tanka [Creator] does not make two birds, or animals, or human beings exactly alike is because each is placed here by Wakan Tanka to be an independent individuality and to rely upon itself" (Deloria, 89). The values of balance with the patterns and ways of life, individuality, diversity, and interdependent relationships can be compromised by motivations for cloning.

Indigenous Cultures. What support that does exist among Native American cultures for human cloning may pertain to the preservation of endangered indigenous peoples. The Rev. Abraham A. Akaka, a Native American Hawaiian pastor, has commented: "For aboriginal people of our planet who see themselves as a dwindling and endangered species, cloning of the best of their race will be a blessing—a viable avenue for preserving and perpetuating their unique identities and individualities upon lands they revere as Father and Mother" (Akaka). This qualified support for human cloning is consistent with the Native emphasis of maintaining the balance of the ways of life given to peoples at creation. It does not, however, warrant individualist desires for cloning that have little bearing on the perpetuation of a species or culture.

Cloning Research: Flashing Red
Human Cloning: Flashing Red

Orthodox Christianity

In the United States, the tradition of Orthodox Christianity is institutionalized in two prominent denominational bodies, the Greek Orthodox Archdiocese of America and the Orthodox Church in America. About 3% of the U.S. religious population is affiliated with these denominations. The Bible and the wisdom of the tradition provide grounds for the ecclesiastical teaching content of Orthodox Christianity. Theologians within both denominations, as well as the Orthodox Church in America itself, have addressed the subject of cloning.

The Image of God. The concept of the person within Orthodox tradition is rooted in the *imago Dei*, with the ultimate purpose of life to realize *theosis*, or God-likeness, in union and communion with others. The image of God influences judgments about reproductive technologies and cloning. Reproductive technologies used outside the context of marriage may be viewed as attempts to recreate human beings in man's image and preferred characteristics, rather than God's image. One theologian, while acknowledging the tremendous promise that cloning holds out for agricultural development, indicates that it must be condemned "as grotesque genetic manipulation when practiced on human beings."

The image of God is also invoked as the central theological claim in a public statement on cloning, issued on 11 March 1997, by the Orthodox Church in America. The Orthodox Church believes cloning use will inevitably be abused, through such examples as "the commercialization of 'prime' DNA, production of children for the purpose of providing 'spare parts,' and movement toward creation of a 'superior' class of human beings." The statement concludes with an emphatic request that "a government ban be imposed on all forms of experimentation to produce human clones and that government funding for such activity be denied." This does not preclude public support and funding for animal cloning to produce therapeutic medical products. The call for a prohibition is addressed directly to publicly funded research, whether animal or human embryonic, that is developed for the purpose of human cloning.

The *imago Dei* requires that human beings be treated with dignity and respect. These values underlie not only treatment of the person, but the method by which the person comes into existence. Cloning creates human beings for human rather than divine purposes and thereby is a form of disrespect. Since on Orthodox understanding, the person is an embodied soul, experimentation on the body, including cloning, would necessarily enter the realm of the soul and the spiritual essence of the self. Cloning cannot be reduced to a scientific procedure on a biological organism.

Sacramental Relationships. A central concern within the Orthodox tradition is the sacramental (revelations of the sacred in human experience) dimensions of marriage, procreation, and the rearing of children. The holiness of marriage and the family is the proper context for procreation and nurture of a child. It is not permissible in Orthodox teaching to introduce the gametic or gestational contributions of third parties in human reproduction. Cloning in particular is deemed to depersonalize the human being; the prospect of manufacturing children transforms a sacred mystery into a sterile technological achievement. While a clone would be considered a person with a soul, based on its capacities for intelligence, self-determination, self-consciousness, and interpersonal and spiritual relationships, Orthodox theologians believe that a cloned human being would be valued only for extrinsic purposes, as an object for the use and exploitation of others.

Cloning Research. Orthodox theologians extend the dignity and respect owed to the person to the human embryo. This does not depend on a claim about ensoulment, but rather exhibits human finitude and fallibility: "We must treat the developing embryo with dignity and respect, because we do not know when it becomes a person" (Demopulos). Moreover, the inefficiency of current cloning techniques, if applied to human embryos, would constitute a tragedy of loss of potential human life. Such positions necessarily preclude cloning research on the embryo.

Cloning Research: Red
Human Cloning: Red

Protestant Christianity: Conservative Evangelical

The diversity of Protestantism is illustrated by the different views of Joseph Fletcher (Episcopal) and Paul Ramsey (Methodist) on human cloning. This report will try to illuminate some of the diversity, while avoiding oversimplification, by distinguishing between conservative evangelical and mainline Protestantism.

The conservative evangelical denominations considered in this report account for some 15% of the American religious population. This includes the largest Protestant body, the Southern Baptist Convention (SBC), which claims over 16 million adherents. The Christian Life Commission of the SBC issued a resolution against human cloning on 6 March 1997. While evangelical theologians and denominations do not speak as one voice, they are united in relying heavily on the Bible as the principal authority for spiritual and moral life. Protestant evangelicals began to take a serious interest in biomedical ethics following the Roe v. Wade

decision legalizing abortion in 1973, and their writings continue to focus on ethical questions at the beginning and ending of life. However, partly as a response to the influence of secular, philosophical models in medicine, evangelical ethicists have begun to address all the major questions of biomedical ethics.

The Sanctity of Life. Given evangelical emphasis on the sanctity of human life, it is not surprising that J. Kerby Anderson, perhaps the first evangelical author to address human cloning, set it within the context of the right-to-life controversy. Anderson argued that the sanctity of life is violated by cloning in two different ways. First, cloning research would inevitably result in loss of embryonic life. Secondly, although Anderson believes a clone would have a soul, he holds that societal disregard for the sanctity of human life would lead to a redefinition of humanity. In that way, society could treat the clone as a repository for spare organs and tissues.

More recent evangelical commentary has reiterated concern about the diminished personhood or humanity of the clone without invoking the sanctity of human life value. The framing context has instead been a critique of the kind of society that makes cloning a valued cultural project, namely, a society that arbitrarily projects certain traits as preferable, particularly those traits having to do with bodily appearance.

Parenthood. Evangelical discourse affirms the intrinsic connection between marriage and parenthood delineated in the *Genesis* creation story. Human cloning is theologically misguided because it breaks this connection so completely. In so doing, cloning no less ruptures critical connections between parent and child. Gilbert Meilaender argues that a marital context of giving and receiving in love is the ideal context for procreation and nurture of a child. This relational context is emphatically severed in human cloning, which "aims directly at the heart of the mystery that is the child." Thus, the idea of a child as a "gift" is effaced as the child becomes both a project and a projection of the self.

Oliver O'Donovan's argument to root the sanctity of parenthood within the Christian liturgical tradition has been especially influential in evangelical scholarship. O'Donovan contrasts the "begetting" of procreation with scientific "making" in human reproduction; the latter is exemplified by human cloning. Cloning diminishes humanity to "raw material" out of which an artifice can be designed and constructed in our image.

Southern Baptist scholars portray human cloning as distinctive and discontinuous from previous methods of human procreation; indeed, it is represented as a "radical break with the human past, and with the established patterns of human life." The distinctiveness of cloning is manifested in what R. Albert Mohler, Jr. refers to as "consumer eugenics" in which "direct genetic customization" of the human embryo is performed. Moreover, the secular principles of procreative liberty and autonomy that support cloning assault the integrity and social necessity of the family and of marital love: "The possibility of human cloning allows for the final emancipation of human reproduction from the marital relationship. Indeed, cloning would allow for the emancipation of human reproduction from *any* relationship" (Mohler, Jr.).

The Image of God. Evangelical authors directly connect issues of diminished humanity and relationality embedded in human cloning with a violation of the *imago Dei*. One author, drawing on neo-orthodox theologian Karl Barth, delineates the *imago Dei* in terms of freedom for self-determination, equality, relationality, mutual respect, and solidarity. Scientific inquiry that issues in a research project to clone human beings violates individual freedom by subordinating self-determination to scientific predetermination. The *imago Dei* is substantively compromised in a clone because of diminished solidarity and the potential deprivation of equality and relationality. Human cloning risks devaluing the person by suggesting genetics is the essence of personhood, or by valuing the clone because of its replication of valued characteristics of another person. In evangelical understandings, society could grant the clone only derivative value, not inherent value.

Religious thinkers within the Southern Baptist Convention also invoke the *imago Dei* as a bar against human cloning. As bearers of this image, human beings gain insight into self-understanding and human uniqueness and receive a distinctive status relative to the rest of creation. This sacred uniqueness is compromised by efforts at human cloning. On 6 March 1997, the Christian Life Commission of the Southern Baptist Convention issued a resolution entitled "Against Human Cloning" that supported the decision of President Clinton to prohibit federal funding for human cloning research and requested "that the Congress of the United States make human cloning unlawful." The resolution also called on "all nations of the world to make efforts to prevent the cloning of any human being."

Evangelical ethicists contend that cloning can contradict human creativity and innovation embedded in the image of God, rather than express it (as claimed by some mainline Protestant theologians). Instead of reflecting an openness to the future, cloning in fact involves a replication of the past. Thus, it should not be interpreted as creative but rather as "reactionary biological conservatism" (Jones). Cloning perpetuates the past and thereby belies our unwillingness to accept contingency and the unknown.

Cloning Research. Research on the human pre-embryo is assessed as "immoral" because of the ascription of personhood with full moral status to the conceptus. Echoing Ramsey's concern, evangelical authors describe cloning as an immoral experiment on a person without his or her consent. Moreover, cloning procedures are likely to ensue in embryonic death due to abnormalities in the embryo or practical difficulties in transferring the embryo to a host womb.

Cloning Research: Red
Human Cloning: Red

Protestant Christianity: Mainline

The religious witness of mainline Protestantism focuses on questions of peace and social justice rather than the right to life. The seven principal denominations designated as "mainline" Protestant (American Baptist, Christian Church [Disciples of Christ], Episcopal, Evangelical

Lutheran, United Methodist, Presbyterian, United Church of Christ) claim approximately 17% of the U.S. religious population.

These denominations have been very active in developing ecclesiastical position statements and convening working groups to address theological and ethical issues in biomedicine. Moreover, ecclesiastical leaders and theologians have been prominent in bringing such issues to the consideration of more global bodies, such as the National Council of Churches in Christ and the World Council of Churches. However, the primacy of freedom of conscience in Protestantism means that theologians engaged in biomedical ethics may not agree with the views of denominational bodies or their theological peers. This summary will reflect this theological diversity rather than resolve it.

Creative Freedom. An important question within mainline Protestant thought is whether there are any adequate precedents to guide ethical reflection for the advent of reproductive and genetic technologies, or what one scholar has described as the "new genesis." A first position affirms that we are free to engage in exploratory ethics because human destiny lies in the future rather than being determined by the past. Theological ethics begins by God giving human beings a future to shape and create in partnership with God. Genetic and reproductive technologies express the creative dimensions of the *imago Dei* insofar as they promote human dignity and welfare. Within this understanding, no theological principle stands as a bar to human cloning.

The Christian vocation of freedom warrants the pursuit of scientific freedom. However, freedom is not unlimited but is to be used to fulfill divine purposes. Moreover, freedom has a correlative obligation of accountability. Thus, regulation of research is justified especially given the current imprecision of the technology and the consequent loss of animal or human embryonic life. While researchers should ensure respect for the pre-embryo, and adopt procedures to minimize discarded embryos, the efficacy of such research is ultimately an issue of scientific procedure rather than of theological principle.

Even though sin will manifest itself in an ongoing disparity between a designed future and its reality, Christians are given permission to "sin bravely" in the pursuit of progress. Thus, if further research on human cloning can establish a reasonable expectation of benefits, and ensure human dignity, then both research and eventually human cloning seem warranted. The prospects of private, entrepreneurial interests establishing various cloning services could, however, culminate in diminished dignity.

Research Criteria. A second position distinguishes between the ethics of cloning research and the ethics of cloning human beings for purposes of transfer and birth. Research on cloned embryos can be justifiable, using the precedent of current standards for the regulation and protection of human and animal subjects. However, cloning of humans involves creation after our image rather than God's and can lead to power over humans rather than enhanced choices. Moreover, this position criticizes the appeal to "human" dignity as a warrant for cloning as too global and impersonal. Decision makers should instead focus on the interests of children, that is, on those persons living in the future created for them. At a minimum, society should engage in a sustained

and substantive debate on the possible benefits and the likely harms of human cloning, with a burden of proof imposed on the research community to establish a compelling case for the beneficial and therapeutic uses of the technology.

Research Moratorium. Public discourse is necessary but insufficient: A third position supports implementing a long-term moratorium on cloning research until the scientific, ethical, and social issues have been fully debated. Without a moratorium, it is entirely likely that new research discoveries could outpace discussion and thereby change the issues under debate. Both issues of cloning research on pre-embryos and cloning human beings should be subjected to ethical and theological scrutiny as well as tests of political and legal feasibility. Christians bring to this social discussion an emphasis on human creative possibility, to be sure, but also a "hermeneutics of suspicion" (Nelson) that stresses human fallibility, misplaced self-confidence, and the risks of arrogance.

Prohibitions. A fourth position places cloning within the context of positive eugenics and offers a critique of both research process and product based on the ethical precedents and prohibitions established with respect to genetic enhancements. In particular, cloning raises issues about the substantive characteristics desired in a person, the control of enormous powers of manipulation by a very small circle of experts, and whether human life will assume instrumental rather than inherent value.

Cloning Research: Green/Amber
Human Cloning: Amber

Roman Catholic Christianity

The Roman Catholic Church is the largest denomination in the U.S., with approximately 40% of the religious population and over 20% of the general population. The religious and moral authority for Roman Catholicism is grounded in the witness of God and Jesus Christ in the Bible, as interpreted through the teaching office (magisterium) of the Church. In the United States, Roman Catholic teaching is coordinated by the National Conference of Catholic Bishops (NCCB). Roman Catholic theologians, though not always in agreement with magisterial teaching, have been among the most influential contributors in biomedical ethics, and have addressed the possibility of human cloning since the 1960s.

Magisterial Teaching. *Donum Vitae*, an encyclical issued in 1987 by the Congregation for the Doctrine of the Faith condemned cloning (blastomere separation) as a violation of the dignity of the human embryo and of the intrinsic goods of human sexuality: "...attempts or hypotheses for obtaining a human being without any connection with sexuality through 'twin fission,' cloning, or parthenogenesis are to be considered contrary to the moral law, since they are in opposition to the dignity both of human procreation and of the conjugal union." While some traditions have addressed the possible abuses of cloning technology, Roman Catholic teaching maintains that the *use* of cloning techniques with respect to human beings is itself contrary to human dignity.

Scientific research on cloning since *Donum Vitae* has issued in ecclesiastical condemnation and a request to governments to enact legislation to prohibit non-therapeutic research on human embryos and cloning of human beings. In the wake of the cloning of "Dolly," a Vatican statement reiterated the basic teaching of *Donum Vitae:* "A person has the right to be born in a human way. It is to be strongly hoped that states...will immediately pass a law that bans the application of cloning on humans and that in the face of pressures, [states] have the force to make no concessions."

National Conference of Catholic Bishops. In the United States, the NCCB released a statement in March 1997 rejecting human cloning on several grounds, including an appeal to the rights of children to have real parents and not to be manufactured as copies. Moreover, research involving the cloning of human embryos is deemed unethical due to its risks and nontherapeutic objectives. The NCCB also issued support for the testimony of John Cardinal O'Connor before the New York State Senate (13 March 1997). Cardinal O'Connor criticized cloning as contrary to human parenthood and human wisdom. Human cloning violates the norms of procreation and parenthood through a process that removes "the humanism from human parents and the human child." A serious survey of the state of our degraded external environment reveals that human beings lack the wisdom to experiment with the internal human environment. O'Connor emphasizes in particular questions of technical inefficiency and issues of the character and qualifications of those who would direct the research and process of cloning, concluding that these are not matters to be left to technical specialists. O'Connor also observes that cloning falls beyond the parameters of the vocation of medicine: "The act of human cloning itself cures no pathology. Thus, we are not doctoring the patient but doctoring the race." While Roman Catholicism encourages scientific development in the service of the person and human dignity, proposals for research "that are hostile to human parenthood, unknown in deleterious consequences, and cure no disease...are not medicine and are not welcome."

Theologians: Cloning Research. While many Roman Catholic theologians have addressed the subject of human cloning, Richard A. McCormick, S.J., has provided the most constant Catholic commentary on cloning. His themes will be used as illustrative of the central concerns of theologians within the tradition. McCormick has invoked the themes of sanctity, wholeness, and individuality in criticizing cloning research on human pre-embryos. Cloning is not merely a question of scientific technique, but also involves matters of the public interest. McCormick is concerned that such research will erode respect for the human pre-embryo and pre-nascent life, and diminish the wonder of human diversity and uniqueness.

Parenthood. McCormick has also argued that human cloning is contrary to the meaning of marriage and the family. The purpose of marriage includes the binding of the unitive and procreative purposes of sexuality. Reproductive technologies, including cloning, suggest that embodiment is extrinsic rather than intrinsic to personhood. Such procedures depersonalize the family, "debodify" marital love, and violate the sacramental covenant of marriage. Moreover, natural law encompasses duties for both procreation *and* education of offspring; parental nurture

is required to enable a child to develop morally and spiritually and to assume interpersonal commitments.

Roman Catholic theologians have emphasized the sins of pride and self-interest, and the human conditions of finitude and fallibility, in assessing the prospects of human cloning. However, avoiding pride should not mean falling into the sin of sloth. Human beings have a divine responsibility for dominion that can be expanded through justified scientific research.

Cloning Research: Red
Human Cloning: Red

APPENDICES

APPENDIX A: ANNOTATED BIBLIOGRAPHY

RELIGION and CLONING

J. Kerby Anderson, *Genetic Engineering,* Grand Rapids, MI: Zondervan Publishing House, 1982.

The fundamental issue of cloning is the sanctity of life, because the potential for loss of life and genetic abnormality is very high. While clones would be creations in God's image and have souls, the major question is whether their humanity would be redefined. Because of societal disregard for the sanctity of life, clones will likely be used for spare parts and be abused.

John Breck, "Genetic Engineering: Setting the Limits," in *Health and Faith: Medical, Psychological, and Religious Dimensions,* John T. Chirban (ed.), Washington, DC: University Press of America, 1991, 51–55.

Breck contends that cloning technology holds out tremendous promise for agriculture, but that the Orthodox Church must condemn it as a grotesque manipulation were it to be practiced on human beings.

R. Geoffrey Brown, "Clones, Chimeras, and the Image of God: Lessons from Barthian Bioethics," in *Bioethics and the Future of Medicine: A Christian Appraisal,* John F. Kilner, Nigel M. de S. Cameron, David Schiedermayer (eds.), Grand Rapids, MI: William B. Eerdmans Publishing Company, 1995, 238–249.

The principles of the image of God give a decisive command to the person for prohibition of "creative (non-therapeutic) genetic predetermination of a human being" through cloning or chimeras on the grounds that human freedom is denied, respect for life is disregarded, and the relational self is violated. Human freedom for self-determination is theologically subject to the image and sovereignty of God. Scientific freedom that results in a project of human cloning "would be blatant disregard for individual freedom," because it subordinates self-determination to scientific determination. Moreover, a clone lacking the characteristics of freedom, which in turn diminishes equality, relationality, and fellow humanity, would be compromised as a person in the image of God.

Ronald Cole-Turner, "Dolly Theology," unpublished manuscript.

Cole-Turner recommends a temporary and voluntary ban on all human cloning, which should last well into the next decade in order to allow full public discussion. The role of the church is to prevent trivial and misguided uses of cloning through careful and open consideration of proposed reasons.

Cole-Turner does not see a theologically or morally significant difference between a cloned and an uncloned embryo, but this should be an item for public discussion. Cole-Turner distinguishes selfish, sinister, exploitative, and possessive uses for desiring to reproduce through cloning an

embryo. He cannot, however, imagine any "loving" reasons; non-loving reasons will devalue the identity of the child.

Congregation for the Doctrine of the Faith, *Instruction on Respect for Human Life in Its Origin and on the Dignity of Procreation*, Vatican City, 22 February 1987.

The *Instruction* prohibits human cloning, both as a scientific *outcome* and as a scientific *proposal*: "Attempts or hypotheses for obtaining a human being without any connection with sexuality through 'twin fission,' cloning, or parthenogenesis are to be considered contrary to the moral law, since they are in opposition to the dignity both of human procreation and of the conjugal union." The prohibition is based in the twin and intrinsically linked meanings of sexual intercourse, procreative and unitive sexuality. The violation of the moral law incurred through a cloning hypothesis concerns the usurpation of God's domain by a scientific ideology devoted to mastery of human destiny.

Charles E. Curran, "Moral Theology and Genetics," *Crosscurrents* 20 (Winter 1970): 64–82.

While finding himself in agreement with most of Paul Ramsey's conclusions on genetic engineering, including cloning, Curran believes Ramsey presents a "closed" or static concept of human nature and that he neglects the expanded dominion over human existence that modern science has bequeathed to us. Thus, Ramsey risks the danger of sloth. However, Curran's critique of proposals for human cloning appeals more to human propensities for pride. The Christian understanding of human nature as limited and sinful means the decisions required for clonal reproduction, such as the selection of ideal types, either could not be made because of incomplete information, or would be made arbitrarily.

Richard Doerflinger, "Remarks in Response to News Reports on the Cloning of Mammals," *National Conference of Catholic Bishops*, 25 February 1997.

Speaking on behalf of the NCCB, Doerflinger maintains that Catholic teaching rejects the cloning of human beings because it is not a worthy way to bring a human being into the world. Children have rights to have real parents and not to be manufactured as products. Research on human embryos for cloning purposes is unethical because it violates informed consent and poses risks in non-therapeutic experimentation.

Nancy J. Duff, "Clone with Caution," *The Washington Post*, 2 March 1997, C1, 5.

Duff presents several reasons against cloning from a theological perspective. These include: (1) Cloning represents an insidious form of pride, insofar as we may seek to create a more perfect humanity, or a humanity created after our own image. Power to clone human beings means power over human beings; (2) Human beings are not their own creators, but cloning raises the prospect of humanity acting as its own destroyer; (3) Human cloning may challenge traditional forms of human procreation; (4) There is a potential risk of harm to the identity of the cloned child; (5) The presumed ownership and manipulation of animal life necessary for human cloning may violate the theological claim of dominion.

The Church is called to "forge a responsible path for this new technology." Duff opposes actual cloning of humans, but believes research on cloning may be encouraged if science will proceed cautiously, openly, and with a willingness to be subject to regulations for the protection of the public good.

Sri Eknath Easwaran, "Brave New World," *Blue Mountain: A Journal for Spiritual Living* (March 1997).

From within Hindu spirituality, Easwaran believes we must ask of cloning technology: "Will this help me in my search for realizing God, who is enshrined in the depths of my consciousness?"

Kenneth D. Eberhard, "Genetics and Human Survival," *Linacre Quarterly* 40:3 (August 1973), 167–181.

Cloning reduces humankind to a material and scientific object to such an extent that the humanity of all is placed under attack. It could not be justifiable to have a cloned child unless human beings were considered merely as material objects. A world of scientific reductionism is not a world the Christian wishes to live in.

John S. Feinberg, Paul D. Feinberg, *Ethics for a Brave New World*, Wheaton, IL: Crossway Books, 1993.

The authors view cloning as impractical and immoral. It is impractical, because research procedures are likely to cause embryo death due to abnormality or failure to transfer to a host womb successfully. It is immoral because a person is present at conception. Cloning therefore involves an immoral experiment on a person without his or her consent.

Joseph Fletcher, *Humanhood: Essays in Biomedical Ethics*, Buffalo, NY: Prometheus Books, 1979; *The Ethics of Genetic Control*, Garden City, NY: Anchor, 1974; "New Beginnings in Life: A Theologian's Response," in The New Genetics and the Future of Man, Michael Hamilton (ed.), Grand Rapids, MI: Wm. B. Eerdmans Publishing, 1972, 78–89.

Fletcher argued the "real moral question" is not whether or not to engage in cloning, but when and why. His own reply is that "There is no ethical objection to cloning when it is *morally* (that is, humanely) employed."

Fletcher portrays cloning as one among many methods of "reproduction," useful under appropriate circumstances: "It can alternate with sexual reproduction as need suggests, in one generation or another." Indeed, according to the criteria of humanness, "laboratory reproduction is radically human" because it is rational and deliberate. Human beings should exercise the same kind of reproductive choice and control over themselves that they do over non-humans: "What men can do by cloning with their plants and animals they could and sometimes should do for themselves."

Among moral or humane uses of cloning technology are (1) to provide "clonants" (instructively, Fletcher never uses the language of "person") with sources of immunologically compatible

life-saving organs; (b) perpetuation of the "finest genotypes" in our species; (c) cloning a child's sex to avoid a genetic-linked disease or to insure family survival; (d) selective reproduction of individuals (e.g., top scientists) for social vocations that require specific characteristics; (e) reparation of a diminished gene pool; or (f) safeguarding those (e.g., soldiers) who assume risks or dangerous roles on behalf of the society.

Bernard Häring, *Ethics of Manipulation: Issues in Medicine, Behavior Control, and Genetics*, New York: Seabury Press, 1975.

Haring raises specific objections to human cloning: (1) it would disrupt human procreative responsibilities: "The total severance of the unitive and procreative purposes of sexuality would have profound repercussions on all human relationships"; (2) a clone may have a compromised sense of identity, belonging, and continuity, which would make it difficult to achieve a willingness to accept interpersonal responsibility and commitment; (3) widespread cloning would undermine the stability of marriage and family.

Maher Hathout, "Cloning: Who Will Set the Limits?" *The Minaret* 19:3 (March 1997), 8.

Hathout argues that the Qur'an and Islam encourage scientific inquiry: Scientific knowledge becomes a symbol or sign of God's creation. Cloning research imitates creation by manipulation of elements created by God (*khaliq*), but does not change creation (*bari*).

The larger question within Islam concerns the application of research. Human beings do have responsibility before God for how they apply research findings. Human dignity must be protected from abuse. Thus, application must be complemented with ethical and sociological studies on possible harm to humans. Moreover, the commodification of knowledge, when it is traded, bought, and sold, is a "violation of the divine principles of serving God and his creation." A similar judgment would be made of uses of cloning for purposes of political and cultural superiority.

Philip Hefner, "Cloning as Quintessential Human Act," forthcoming in *Insights*, June 1997.

Hefner believes the significance of cloning lies in its revelation to us of fundamental realities: Human beings are created co-creators; we are thoroughly natural creatures; and cloned humans are natural persons.

Theologically, Hefner contends that life is God's gift; that humans are to be good stewards of God's gifts; humans are free and accountable to God; and that human experience is inevitably sinful. Policies on cloning should reflect these realities, allowing considerable time for public discussion, attending to the complex sets of values, and accounting for our fallible judgments.

D. Gareth Jones, *Brave New People: Ethical Issues at the Commencement of Life*, Grand Rapids, MI: Wm. B. Eerdmans Publishing, 1985.

Jones argues that cloning is unacceptable to Christians. Creativity and change are intrinsic to human life and reflect our likeness of God, who is creative and innovative. Cloning by contrast

involves a replication of the past, and therefore, is a form of "reactionary biological conservatism."

The value of clones lies in their replication of characteristics of other persons; clones are valued for others, rather than for themselves. Thus, they are creatures in "our" likeness, rather than God's. Jones fears that human cloning will result in a lost humanness. In addition, Jones believes that society is incapable of addressing the ethical issues raised by implementation of cloning.

Damien Keown, *Buddhism and Bioethics,* New York: St. Martin's Press, 1995.
In a short discussion of asexual reproduction, Keown contends that human cloning will merely illustrate the variety of ways that life can be generated, consistent with teaching in Buddhist texts. The Buddhist narrative tradition relates stories of "spontaneous generation" in which sages and supernatural beings have power to "materialize a human form for themselves at will." On Keown's view, both the clone and the host are ontological individuals entitled to full respect.

Andrew Kimbrell, *The Human Body Shop: The Engineering and Marketing of Life,* New York: HarperCollins Publishers, 1993.
Kimbrell recommends a "complete ban on the cloning of human beings." This policy is based on an appeal to the "sacred image of the human form," suggesting conceptions of embodiment and the image of God.

C.S. Lewis, *The Abolition of Man,* New York: Macmillan Publishing Co., 1973.
The consequences of designing our descendants would be less freedom: "If any one age really attains, by eugenics and scientific education, the power to make its descendants what it pleases, all men who live after that are patients of that power."

Richard A. McCormick, S.J., *How Brave a New World: Dilemmas in Bioethics,* Garden City, NY: Doubleday & Company, Inc., 1981.
McCormick argues that Fletcher distorts the notion of humanness by equating "rational control" with "good" in discussions of asexual reproduction. The criteria of deliberation and rationality tell us only that a person is acting, not that the person is acting humanly. McCormick then offers his own view that reproductive procedures such as IVF and cloning are "inimical to marriage and the family." There is no justification for such steps "unless a value the equivalent of survival demands it."

McCormick finds himself in agreement with Ramsey (and Leon Kass) on the issue of whether such procedures depersonalize and dehumanize the family and its members. First, they suggest that embodiment is extrinsic rather than intrinsic to personhood. Moreover, laboratory control of reproduction undermines the biological and moral bonds of the family.

Richard A. McCormick, S.J., "Should We Clone Humans," *The Christian Century* November 17–24, 1993, 1148–1149; "Blastomere Separation: Some Concerns," *Hastings Center Report* 24:2 (1994), 14–16.

McCormick argues in his original article, and in a subsequent rejoinder to John Robertson, that cloning is capable of imposing irreparable harm to "our cherished sense of the sanctity, wholeness, and individuality of human life." The status of the human preembryo used in human cloning research at George Washington University is of substantial public importance because it reflects basic attitudes toward human life. McCormick is concerned that support for autonomous choices regarding preferential breeding will be detached from social contexts of eugenics. We will reduce the totality to a part and begin to value a person in terms of the particular trait he or she was programmed to have. Finally, cloning may "shatter our wonder at human diversity and individuality."

C. Ben Mitchell, as cited in "Cloning of Embryos Stirs Ethical Concerns," *The Christian Century* November 10, 1993, 1117.

Responding to the George Washington University experiment, ethicist Ben Mitchell of the Christian Life Commission of the Southern Baptist Convention argues, "It is difficult to see how this technology could be used without devaluing the sanctity of human life. Human beings are more than the sum of genetic parts."

Oliver O'Donovan, *Begotten or Made?*, Oxford: Clarendon Press, 1984.

Using the Nicene Creed as a point of departure, O'Donovan contrasts the theological use of "begotten" with "making." Begetting generates that which is like ourselves (in the way the Son was like the Father), while making produces that which is unlike ourselves. Cloning represents the culmination of scientific making in human reproduction. The use of scientific capacity comes at the cost of natural humanity: "Cloning techniques demonstrate that mankind does have the awesome technical power to exchange the humanity which God has given him for something else, to treat natural humanity itself as a raw material for constructing a form of life that is *not* natural humanity but is an artificial development *out of* humanity."

Orthodox Church in America, "Statement on Recent Developments in Cloning Technology," 11 March 1997.

This denominational statement holds that the prospect of human cloning raises the prospect of an ominous slippery slope, in which use of cloning will inevitably lead to abuse. "Prime" DNA will be commercialized, children will be produced for their spare parts, and there will be movement to create a superior race of human beings.

The statement concludes by emphatically requesting that a government ban be imposed on all forms of experimentation to produce human clones and that government funding for such activity be denied.

Paul Ramsey, *Fabricated Man: The Ethics of Genetic Control*, New Haven: Yale University Press, 1970, especially pp. 60–103, "Shall We Clone A Man?"; "Moral and Religious Implications of Genetic Control," in *Genetics and the Future of Man*, John D. Roslansky (ed.), New York: Appleton-Century-Croffs, 1966, 107–169.

Ramsey portrayed clonal reproduction as a "borderline" for medicine and society. Cloning seeks to modify the genetic conditions of life in the service of non-patients—the human species or control of evolution—and thus risks changing medicine's vocation of service to life and to real patients.

> As part of a general critique of asexual reproduction, Ramsey identified three "horizontal" (person-person) and two "vertical" (person-God) violations of cloning on moral norms: (1) Clonal reproduction would inevitably require "coercive" or "dictated breeding" in order to ensure a controlled gene pool. (2) Scientific optimism for eugenic improvement of the species would neglect injustices and "mishaps" perpetrated on individuals. (3) Cloning represents an assault on human parenthood. Cloning technology alienate the person from his or her embodied personhood through a technical, non-relational, and dehumanized process. The two vertical violations of hubris and playing God explicitly invoke a theological anthropology. With the death of God in secular culture, human beings who enact their self-modifying freedom assume the role of man-God. (92).

Fred Rosner, *Modern Medicine and Jewish Ethics*, New York: Yeshiva University Press, 1986.

Rosner suggests three questions are involved in Jewish discussion of cloning: (1) Are we encroaching on the domain of the Creator? (2) Are we allowed to tamper with our essence in creating an "artificial" human? (3) Do we have permission to alter humanhood and humanity? Such issues deserve "extensive consideration" within the Jewish community.

Thomas A. Shannon, "Cloning, Uniqueness, and Individuality," *Louvain Studies* 19 (1994), 283–306.

Shannon examines the implications of cloning for genetic uniqueness and individuality in the wake of the George Washington University studies. Drawing on the scholastic theologian John Duns Scotus, Shannon argues for a difference between genetic uniqueness, i.e., the genome which constitutes a common nature for the human species, and individuality, which begins through cellular division and continues through the life experiences of a person. Persons may then be genetically but not individually interchangeable. Shannon holds that the pre-embryo is not morally mistreated through the technical process of cloning, but individuals will be, because they are valued for reasons other than their inherent worth and dignity.

Seymour Siegel, "Genetic Engineering: Some Reflections," address to the Rabbinical Assembly Convention, New York, 1978, as cited in Martin Ebon, *The Cloning of Man: A Brave New Hope or Horror,* New York: Signet Books, 1978.

Siegel addressed the prospects of cloning in the future. He argued that we cannot play God, but that humankind is challenged by God to use its reason, its imagination, and its daring in an effort to improve the health and welfare of the human species.

Charles Stinson, "Theology and the Baron Frankenstein: Cloning and Beyond," *The Christian Century* 89 (January 19, 1972), 60–63.

In opposition to Ramsey, Stinson envisions "socially regulated cloning of individuals deemed especially valuable to the community" within the next century. He offers a "key theological concept for the future": The spiritual significance of life lies in the ongoing content of human life, not its origin, whether natural or artificial.

Stinson contends that clones would have a "soul"—insofar as they would be capable of personal, ethical, aesthetic, and religious experience. So long as a clone is raised in a loving familial environment, Stinson believes there is little question about the genuineness of the humanity of a clone.

Allen D. Verhey, "Cloning: Revisiting an Old Debate," *Kennedy Institute of Ethics Journal* 4:3 (September 1994), 227–234; "Theology after Dolly," *The Christian Century*, March 19–26, 1997, 285–286.

Verhey contrasts the views of Joseph Fletcher and Paul Ramsey on five major themes:

1) **Freedom**: Fletcher understood freedom to be a sufficient principle of morality, while Ramsey held it to be insufficient and limited by our embodied and social nature.

2) **Good and Evil:** Fletcher assessed "good" in terms of the maximization of happiness. Ramsey believed that happiness was not sufficient to account for the good life in a family, and that we must be concerned with how happiness is distributed.

3) **Embodiment:** Fletcher located the person in our capacity for rational choice and control. Ramsey emphasized our embodied selfhood, including sexuality as intrinsic to self.

4) **Nature:** Fletcher followed in the Baconian tradition of celebrating technology and human mastery over nature. Ramsey recognized that technology is also the power of some people over other people.

5) **Parenthood**: Fletcher emphasized the social parent, while Ramsey argued for the significance of biological parenting. We are called to see children as gifts, not products.

World Council of Churches, *Faith and Science in an Unjust World*, Geneva: World Council of Churches, 1979.

A working group of the World Council of Churches examining ethics and the biological sciences believed cloning raised ethical objections similar to those of positive eugenics—namely, that there is no societal, let alone global, consensus on "superior" human qualities, and that cloning technology places enormous powers of manipulation in the hands of a few experts, who require control by other experts.

APPENDIX B: BIBLIOGRAPHY

Endnotes: Sections 1 and 2

[1] Cahill, L.S., Cloning: Religious-Based Perspectives, Testimony before the National Bioethics Advisory Commission, March 13, 1997.

[2] Childress, J.F., *Practical Reasoning in Bioethics*, Bloomington, IN: Indiana University Press, 1997.

[3] Cole-Turner, R., Dolly Theology, Unpublished manuscript.

[4] ———, Is genetic engineering co-creation?, *Theology Today*, 44:338-349, 1987.

[5] Congregation for the Doctrine of the Faith, Instruction on respect for human life in its origin and on the dignity of procreation, *Origins*, 16(40):698-711, 1987.

[6] Dorff, R.E.N., Human Cloning: A Jewish Perspective, Testimony before the National Bioethics Advisory Commission, March 14, 1997.

[7] Einstein, A., Strange is our situation here upon Earth, in *The World Treasury of Modern Religious Thought*, J. Pelikan (ed.), Boston: Little, Brown and Company, 1990, 202-205.

[8] Fadlallah, M.H., as cited in Cloning should be punishable by death or amputation: Saudi cleric, *Agence France Presse*, March 13, 1997.

[9] Fletcher, J., *Humanhood: Essays in Biomedical Ethics*, Buffalo, NY: Prometheus Books, 1979.

[10] ———, *The Ethics of Genetic Control*, Garden City, NY: Anchor Press, 1974.

[11] ———, New beginnings in human life: A theologian's response, in *The New Genetics and the Future of Man*, M. Hamilton (ed.), Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1972, 78-89.

[12] ———, Ethical aspects of genetic controls, *N Engl J Med*, 285(14):776-783, 1971.

[13] Freundel, R.B., Judaism, in *On the New Frontiers of Genetics and Religion*, J.R. Nelson (ed.), Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1994, 120-136; Personal communication, March 6, 1997.

[14] Gustafson, J.M., Where theologians and geneticists meet, *dialog*, 33(1):7-16, 1994.

[15] ———, Genetic therapy: Ethical and religious reflections, *J Contemp Health Law Policy*, 8(Spring):183-206, 1992.

[16] Hathout, M., Cloning: Who will set the limits?, *The Minaret*, 19(3):8, 1997.

[17] Hefner, P., Cloning as quintessential human act, *Insights*, June 1997.

[18] Lewis, C.S., *The Abolition of Man*, New York: Macmillan Publishing Company, 1973, 70, 71.

[19] Lynn, B., *Genetic Manipulation*, New York: Office for Church in Society, United Church of Christ, 1977.

[20] McCormick, R.A., Should we clone humans?, *The Christian Century*, Nov. 17-24, 1993, 1148-1149.

[21] ———, Blastomere separation: Some concerns, *Hastings Center Report*, 24(2):14-16, 1994.

[22] Meilaender, G.C., Testimony before the National Bioethics Advisory Commission, March 13, 1997.

[23] Moraczewski, A.S., Cloning and the Church, Testimony before the National Bioethics Advisory Commission, March 13, 1997.

[24] ———, On human cloning, *Ethics and Medics*, 19(6):3-4, 1994.

[25] O'Donovan, O., *Begotten or Made?*, Oxford: Clarendon Press, 1984, 16.

[26] Peters, T., *Playing God? Genetic Discrimination and Human Freedom*, New York: Routledge, 1997; Personal communication, March 13, 16, 1997.

[27] Ramsey, P., *Fabricated Man: The Ethics of Genetic Control*, New Haven, CT: Yale University Press, 1970.

[28] ———, Moral and religious implications of genetic control, in *Genetics and the Future of Man*, J.D. Roslansky (ed.), New York: Appleton-Century-Crofts, 1966, 107-169.

[29] Reformed Church in America, Genetic engineering, in *Minutes of General Synod*, New York: Office of Social Witness and Worship, 1988, 61-74.

[30] Rorvik, D.M., *In His Image: The Cloning of a Man*, Philadelphia: J.B. Lippincott Company, 1978.

[31] Sachedina, A., Islamic Perspectives on Cloning, Testimony before the National Bioethics Advisory Commission, March 14, 1997.

[32] Shannon, T.A., Cloning, uniqueness, and individuality, *Louvain Studies*, 19:283-306, 1994.

[33] Shinn, R.L., *Forced Options: Social Decisions for the 21st Century*, San Francisco: Harper & Row Publishers, 1982, 142.

[34] Tendler, R.M., Testimony before the National Bioethics Advisory Commission, March 14, 1997.

[35] ———, as quoted in A.R. Melnick, Cloning a difficult issue for churches, *Pittsburgh Post-Gazette*, March 1, 1997, A-1.

[36] Verhey, A.D., Theology after Dolly, *The Christian Century*, March 19-26, 1997, 285-286.

[37] ———, Playing God and invoking a perspective, *J Med Philos* 20:347-364, 1995.

[38] ———, Cloning: Revisiting an old debate, *Kennedy Institute of Ethics Journal*, 4(3):227-234, 1994.

References: Section 3

Akaka, A.K., Cloning: A Native American Hawaiian Comment, Personal letter, April 5, 1997.

Anderson, J.K., *Genetic Engineering*, Grand Rapids, MI: Zondervan Publishing House, 1982.

Antes, P., Medicine and the living tradition of Islam, in *Healing and Restoring: Health and Medicine in the World's Religious Traditions*, L.E. Sullivan (ed.), New York: Macmillan Publishing Company, 1989, 173-202.

Athar, S. (ed.), *Islamic Perspectives in Medicine*, Indianapolis, IN: American Trust Publications, 1993.

Avery, C., Native American medicine: Traditional healing, *JAMA*, 265(17):2271, 2273, 1991.

Berg, S., Begotten, not made?, *Star Tribune* (Minneapolis), April 26, 1997, 7B.

Breck, J., Genetic Engineering: Setting the limits, in *Health and Faith: Medical, Psychological and Religious Dimensions*, J.T. Chirban (ed.), Washington, DC: University Press of America, 1991, 51-55.

Brown, R.G., Clones, chimeras, and the image of God: Lessons from Barthian ethics, in *Bioethics and the Future of Medicine: A Christian Appraisal*, J.F. Kilner, N.M.deS. Cameron, D.L. Scheidermayer (eds.), Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1995, 238-249.

Cahill, L.S., Cloning: Religion-Based Perspectives, Testimony before the National Bioethics Advisory Commission, March 13, 1997.

Carrese, J.A., L.A. Rhodes, Western bioethics on the Navajo reservation: Benefit or harm?, in *Bioethics: An Introduction to the History, Methods, and Practice*, N.S. Jecker, A.R. Jonsen, R.A. Pearlman (eds.), Sudbury, MA: Jones and Bartlett Publishers, 1997, 383-391.

Christian Life Commission, Southern Baptist Convention, Against Human Cloning, March 6, 1997.

Cohen, C.B., The moral hazards of human cloning, *Episcopalian Life*, June 1997, 24.

Cole-Turner, R., *The New Genesis: Theology and the Genetic Revolution*, Louisville, KY: Westminster/John Knox Press, 1993.

Congregation for the Doctrine of the Faith, *Instruction on Respect for Human Life in Its Origin and on the Dignity of Procreation*, 1987.

Cordova, V.F., Clones, Test Tubes, and Human Litters: A Native American Perspective, Personal statement, March 25, 1997.

Curran, C., Moral theology and genetics, *CrossCurrents*, 20(Winter):64-82, 1970.

Deloria, V. Jr., *God Is Red: A Native View of Religion*, Golden, CO: Fulcrum Publishing, 1994.

Demopulos, D., Personal statement, March 20, 1997.

Desai, P.N., Medical ethics in India, *J Med Phil*, 13(3):231-256, 1988.

———, Hinduism and bioethics in India: A tradition in transition, in *Theological Developments in Bioethics: 1988-1990*, B.A. Lustig (ed.), Dordrecht, The Netherlands: Kluwer Academic Publishers, 1991, 41-60.

Dorff, R.E.N., Human Cloning: A Jewish Perspective, Testimony before the National Bioethics Advisory Commission, March 14, 1997.

———, Testimony before the National Bioethics Advisory Commission, March 13, 1997.

———, Personal correspondence, March 5, 1997.

Duff, N.J., Clone with caution, *The Washington Post*, March 2, 1997, C1.

Easwaran, S.E., Brave new world, *Blue Mountain: A Journal for Spiritual Living*, May 1997, 11.

———, Personal correspondence, March 16, 1997.

Ellis, R.G., as cited in L. Scanlon, Cloning technology spawns moral dilemma, words of caution, *[Louisville] Courier-Journal*, April 7, 1997.

Fadlallah, M.H., as cited in Cloning should be punishable by death or amputation: Saudi cleric, *Agence France Presse*, March 13, 1997.

Feinberg, J.S., P.D. Feinberg, *Ethics for a Brave New World*, Wheaton, IL: Crossway Books, 1993.

Flack, H.E., E.D. Pellegrino (eds.), *African American Perspectives on Biomedical Ethics*, Washington, DC: Georgetown University Press, 1992.

For the president, Mr. Bill Clinton, *Hinduism Today*, April 1, 1997.

Freundel, R.B., Personal communication, March 6, 1997.

———, Judaism, in *On the New Frontiers of Genetics and Religion*, J.R. Nelson (ed.), Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1994, 120-136.

Gbadegasin, S., Personal communication, March 18, 1997.

Harakas, S.S., Questions about cloning, *Hellenic Chronicle*, 14(April 3):4, 1997.

———, Personal correspondence, March 18, 23, 1997.

———, Eastern Orthodox bioethics, in *Theological Developments in Bioethics: 1990-1992*, B.A. Lustig (ed.), Dordrecht, The Netherlands: Kluwer Academic Publishers, 1993, 117-132.

Häring, B., *Ethics of Manipulation: Issues in Medicine, Behavior Control, and Genetics*, New York: The Seabury Press, 1975.

Hathout, H., Islamic concepts and bioethics, in *Theological Developments in Bioethics: 1988-1990*, B.A. Lustig (ed.), Dordrecht, The Netherlands: Kluwer Academic Publishers, 1991, 103-118.

Hathout, H., B.A. Lustig, Bioethical developments in Islam, in *Theological Developments in Bioethics: 1990-1992*, B.A. Lustig (ed.), Dordrecht, The Netherlands: Kluwer Academic Publishers, 1993, 133-148.

Hathout, M., Cloning: Who will set the limits?, *The Minaret*, 19(3):8, 1997.

Hefner, P., Cloning as quintessential human act, in *Philosophy of Biology*, M. Ruse (ed.), Amherst, NY: Prometheus Books, 1998, 352-358.

Hultkrantz, A., Health, religion, and medicine in Native North American traditions, in *Healing and Restoring: Health and Medicine in the World's Religious Traditions*, L.E. Sullivan (ed.), New York: Macmillan Publishing Company, 1989, 327-358.

Jakobovits, R.I., Some letters on Jewish medical ethics, *J Med Philos*, 8:217-224, 1983.

John Paul II, The ethics of genetic manipulation, in *Medical Ethics: Sources of Catholic Teaching*, 2nd ed., K.D. O'Rourke, P. Boyle (eds.), Washington, DC: Georgetown University Press, 1993, 132-133.

Jones, D.G., *Brave New People: Ethical Issues at the Commencement of Life*, Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1985.

Keown, D., Personal communication, April 4, 1997.

———, *Buddhism and Bioethics*, New York: St. Martin's Press, 1995.

King, P., Personal communication, March 18, 1997.

Lipner, J.J., The classical Hindu view on abortion and the moral status of the unborn, in *Hindu Ethics: Purity, Abortion, and Euthanasia*, H.G. Coward, J.J. Lipner, K.K. Young (eds.), Albany, NY: SUNY Press, 1989, pp. 41-70.

Lopez, D., Personal communication, Mar. 18, 1997.

McCormick, R.A., Should we clone humans?, *The Christian Century*, Nov. 17-24, 1993, 1148-1149.

———, *How Brave a New World?: Dilemmas in Bioethics*, Garden City, NY: Doubleday & Company, Inc., 1981.

Meilaender, G.C., Testimony before the National Bioethics Advisory Commission, March 13, 1997.

Mitchell, C.B., as cited in Cloning of embryo stirs ethical concerns, in *The Christian Century*, November 10, 1993, 1117.

Mohler, R.A., Jr., The Brave New World of Cloning: A Christian Worldview Perspective, Unpublished manuscript, March 1997.

Moraczewski, A., Cloning and the Church, Testimony before National Bioethics Advisory Commission, March 13, 1997.

Murphy, N., Personal communication, March 10, 1997.

Murray, R.F., Personal communication, March 18, 1997.

Nakasone, R.Y., *Ethics of Enlightenment*, Fremont, CA: Dharma Cloud Publishers, 1990.

———, Personal communication, March 28, 1997.

National Conference of Catholic Bishops, Secretariat for Pro-Life Activities, *Remarks in Response to News Reports on the Cloning of Mammals*, February 25, 1997.

Nolan, K., Personal communication, March 22, 1997.

———, Buddhism, Zen, and bioethics, in *Theological Developments in Bioethics: 1990-1992*, B.A. Lustig (ed.), Dordrecht, The Netherlands: Kluwer Academic Publishers, 1993, 185-216.

O'Connor, John Cardinal, Testimony at the New York State Senate Committee of Investigation, Hearings on Cloning, March 13, 1997.

O'Donovan, O., *Begotten or Made?* Oxford: Clarendon Press, 1984.

Orthodox Church in America, *Statement on Recent Developments in Cloning Technology*, March 11, 1997.

ibn Saleh al-Othimin, M., as cited in Cloning should be punishable by death or amputation: Saudi cleric, *Agence France Presse*, March 13, 1997.

Palaniswami (ed.), *Hinduism Today*, Personal communication, March 21, 1997.

Paris, P.J., *The Social Teaching of the Black Churches*, Philadelphia: Fortress Press, 1985.

Peters, T., *Playing God? Genetic Determinism and Human Freedom.* New York: Routledge, 1997.

———, Personal communication, March 13, 1997.

Rahner, K., *Theological Investigations*, vol. 9, G. Harrison (trans), New York: The Seabury Press, 1972, 205-252.

Robinson, K.S., Personal letter, March 21, 1997.

Rosner, F., *Modern Medicine and Jewish Ethics*, New York: Yeshiva University Press, 1986, pp. 173-183.

Sachedina, A., Islamic Perspectives on Cloning, Testimony before the National Bioethics Advisory Commission, March 14, 1997.

———, Personal correspondence, March 21, 1997.

Sakim, as cited in J. Weiss, Religions aren't unanimous on cloning, *Dallas Morning News*, March 1, 1997, 1G.

Secundy, M.G., Personal letter, March 27, 1997.

Sharma, A., Personal letter, March 20, 1997.

Shinn, R.L., Personal communication, March 14, 1997.

Tendler, R.M., Testimony before the National Bioethics Advisory Commission, March 14, 1997.

———, as cited in L. David, Cloning of sheep revives ancient cultural fears, *The Columbus Dispatch*, March 16, 1997, 7B.

Tubpa, G.K., as cited in S. Dobee, Cloning poses challenge to religious leaders, Copely News Service, February 27, 1997.

Wassil, N.F., as cited in Egypt top Muslim cleric says cloning satanic, Reuters North American Wire, March 16, 1997.

Williams, P.N., Personal communication, April 7, 1997.

General Sources

Ames, D.A., C.B. Gracey, *Good Genes? Emerging Values for Science, Religion, and Society*, Cincinnati: Forward Movement Publications, 1984.

Blake, D.A., Ethics of biotechnology: Medical biotechnology for the nineties, *The Catholic World*, Sept./Oct. 1991, pp. 234-237.

Bouma, H. III, et al., *Christian Faith, Health, and Medical Practice*, Grand Rapids, MI: Wm. B. Eerdmans Publishing, 1989.

Brody, B., Current religious perspectives on the new reproductive techniques, in *Beyond Baby M: Ethical Issues in New Reproductive Technologies*, D.M. Bartels, et al. (eds.), Clifton, NJ: Human Press, 1990, 45-64.

Carney, T.P., *Instant Evolution*, Notre Dame, IN: University of Notre Dame Press, 1980.

Carrese, J.A., L.A. Rhodes, Western bioethics on the Navajo reservation: Benefit or harm? *JAMA*, 274(10):826-829, 1995.

Church of the Nazarene, Current moral and social issues: Genetic engineering and gene therapy, *Manual 1993-1997*, Kansas City, MO: Nazarene Publishing House, 1993.

Cole-Turner, R., *The New Genesis: Theology and the Genetic Revolution*, Louisville, KY: Westminster/John Knox Press, 1993.

———, Religion and the human genome, *Journal of Religion and Health*, 31(2 Summer):161-173, 1992.

———, Is genetic engineering co-creation?, *Theology Today*, 44:338-349, 1987.

———, Genes, Religion and Society: The Developing Views of the Churches, Unpublished manuscript.

Congregation for the Doctrine of the Faith, *Instruction on Respect for Human Life in Its Origin and on the Dignity of Procreation*, 1987.

Coughlan, M.J., *The Vatican, the Law, and the Human Embryo*, Iowa City: University of Iowa Press, 1990.

Cranor, C.F. (ed.), *Are Genes Us? The Social Consequences of the New Genetics*, New Brunswick, NJ: Rutgers University Press, 1994.

Duster, T., *Backdoor to Eugenics*, New York: Routledge, 1990.

Dyson, A., J. Harris (eds.), *Ethics and Biotechnology*, New York: Routledge, 1994.

Eberhard, K.E., Genetics and human survival, *Linacre Quarterly*, 40(3, August):167-181, 1973.

Ebon, M., Bring on the clones, *Human Behavior,* 8(February), 38-41, 1979.

Einstein, A., Strange is our situation here upon Earth, in *The World Treasury of Modern Religious Thought,* J. Pelikan (ed.), Boston: Little, Brown and Company, 1990, 202-205.

Eisenberg, L., The outcome as cause: Predestination and human cloning, *J Med Philos,* 1(4):318-331, 1976.

Ellison, C.W., *Modifying Man: Implications and Ethics*, Washington, DC: University Press of America, 1978.

Esbjornson, R. (ed.), *The Manipulation of Life*, San Francisco: Harper & Row Publishers, 1984.

Flack, H.E., E.D. Pellegrino, *African-American Perspective on Biomedical Ethics*, Washington, DC: Georgetown University Press, 1992.

Fletcher, J., *Humanhood: Essays in Biomedical Ethics*, Buffalo, NY: Prometheus Books, 1979.

———, *The Ethics of Genetic Control*, Garden City, NY: Anchor Press, 1974.

———, New beginnings in human life: A theologian's response, in *The New Genetics and the Future of Man*, M. Hamilton (ed.), Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1972, 78-89.

———, Ethical aspects of genetic controls, *N Eng J Med*, 285(14):776-783, 1971.

Freundel, R.B., Judaism, in J.R. Nelson, *On the New Frontiers of Genetics and Religion*, Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1994, 120-136.

General Conference of Seventh-day Adventists, Health Department, Christian Principles of Genetic Interventions, Silver Spring, MD, June 13, 1995.

———, Genetic engineering and the study of its implications, *Journal of the General Convention of the Episcopal Church 1985*, New York: General Convention, 1986, 179.

Guidelines in the area of genetic engineering, *Journal of the General Convention of the Episcopal Church 1991*, New York: General Convention, 1992.

Gustafson, J.M., Where theologians and geneticists meet, *dialog,* 33(1):7-16, 1994.

———, Genetic therapy: Ethical and religious reflections, *J Contemp Health Law Policy,* 8(Spring):183-206, 1992.

———, Basic ethical issues in the biomedical fields, *Soundings,* 53:151-180, 1990.

Hamilton, M., New life for old: Genetic decisions, *The Christian Century,* 86:741-744, 1969.

——— (ed.), *The New Genetics and the Future of Man,* Grand Rapids, MI: Wm. B. Eerdmans Publishing, 1972.

Häring, B., *Medical Ethics*, Notre Dame, IN: Fides Publishers, 1973.

Hathout, M., Cloning: Who will set the limits, *The Minaret,* 19(3):8, 1997.

Hefner, P., Cloning as quintessential human act, *Insights,* June 1997.

Heyd, D., *Genethics: Moral Issues in the Creation of People,* Berkeley, CA: University of California Press, 1992.

Hirschorn, K., On re-doing man, *Commonwealth,* 88(May 17):257-261, 1968.

Hughes, J.J., D. Keown, Buddhism and medical ethics: A bibliographic introduction, *Journal of Buddhist Ethics,* 2:105-124, 1995.

Human cloning and Catholic teaching, *The Medical-Moral Newsletter,* 31(1):1-2, 1994.

Hyde, M.E., L.E. Hyde, *Cloning and the New Genetics*, Hillside, NJ: Enslow Publishers, Inc., 1984.

Jacob, W. (ed.), *American Reformed Response,* New York: Center Conference of American Rabbis, 1983.

Jakobovits, R.I., *Jewish Medical Ethics*, New York: Bloch Publishing Co., 1975.

Jones, D.G., *Brave New People: Ethical Issues at the Commencement of Life,* Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1985.

Kahn, C., Can we achieve immortality?: The ethics of cloning and other life-extension technologies, *Free Inquiry,* Spring 1989, 14-18.

Kilner, J.F., N.M.deS. Cameron, D.L. Scheidermeyer (eds.), *Bioethics and the Future: A Christian Appraisal*, Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1995.

Kuhn, H.B., Prospect of carbon-copy humans, *Christianity Today,* 15:639-642, 1971.

Lammers, S., A. Verhey (eds.), *On Moral Medicine: Theological Perspectives in Medical Ethics*, Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1987.

Land, R.D., L.A. Moore (eds.), *Life at Risk: The Crises in Medical Ethics*, Nashville, TN: Broadman & Holman Publishers, 1995.

Langone, J., *Human Engineering: Marvel or Menace?*, Boston: Little, Brown & Co., 1978.

Lauritzen, P., *Pursuing Parenthood: Ethical Issues in Assisted Reproduction*, Bloomington, IN: Indiana University Press, 1993.

LeBar, M., The pros and cons of human cloning, *Thought*, 59(234):319-333, 1984.

Lewis, C.S., *The Abolition of Man*, New York: Macmillan Publishing Company, 1973, 70, 71.

Linzey, A., *Animal Theology*, Chicago: University of Illinois Press, 1994.

———, Human and animal slavery, in *The Bio-Revolution: Cornucopia or Pandora's Box*, P. Wheale, R. McNally (eds.), Winchester, MA: Pluto Press, 1990, 175-188.

Lipkin, M. Jr., P.J. Rowley (eds.), *Genetic Responsibility: On Choosing Our Children's Genes*, New York: Plenum Press, 1974.

Lustig, B.A. (ed.), *Theological Developments in Bioethics, 1990-1992*, vol. 3, Dordrecht, The Netherlands: Kluwer Academic Publishers, 1993.

———, *Theological Developments in Bioethics, 1988-1990*, vol. 1, Dordrecht, The Netherlands: Kluwer Academic Publishers, 1991.

Lynn, B., *Genetic Manipulation*, New York: Office for Church in Society, United Church of Christ, 1977.

Mackenzie, D., A new crusade for science?: Morality in science, *New Scientist*, 13(November):49, 1993.

Mangum, J.M., *The New Faith-Science Debate*, Minneapolis: Fortress Press, 1989.

McCormick, R.A., Blastomere separation: Some concerns, *Hastings Center Report*, 24(2):14-16, 1994.

———, Should we clone humans?, *The Christian Century*, November 17-24, 1993, 1148-1149.

———, *Health and Medicine in the Catholic Tradition*, New York: Crossroad Publishing, 1984.

———, *How Brave a New World? Dilemmas in Bioethics*, Garden City, NY: Doubleday & Company, Inc., 1981.

———, Reproductive technology: Ethical issues, in *Encyclopedia of Bioethics*, W.T. Reich (ed.), New York: Free Press, 1978, 1454-1464.

Meier, R.L., *Jewish Values in Bioethics*, New York: Human Sciences Press, 1986.

Melton, J.G. (ed.), *Encyclopedia of American Religions*, 4th ed., Detroit: Gale Research, 1993.

Meyer, J.R., Cloning human embryos: Why artificial human procreation is immoral, *Linacre Quarterly*, 62(2):22-29, 1995.

Mitchell, C.B., Genetic engineering: Bane or blessing?, Nashville, TN: Christian Life Commission of the Southern Baptist Convention, 1994.

———, Was Jesus an embryo?: The ethics of human embryo research and the *Brave New World*, Nashville, TN: Christian Life Commission of the Southern Baptist Convention, 1994.

National Council of Churches in Christ, *Genetic Science for Human Benefit*, New York: National Council of Churches, 1986.

———, *Genetic Engineering: Social and Ethical Consequences*, New York: National Council of Churches, 1983.

———, *Human Life and the New Genetics*, New York: National Council of Churches, 1980.

Nelson, J.R., The role of religions in the analysis of the ethical issues of gene therapy, *Human Gene Therapy*, 1:43-48, 1990.

———, *Human Life: A Biblical Perspective for Bioethics*, Philadelphia: Fortress Press, 1984.

———, Genetic science: A menacing marvel, *The Christian Century*, July 6-13, 1983, pp. 636-638.

———, *Science and Our Troubled Conscience*, Philadelphia: Fortress Press, 1980.

———, (ed.), *On the New Frontiers of Genetics and Religion*, Grand Rapids, MI: Wm. B. Eerdmans Publishing Company, 1994.

Niebuhr, G., Suddenly, religious ethicists face a quandary on cloning, *New York Times*, March 1, 1997, 1, 10.

O'Donovan, O., *Begotten or Made?*, Oxford: Clarendon Press, 1984.

Peters, T., *Playing God? Genetic Discrimination and Human Freedom*, New York:Routledge, 1997.

———, 'Playing God' and germline intervention, *J Med Philos*, 20:365-386, 1995.

Peters, T.F., R.J. Russell, The Human Genome Project: What questions does it raise for theology and ethics? *Midwest Medical Ethics*, 8(1 Summer):12-17, 1992.

Playing God, *Hinduism Today*, June 1997, 22-25.

Rahman, F., *Health and Medicine in the Islamic Tradition: Change and Identity*, New York: Crossroad Publishing, 1989.

Rahner, K., *Theological Investigations*, vol. 9, G. Harrison (trans.), New York: Crossroad, 1972.

Ramsey, P., *Fabricated Man: The Ethics of Genetic Control*, New Haven, CT: Yale University Press, 1970.

———, Moral and religious implications of genetic control, in *Genetics and the Future of Man*, J.D. Roslansky (ed.), New York: Appleton-Century-Crofts, 1966, 107-169.

Ratanakul, P., Bioethics in Thailand: The struggle for Buddhist solutions, *J Med Philos*, 13(3):301-312, 1988.

Reformed Church in America, Genetic engineering, in *Minutes of General Synod*, New York: Office of Social Witness and Worship, 1988, 61-74.

Reiss, M.J., R. Straughan, *Improving Nature?: The Science and Ethics of Genetic Engineering*, Cambridge, UK: Cambridge University Press, 1996.

Roberts, M.A., Human cloning: A case of no harm done?, *J Med Philos*, 21(October):537-554, 1996.

Rorvik, D., *In His Image: The Cloning of a Man*, Philadelphia: J.B. Lippincott Company, 1978.

Roslansky, J.D. (ed.), *Genetics and the Future of Man*, New York: Appleton-Century-Crofts, 1966.

Rosner, F., J.D. Bleich (eds.), *Jewish Bioethics*, New York: Sanhedrin Press, 1979.

Shannon, T.A., Testimony before Senate Hearing on Human Cloning, Commonwealth of Massachusetts, March 10, 1997.

———, *Made in Whose Image?: Genetic Engineering and Christian Ethics*, Atlantic Highlands, NJ: Humanities Press, 1997.

———, Cloning, uniqueness, and individuality, *Louvain Studies*, 19:283-306, 1994.

Shinn, R.L., *The New Genetics: Challenges for Science, Faith, and Politics*, Wakefield, RI: Moyer Bell, 1996.

———, *Forced Options: Social Decisions for the 21st Century*, San Francisco: Harper & Row Publishers, 1982, 142.

———, Perilous progress in genetics, *Social Research*, 40(1):83-103, 1974.

Shinn, R.L., P. Albrecht (eds.), *Faith and Science in an Unjust World*, Philadelphia: Fortress Press, 1980.

Simmons, P.D., *Birth and Death: Bioethical Decision-making*, Philadelphia: The Westminster Press, 1983.

Steinfels, P., Beliefs, *New York Times*, March 8, 1997, 15.

Stinson, C., Theology and the Baron Frankenstein: Cloning and beyond, *The Christian Century*, January 19, 1972, 60-63.

Studdard, A., The lone clone, *Man and Medicine*, 3(2):109-117, 1978.

United Church of Christ, General Synod 17, A Pronouncement on the Church and Genetic Engineering, Cleveland: United Church of Christ, 1989.

United Methodist Church, New developments in genetic science, *The Book of Resolutions of the United Methodist Church*, Nashville, TN: United Methodist Publishing House, 1992, 325-340.

Vaux, K. (ed.), *Who Shall Live?: Medicine, Technology, Ethics*, Philadelphia: Fortress Press, 1970.

Verhey, A.D., Cloning: Revisiting an old debate, *Kennedy Institute of Ethics Journal*, 4(3):227-234, 1994.

Weir, R.F. (ed.), *Genes and Human Self-Knowledge*, Iowa City: University of Iowa Press, 1994.

Wheale, P., R. McNally, *Genetic Engineering: Catastrophe or Utopia?*, New York: St. Martin's Press, 1988.

Williams, P.N. (ed.), *Ethical Issues in Biology and Medicine*, Cambridge, MA: Schenkman Publishing Company, 1973.

Woodward, K.L., Today the sheep..., *Newsweek*, March 10, 1997, 60.

World Council of Churches, *Biotechnology: Challenge to the Churches*, Geneva: World Council of Churches, 1989.

———, *Manipulating Life: Ethical Issues in Genetic Engineering*, Geneva, World Council of Churches, 1982.

CLONING HUMAN BEINGS

An Assessment of the Ethical Issues Pro and Con

Commissioned Paper
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CONTENTS

INTRODUCTION

The world of science and the public at large were both shocked and fascinated by the announcement in the journal *Nature* by Ian Wilmut and his colleagues that they had successfully cloned a sheep from a single cell of an adult sheep (Wilmut 1997). Scientists were in part surprised, because many had believed that after the very early stage of embryo development at which differentiation of cell function begins to take place, it would not be possible to achieve cloning of an adult mammal by nuclear transfer. In this process, the nucleus from the cell of an adult mammal is inserted into an ennucleated ovum, and the resulting embryo develops following the complete genetic code of the mammal from which the inserted nucleus was obtained. But some scientists and much of the public were troubled or apparently even horrified at the prospect that if adult mammals such as sheep could be cloned, then cloning of adult humans by the same process would likely be possible as well. Of course, the process is far from perfected even with sheep—it took 276 failures by Wilmut and his colleagues to produce Dolly, their one success. Whether the process can be successfully replicated in other mammals, much less in humans, is not now known. But those who were horrified at the prospect of human cloning were not assuaged by the fact that the science with humans is not yet there, for it looked to them now perilously close.

The response of most scientific and political leaders to the prospect of human cloning, indeed of Dr. Wilmut as well, was of immediate and strong condemnation. In the United States, President Clinton immediately banned federal financing of human cloning research and asked privately funded scientists to halt such work until the newly formed National Bioethics Advisory Commission could review the "troubling" ethical and legal implications. The Director-General of the World Health Organization (WHO) characterized human cloning as "ethically unacceptable as it would violate some of the basic principles which govern medically assisted reproduction. These include respect for the dignity of the human being and the protection of the security of human genetic material" (WHO 1997). Around the world similar immediate condemnation was heard, as human cloning was called a violation of human rights and human dignity. Even before Wilmut's announcement, human cloning had been made illegal in nearly all countries in Europe and had been condemned by the Council of Europe (Council of Europe 1986).

A few more cautious voices were heard, both suggesting some possible benefits from the use of human cloning in limited circumstances and questioning its too quick prohibition, but they were a clear minority. In the popular media, nightmare scenarios of laboratory mistakes resulting in monsters, the cloning of armies of Hitlers, the exploitative use of cloning for totalitarian ends as in Huxley's *Brave New World*, and the murderous replicas of the film *Blade Runner*, all fed the public controversy and uneasiness. A striking feature of these early responses was that their strength and intensity seemed to far outrun the arguments and reasons offered in support of them—they seemed often to be "gut level" emotional reactions rather than considered reflections on the issues. Such reactions should not be simply dismissed, both because they may point us to important considerations otherwise missed and not easily articulated, and because they often have a major impact on public policy. But the formation of public policy should not ignore the moral reasons and arguments that bear on the practice of human cloning—these must be articulated in

order to understand and inform people's more immediate emotional responses. This paper is an effort to articulate, and to evaluate critically, the main moral considerations and arguments for and against human cloning. Though many people's religious beliefs inform their views on human cloning, and it is often difficult to separate religious from secular positions, I shall restrict myself to arguments and reasons that can be given a clear secular formulation and will ignore explicitly religious positions and arguments pro or con. I shall also be concerned principally with cloning by nuclear transfer, which permits cloning of an adult, not cloning by embryo splitting, although some of the issues apply to both (Cohen and Tomkin 1994).

I begin by noting that on each side of the issue there are two distinct kinds of moral arguments brought forward. On the one hand, some opponents claim that human cloning would violate fundamental moral or human rights, while some proponents argue that its prohibition would violate such rights. On the other hand, both opponents and proponents also cite the likely harms and benefits, both to individuals and to society, of the practice. While moral and even human rights need not be understood as absolute, that is, as morally requiring people to respect them no matter how great the costs or bad consequences of doing so, they do place moral restrictions on permissible actions that appeal to a mere balance of benefits over harms. For example, the rights of human subjects in research must be respected even if the result is that some potentially beneficial research is made more difficult or cannot be done, and the right of free expression prohibits the silencing of unpopular or even abhorrent views; in Ronald Dworkin's striking formulation, rights trump utility (Dworkin 1978). I shall take up both the moral rights implicated in human cloning, as well as its more likely significant benefits and harms, because none of the rights as applied to human cloning is sufficiently uncontroversial and strong to settle decisively the morality of the practice one way or the other. But because of their strong moral force, the assessment of the moral rights putatively at stake is especially important. A further complexity here is that it is sometimes controversial whether a particular consideration is merely a matter of benefits and harms, or is instead a matter of moral or human rights. I shall begin with the arguments in support of permitting human cloning, although with no implication that it is the stronger or weaker position.

Moral Arguments in Support of Human Cloning

A. Is There a Moral Right to Use Human Cloning?

What moral right might protect at least some access to the use of human cloning? Some commentators have argued that a commitment to individual liberty, as defended by J. S. Mill, requires that individuals be left free to use human cloning if they so choose and if their doing so does not cause significant harms to others, but liberty is too broad in scope to be an uncontroversial moral right (Mill 1859; Rhodes 1995). Human cloning is a means of reproduction (in the most literal sense), and so the most plausible moral right at stake in its use is a right to reproductive freedom or procreative liberty (Robertson 1994a; Brock 1994). Reproductive freedom includes not only the familiar right to choose not to reproduce, for example by means of contraception or abortion, but also the right to reproduce. The right to reproductive freedom is

properly understood to include as well the use of various artificial reproductive technologies, such as in vitro fertilization (IVF), oocyte donation, and so forth. The reproductive right relevant to human cloning is a negative right, that is, a right to use assisted reproductive technologies without interference by the government or others when made available by a willing provider. The choice of an assisted means of reproduction, such as surrogacy, can be defended as included within reproductive freedom, even when it is not the only means for individuals to reproduce, just as the choice among different means of preventing conception is protected by reproductive freedom. However, the case for permitting the use of a particular means of reproduction is strongest when that means is necessary for particular individuals to be able to procreate at all. Sometimes human cloning could be the only means for individuals to procreate while retaining a biological tie to the child created, but in other cases different means of procreating would also be possible.

It could be argued that human cloning is not covered by the right to reproductive freedom, because whereas current assisted reproductive technologies and practices covered by that right are remedies for inabilities to reproduce sexually, human cloning is an entirely new means of reproduction; indeed, its critics see it as more a means of manufacturing humans than of reproduction. Human cloning is a different means of reproduction than sexual reproduction, but it is a means that can serve individuals' interest in reproducing. If it is not covered by the moral right to reproductive freedom, I believe that must be not because it is a new means of reproducing, but instead because it has other objectionable moral features, such as eroding human dignity or uniqueness. We shall evaluate these other ethical objections to it below.

When individuals have alternative means of procreating, human cloning typically would be chosen because it replicates a particular individual's genome. The reproductive interest in question then is not simply reproduction itself, but a more specific interest in choosing what kind of children to have. The right to reproductive freedom is usually understood to cover at least some choice about the kind of children one will have; for example, genetic testing of an embryo or fetus for genetic disease or abnormality, together with abortion of an affected embryo or fetus, are now used to avoid having a child with that disease or abnormality. Genetic testing of prospective parents before conception to determine the risk of transmitting a genetic disease is also intended to avoid having children with particular diseases. Prospective parents' moral interest in self-determination, which is one of the grounds of a moral right to reproductive freedom, includes the choice about whether to have a child with a condition that is likely to place severe burdens on them and cause severe burdens to the child itself.

The more a reproductive choice is not simply the determination of oneself and one's own life but the determination of the nature of another, as in the case of human cloning, the more moral weight the interests of that other person, that is, the cloned child, should have in decisions that determine its nature (Annas 1994). But even then parents are typically taken properly to have substantial, but not unlimited, discretion in shaping the persons their children will become, for example, through education and other childrearing decisions. Even if not part of reproductive freedom, the right to raise one's children as one sees fit, within limits mostly determined by the interests of the children, is also a right to determine within limits what kinds of persons one's

children will become. This right includes not just preventing certain diseases or harms to children, but selecting and shaping desirable features and traits in one's children. The use of human cloning is one way to exercise that right.

It's worth pointing out that current public and legal policy permits prospective parents to conceive, or to carry a conception to term, when there is a significant risk, or even certainty, that the child will suffer from a serious genetic disease. Even when others think the risk or presence of genetic disease makes it morally wrong to conceive, or to carry a fetus to term, the parents' right to reproductive freedom permits them to do so. Most possible harms to a cloned child that I shall consider below are less serious than the genetic harms with which parents can now permit their offspring to be conceived or born.

I conclude that there is good reason to accept that a right to reproductive freedom presumptively includes both a right to select the means of reproduction, as well as a right to determine what kind of children to have, by use of human cloning. However, the particular reproductive interest of determining what kind of children to have is less weighty than other reproductive interests and choices whose impact falls more directly and exclusively on the parents rather than the child. Accepting a moral right to reproductive freedom that includes the use of human cloning does not settle the moral issue about human cloning, however, since there may be other moral rights in conflict with this right, or serious enough harms from human cloning to override the right to use it; this right can be thought of as establishing a serious moral presumption supporting access to human cloning.

There is a different moral right which might be thought to be at stake in the dispute about human cloning—the right to freedom of scientific inquiry and research in the acquisition of knowledge. If there is such a right, it would presumably be violated by a legal prohibition of research on human cloning, although the government could still permissibly decide not to spend public funds to support such research. Leaving aside for the moment human subject ethical concerns, research on human cloning might provide valuable scientific medical knowledge beyond simply knowledge about how to carry out human cloning. Whether or not there is a moral right to freedom of scientific inquiry—for example, as part of a right to free expression—prohibiting and stopping scientific research and inquiry is a serious matter and precedent which should only be undertaken when necessary to prevent grave violations of human rights or to protect fundamental interests. But even for opponents of human cloning, the fundamental moral issue is not acquiring the knowledge that would make it possible, but using that knowledge to do human cloning. Since it is possible to prohibit human cloning itself, without prohibiting all research on it, it is not necessary to limit the freedom of scientific inquiry in order to prevent human cloning from taking place. But this means as well that a right to freedom of scientific inquiry could only protect research on human cloning, not its use. For this reason, I believe the fundamental moral right which provides presumptive moral support for permitting the use of human cloning is the right to reproductive freedom, not the right to freedom of scientific inquiry. My discussion in what follows will principally concern the moral issues in the use of human cloning, not those restricted to research on it.

B. What Individual or Social Benefits Might Human Cloning Produce?

Largely Individual Benefits

The literature on human cloning by nuclear transfer, as well as the literature on embryo splitting where it is relevant to the nuclear transfer case, contains a few examples of circumstances in which individuals might have good reasons to want to use human cloning. However, a survey of that literature strongly suggests that human cloning is not the unique answer to any great or pressing human need and that its benefits would at most be limited. What are the principal benefits of human cloning that might give persons good reasons to want to use it?

1. Human cloning would be a new means to relieve the infertility some persons now experience. Human cloning would allow women who have no ova or men who have no sperm to produce an offspring that is biologically related to them (Eisenberg 1976; Robertson 1994b and 1997; LaBar 1984). Embryos might also be cloned, either by nuclear transfer or embryo splitting, in order to increase the number of embryos for implantation and improve the chances of successful conception (NABER 1994). While the moral right to reproductive freedom creates a presumption that individuals should be free to choose the means of reproduction that best serves their interests and desires, the benefits from human cloning to relieve infertility are greater the more persons there are who cannot overcome their infertility by any other means acceptable to them. I do not know of data on this point, but they should be possible to obtain or gather from national associations concerned with infertility.

It is not enough to point to the large number of children throughout the world possibly available for adoption as a solution to infertility, unless we are prepared to discount as illegitimate the strong desire many persons, fertile and infertile, have for the experience of pregnancy and for having and raising a child biologically related to them. While not important to all infertile (or fertile) individuals, it is important to many and is respected and met through other forms of assisted reproduction that maintain a biological connection when that is possible; there seems no good reason to refuse to respect and respond to it when human cloning would be the best or only means of overcoming an individual's infertility.

2. Human cloning would enable couples in which one party risks transmitting a serious hereditary disease, a serious risk of disease, or an otherwise harmful condition to an offspring, to reproduce without doing so (Robertson 1994b). Of course, by using donor sperm or egg donation, such hereditary risks can generally be avoided now without the use of human cloning. These procedures may be unacceptable to some couples, however, or at least considered less desirable than human cloning, because they introduce a third party's genes into reproduction, instead of giving the couple's offspring only the genes of one of them. Thus, in some cases human cloning would be a means of preventing genetically transmitted harms to offspring. Here, too, there are not data on the likely number of persons who would wish to use human cloning for this purpose instead of either using other available means of avoiding the risk of genetic transmission of the harmful condition or accepting the risk of transmitting the harmful condition.

3. Human cloning a later twin would enable a person to obtain needed organs or tissues for transplantation (Robertson 1994b, 1997; Kahn 1989; Harris 1992). Human cloning would solve the problem of finding a transplant donor who is an acceptable organ or tissue match and would eliminate, or drastically reduce, the risk of transplant rejection by the host. The availability of human cloning for this purpose would amount to a form of insurance policy to enable treatment of certain kinds of medical needs. Of course, sometimes the medical need would be too urgent to permit waiting for the cloning, gestation, and development of the later twin necessary before tissues or organs for transplant could be obtained. In other cases, the need for an organ, such as a heart or a liver, that the later twin would need to maintain life would preclude cloning and then taking the organ from an even later twin.

Such a practice has been criticized on the ground that it treats the later twin not as a person valued and loved for his or her own sake, as an end in itself in Kantian terms, but simply as a means for benefiting another. This criticism assumes, however, that only this one motive would determine the relation of the person to his or her later twin. The well-known case some years ago in California of the Ayala family, who conceived in the hopes of obtaining a source for a bone marrow transplant for their teenage daughter suffering from leukemia, illustrates the mistake in this assumption. They argued that whether or not the child they conceived turned out to be a possible donor for their daughter, they would value and love the child for itself, and treat it as they would treat any other member of their family. That one reason it was wanted was as a means to saving their daughter's life did not preclude its also being loved and valued for its own sake; in Kantian terms, it was treated as a possible means to saving their daughter, but not *solely as a means*, which is what the Kantian view proscribes.

Indeed, when people have children, whether by sexual means or with the aid of assisted reproductive technologies, their motives and reasons for doing so are typically many and complex, and include reasons less laudable than obtaining life-saving medical treatment, such as having a companion like a doll to play with, enabling one to live on one's own, qualifying for public or government benefit programs, and so forth. While these other motives for having children sometimes may not bode well for the child's upbringing and future, public policy does not assess prospective parents' motives and reasons for procreating as a condition of their doing so.

One commentator has proposed human cloning for obtaining even life-saving organs (Kahn 1989). After cell differentiation, some of the brain cells of the embryo or fetus would be removed so that it could then be grown as a brain-dead body for spare parts for its earlier twin. This body clone would be like an anencephalic newborn or presentient fetus, neither of whom arguably can be harmed, because of their lack of capacity for consciousness. Most people would likely find this practice appalling and immoral, in part because here the cloned later twin's capacity for conscious life is destroyed *solely as a means* for the benefit of another. Yet if one pushes what is already science fiction quite a bit further in the direction of science fantasy, and imagines the ability to clone and grow in an artificial environment only the particular life-saving organ a person needed for transplantation, then it is far from clear that it would be morally impermissible to do so.

4. Human cloning would enable individuals to clone someone who had special meaning to them, such as a child who had died (Robertson 1994b). There is no denying that if human cloning were available, some individuals would want to use it in order to clone someone who had special meaning to them, such as a child who had died, but that desire usually would be based on a deep confusion. Cloning such a child would not replace the child the parents had loved and lost, but rather would create a new and different child with the same genes. The child they loved and lost was a unique individual who had been shaped by his or her environment and choices, not just his or her genes, and more important, who had experienced a particular relationship with them. Even if the later cloned child could have not only the same genes but also be subjected to the same environment, which of course is in fact impossible, it would remain a different child than the one they had loved and lost, because it would share a different history with them (Thomas 1974). Cloning the lost child might help the parents accept and move on from their loss, but another already existing sibling or another new child who was not a clone might do this equally well; indeed, it might do so better, since the appearance of the cloned later twin would be a constant reminder of the child they had lost. Nevertheless, if human cloning enabled some individuals to clone a person who had special meaning to them and doing so gave them deep satisfaction, that would be a benefit to them even if their reasons for wanting to do so, and the satisfaction they in turn received, were based on confusion.

Largely Social Benefits

5. Human cloning would enable the duplication of individuals of great talent, genius, character, or other exemplary qualities. The first four reasons for human cloning considered above looked to benefits to specific individuals, usually parents, from being able to reproduce by means of human cloning. This fifth reason looks to benefits to the broader society from being able to replicate extraordinary individuals—a Mozart, Einstein, Gandhi, or Schweitzer (Lederburg 1966; McKinnell 1979). Much of the appeal of this reason, like much thinking both in support of and in opposition to human cloning, rests on a confused and mistaken assumption of genetic determinism, that is, that one's genes fully determine what one will become, do, and accomplish. What made Mozart, Einstein, Gandhi, and Schweitzer the extraordinary individuals they were was the confluence of their particular genetic endowments with the environments in which they were raised and lived and the particular historical moments they in different ways seized. Cloning them would produce individuals with the same genetic inheritances (nuclear transfer does not even produce 100% genetic identity, although for the sake of exploring the moral issues, I have followed the common assumption that it does). But neither by cloning, nor by any other means, would it be possible to replicate their environments or the historical contexts in which they lived and their greatness flourished. We do not know, either in general or with any particular individual, the degree or specific respects in which their greatness depended on their "nature" or their "nurture," but we do know in all cases that it depended on an interaction of them both. Thus, human cloning could never replicate the extraordinary accomplishments for which we admire individuals like Mozart, Einstein, Gandhi, and Schweitzer.

If we make a rough distinction between the extraordinary capabilities of a Mozart or an Einstein and how they used those capabilities in the particular environments and historical settings in which they lived, it would also be a mistake to assume that human cloning could at least replicate their extraordinary capabilities, if not the accomplishments they achieved with them. Their capabilities, too, were the product of their inherited genes and their environments, not of their genes alone, and so it would be a mistake to think that cloning them would produce individuals with the same capabilities, even if they would exercise those capabilities at different times and in different ways. In the case of Gandhi and Schweitzer, whose extraordinary greatness lies more in their moral character and commitments, we understand even less well the extent to which their moral character and greatness was produced by their genes.

None of this is to deny that Mozart's and Einstein's extraordinary musical and intellectual capabilities, nor even Gandhi's and Schweitzer's extraordinary moral greatness, were produced in part by their unique genetic inheritances. Cloning them might well produce individuals with exceptional capacities, but we simply do not know how close their clones would be in capacities or accomplishments to the great individuals from whom they were cloned. Even so, the hope for exceptional, even if less and different, accomplishment from cloning such extraordinary individuals might be a reasonable ground for doing so.

I have used examples above of individuals whose greatness is widely appreciated and largely uncontroversial, but if we move away from such cases, we encounter the problem of whose standards of greatness would be used to select individuals to be cloned for the benefit of society or humankind at large. This problem inevitably connects with the important issue of who would control access to and use of the technology of human cloning, since those who control its use would be in a position to impose their standards of exceptional individuals to be cloned. This issue is especially worrisome if particular groups or segments of society, or if government, controlled the technology, for we would then risk its use for the benefit of those groups, segments of society, or governments under the cover of benefiting society or even humankind at large.

6. Human cloning and research on human cloning might make possible important advances in scientific knowledge, for example about human development (Walters 1982; Smith 1983). While important potential advances in scientific or medical knowledge from human cloning or human cloning research have frequently been cited in some media responses to Dolly's cloning, there are at least three reasons why these possible benefits are highly uncertain. First, there is always considerable uncertainty about the nature and importance of the new scientific or medical knowledge to which a dramatic new technology like human cloning will lead; the road to that new knowledge is never mapped in advance and takes many unexpected turns. Second, we also do not know what new knowledge from human cloning or human cloning research could also be gained by other methods and research that do not have the problematic moral features of human cloning to which its opponents object. Third, what human cloning research would be compatible with ethical and legal requirements for the use of human subjects in research is complex, controversial, and largely unexplored. For example, in what contexts and from whom would it be necessary, and how would it be possible, to secure the informed consent of parties involved in human cloning?

No human cloning should ever take place without the consent of the cloned and the woman receiving a cloned embryo, if they are different. But we could never obtain the consent of the later twin to being cloned, so research on human cloning that produces a cloned individual might be barred by ethical and legal regulations for the use of human subjects in research (Ramsey 1970). Moreover, creating human clones solely for the purpose of research would be to use them solely for the benefit of others without the clones' consent, and therefore unethical. Of course, once human cloning was established to be safe and effective, then new scientific knowledge might be obtained from its use for legitimate, non-research reasons. How human subjects regulations would apply to research on human cloning needs much more exploration than I can give it here in order to help clarify how significant and likely the potential gains are in scientific and medical knowledge from human cloning research and human cloning.

Although there is considerable uncertainty concerning most of the possible individual and social benefits of human cloning that I have discussed above, and although no doubt it may have other benefits or uses that we cannot yet envisage, I believe it is reasonable to conclude that human cloning at this time does not seem to promise great benefits or uniquely to meet great human needs. Nevertheless, a case can be made that scientific freedom supports permitting research on human cloning to go forward and that freedom to use human cloning is protected by the important moral right to reproductive freedom. We must therefore assess what moral rights might be violated, or harms produced, by research on or use of human cloning.

Moral Arguments Against Human Cloning

A. Would the Use of Human Cloning Violate Important Moral Rights?

Many of the immediate condemnations of any possible human cloning following Wilmut's cloning of an adult sheep claimed that it would violate moral or human rights, but it was usually not specified precisely, or often even at all, what the rights were that would be violated. I shall consider two possible candidates for such a right: a right to have a unique identity and a right to ignorance about one's future or to an "open future." The former right is cited by many commentators, but I believe even if any such a right exists, it is not violated by human cloning. The latter right has only been explicitly defended to my knowledge by two commentators, and in the context of human cloning, only by Hans Jonas; it supports a more promising, even if in my view ultimately unsuccessful, argument that human cloning would violate an important moral or human right.

Is there a moral or human right to a unique identity, and if so, would it be violated by human cloning? For human cloning to violate a right to a unique identity, the relevant sense of identity would have to be genetic identity, that, is a right to a unique unrepeated genome. This would be violated by human cloning, but is there any such right? It might be thought there could not be such a right, because it would be violated in all cases of identical twins, yet no one claims in such cases that the moral or human rights of each of the twins have been violated. Even the use of fertility drugs, which increases the probability of having twins, is not intended to produce

twins. However, this consideration is not conclusive (Kass 1985; NABER 1994). It is commonly held that only deliberate human actions can violate others' rights, but outcomes that would constitute a rights violation if those outcomes if done by human action are not a rights violation if those outcomes result from natural causes. For example, if Arthur deliberately strikes Barry on the head so hard as to cause his death, Arthur violates Barry's right not to be killed. But if lightening strikes Cheryl, causing her death, then we would not say that her right not to be killed has been violated. The case of twins does not show there could not be a right to a unique genetic identity.

What is the sense of identity that might plausibly be each person has a right to have uniquely, which constitutes the special uniqueness of each individual (Macklin 1994; Chadwick 1982)? Even with the same genes, two individuals, for example homozygous twins, are numerically distinct and not identical, so what is intended must be the various properties and characteristics that make each individual qualitatively unique and different than others. Does having the same genome as another person undermine that unique qualitative identity? Only in the crudest genetic determinism, a genetic determinism according to which an individual's genes completely and decisively determine everything about the individual, all his or her other non-genetic features and properties, together with the entire history or biography that will constitute his or her life. But there is no reason whatever to believe in that kind of genetic determinism, and I do not think that anyone does. Even with the same genes, as we know from the cases of genetically identical twins, while there may be many important similarities in the twins' psychological and personal characteristics, differences in these develop over time together with differences in their life histories, personal relationships, and life choices. This is true of identical twins raised together, and the differences are still greater in the cases of identical twins raised apart; sharing an identical genome does not prevent twins from each developing a distinct and unique personal identity of their own.

We need not pursue what the basis or argument in support of a moral or human right to a unique identity might be—such a right is not found among typical accounts and enumerations of moral or human rights—because even if we grant that there is such a right, sharing a genome with another individual as a result of human cloning would not violate it. The idea of the uniqueness, or unique identity, of each person historically predates the development of modern genetics and the knowledge that except in the case of homozygous twins, each individual has a unique genome. A unique genome thus could not be the grounds of this long-standing belief in the unique human identity of each person.

I turn now to whether human cloning would violate what Hans Jonas called "a right to ignorance," or what Joel Feinberg called "a right to an open future" (Jonas 1974; Feinberg 1980). Jonas argued that human cloning in which there is a substantial time gap between the beginning of the lives of the earlier and later twins is fundamentally different from the simultaneous beginning of the lives of homozygous twins that occur in nature. Although contemporaneous twins begin their lives with the same genetic inheritance, they also begin their lives or biographies at the same time, and so in ignorance of what the other who shares the same genome will by his or her choices

make of his or her life. To whatever extent one's genome determines one's future, each begins ignorant of what that determination will be and so remains as free to choose a future, to construct a particular future from among open alternatives, as are individuals who do not have a twin. Ignorance of the effect of one's genome on one's future is necessary for the spontaneous, free, and authentic construction of a life and self.

A later twin created by human cloning, Jonas argues, knows, or at least believes he or she knows, too much about himself or herself. For there is already in the world another person, one's earlier twin, who from the same genetic starting point has made the life choices that are still in the later twin's future. It will seem that one's life has already been lived and played out by another, that one's fate is already determined, and so the later twin will lose the spontaneity of authentically creating and becoming his or her own self. One will lose the sense of human possibility in freely creating one's own future. It is tyrannical, Jonas claims, for the earlier twin to try to determine another's fate in this way. And even if it is a mistake to believe the crude genetic determinism according to which one's genes determine one's fate, what is important for one's experience of freedom and ability to create a life for oneself is whether one thinks one's future is open and undetermined, and so still to be determined by one's own choices.

One might try to interpret Jonas' objection so as not to assume either genetic determinism, or a belief in it. A later twin might grant that he is not determined to follow in his earlier twin's footsteps, but that nevertheless the earlier twin's life would always haunt him, standing as an undue influence on his life, and shaping it in ways to which others' lives are not vulnerable. But the force of the objection still seems to rest on a false assumption that having the same genome as his earlier twin unduly restricts his freedom to choose a different life than the earlier twin chose. A family environment also importantly shapes children's development. But there is no force to the claim of a younger sibling that the existence of an older sibling raised in that same family is an undue influence on his freedom to make a life for himself in that environment. Indeed, the younger twin or sibling might benefit by being able to learn from the older twin's or sibling's mistakes.

In a different context, and without applying it to human cloning, Joel Feinberg has argued for a child's right to an open future. This requires that others raising a child not close off future possibilities that the child would otherwise have, thereby eliminating a reasonable range of opportunities from which the child may choose autonomously to construct his or her own life. One way this right to an open future would be violated is to deny even a basic education to a child. Another way might be to create him as a later twin, so that he will believe his future has already been set for him by the choices made and the life lived by his earlier twin.

A central difficulty in evaluating the implications for human cloning of a right either to ignorance or to an open future, is whether the right is violated merely because the later twin may be likely to *believe* that his future is already determined, even if that belief is clearly false and supported only by the crudest genetic determinism. I believe that if the twin's future in reality remains open and his to freely choose, then someone acting in a way that unintentionally leads him to believe that his future is closed and determined has not violated his right to ignorance or to an

open future. Likewise, suppose I drive down the twin's street in my new car, which is just like his. I know that when he sees me, he is likely to believe that I have stolen his car, and therefore will abandon his driving plans for the day. I have not violated his property right to his car, even though he may feel the same loss of opportunity to drive that day as if I had in fact stolen his car. In each case, he is mistaken that his open future or car has been taken from him, and so no right of his has been violated. If we know that the twin will believe that his open future has been taken from him as a result of being cloned, even though in reality it has not, then we know that cloning will cause him psychological distress, but not that it will violate his right. Thus, I believe Jonas' right to ignorance, and our employment of Feinberg's analogous right of a child to an open future, turns out not to be violated by human cloning, though they do point to psychological harms that a later twin may be likely to experience and that I will address below.

The upshot of our consideration of a moral or human right either to a unique identity or to ignorance and an open future is that neither would be violated by human cloning. Perhaps there are other possible rights that would make good the charge that human cloning is a violation of moral or human rights, but I am unsure what they might be. I turn now to consideration of the harms that human cloning might produce.

B. What Individual or Social Harms Might Human Cloning Produce?

There are many possible individual or social harms that have been posited by one or another commentator, and I shall only try to cover the more plausible and significant of them.

Largely Individual Harms

1. Human cloning would produce psychological distress and harm in the later twin.

This is perhaps the most serious individual harm that opponents of human cloning foresee, and we have just seen that even if human cloning is no violation of rights, it may nevertheless cause psychological distress or harm. No doubt knowing the path in life taken by one's earlier twin may in many cases have several bad psychological effects (Callahan 1993; LaBar 1984; Macklin 1994; McCormick 1993; Studdard 1978; Rainer 1978; Verhey 1994). The later twin may feel, even if mistakenly, that his or her fate has already been substantially laid out, and so have difficulty freely and spontaneously taking responsibility for and making his or her own fate and life. The later twin's experience or sense of autonomy and freedom may be substantially diminished, even if in actual fact they are diminished much less than it seems to him or her. Together with this might be a diminished sense of one's own uniqueness and individuality, even if once again these are in fact diminished little or not at all by having an earlier twin with the same genome. If the later twin is the clone of a particularly exemplary individual, perhaps with some special capabilities and accomplishments, he or she may experience excessive pressure to reach the very high standards of ability and accomplishment of the earlier twin (Rainer 1978). All of these psychological effects may take a heavy toll on the later twin and be serious burdens under which he or she would live.

One commentator has also cited special psychological harms to the first, or first few, human clones from the great publicity that would attend their creation (LaBar 1984). While public interest in the first clones would no doubt be enormous, medical confidentiality should protect their identity. Even if their identity became public knowledge, this would be a temporary effect only on the first few clones. The experience of Louise Brown, the first child conceived by IVF, suggests this publicity could be managed to limit its harmful effects.

While psychological harms of these kinds from human cloning are certainly possible, and perhaps even likely, they remain at this point only speculative, since we have no experience with human cloning and the creation of earlier and later twins. With naturally occurring identical twins, while they sometimes struggle to achieve their own identities (a struggle shared by many people without a twin), there is typically a very strong emotional bond between the twins, and such twins are, if anything, generally psychologically stronger and better adjusted than non-twins (Robertson 1994b). Scenarios are even possible in which being a later twin confers a psychological benefit. For example, having been deliberately cloned with specific genes might make the later twin feel especially wanted for the kind of person he or she is. Nevertheless, if experience with human cloning confirmed that serious and unavoidable psychological harms typically occurred to the later twin, that would be a serious moral reason to avoid the practice.

In the discussion above of potential psychological harms to later twins, I have been assuming that one later twin is cloned from an already existing adult individual. Cloning by means of embryo splitting, as carried out and reported by Hall and colleagues at George Washington University in 1993, has limits on the number of genetically identical twins that can be cloned (Hall 1993). Nuclear transfer, however, has no limits to the number of genetically identical individuals who might be cloned. Intuitively, many of the psychological burdens and harms noted above seem more likely and serious for a clone who is only one of many identical later twins from one original source, so that the clone might run into another identical twin around every street corner. This prospect could be a good reason to place sharp limits on the number of twins that could be cloned from any one source.

There is one argument that has been used by several commentators to undermine the apparent significance of potential psychological harms to a later twin (Chadwick 1982; Robertson 1994b, 1997; Macklin 1994). The point derives from a general problem, called the non-identity problem, posed by the philosopher Derek Parfit and not originally directed to human cloning (Parfit 1984). Here is the argument. Even if all the psychological burdens and pressures from human cloning discussed above could not be avoided for any later twin, they are not harms to the twin, and so not reasons not to clone the twin. That is because the only way for the twin to avoid the harms is never to be cloned or to exist at all. But no one claims that these burdens and stresses, hard though they might be, are so bad as to make the twin's life, all things considered, not worth living—that is, to be worse than no life at all. So the later twin is not harmed by being given a life with these burdens and stresses, since the alternative of never existing at all is arguably worse—he or she loses a worthwhile life—but certainly not better for the twin. And if the later twin is not harmed by having been created with these unavoidable burdens and stresses, then how

could he or she be wronged by having been created with them? And if the later twin is not wronged, then why is any wrong being done by human cloning? This argument has considerable potential import, for if it is sound, it will undermine the apparent moral importance of any bad consequence of human cloning to the later twin that is not so serious as to make the twin's life, all things considered, not worth living.

Parfit originally posed the non-identity problem, but he does not accept the above argument as sound. Instead, he believes that if one could have a *different* child without these psychological burdens (for example, by using a different method of reproduction which did not result in a later twin), there is as strong a moral reason to do so as there would be not to cause similar burdens to an already existing child; I have defended this position regarding the general case of genetically transmitted handicaps or disabilities (Brock 1995). The theoretical philosophical problem is to formulate the moral principle that implies this conclusion and that also has acceptable implications in other cases involving bringing people into existence, such as issues about population policy. The issues are too detailed and complex to pursue here, and the non-identity problem remains controversial and not fully resolved. Suffice it to say that what is necessary is a principle that permits comparison of the later twin with these psychological burdens and a different person who could have been created instead by a different method and so without such burdens. Choosing to create the later twin with serious psychological burdens instead of a different person who would be free of them, without a weighty overriding reason for choosing the former, would be morally irresponsible or wrong, even if doing so does not harm or wrong the later twin who could only exist with the burdens. At the least, the argument for disregarding the psychological burdens to the later twin, because he or she could not exist without them, is controversial, and in my view mistaken; unavoidable psychological burdens to later twins are reasons against human cloning. Such psychological harms, as I shall continue to call them, do remain speculative, but they should not be disregarded because of the non-identity problem.

2. Human cloning procedures would carry unacceptable risks to the clone.

One version of this objection to human cloning concerns the research necessary to perfect the procedure. The other version concerns the later risks from its use. Wilmut's group had 276 failures before their success with Dolly, indicating that the procedure is far from perfected, even with sheep. Further research on the procedure with animals is clearly necessary before it would be ethical to use the procedure on humans. But even assuming that cloning's safety and effectiveness is established with animals, research would need to be done to establish its safety and effectiveness for humans. Could this research be ethically done (Pollack 1993)? There would be little or no risk to the donor of the cell nucleus to be transferred, and his or her informed consent could and must always be obtained. There might be greater risks for the woman to whom a cloned embryo is transferred, but these should be comparable to those associated with IVF procedures. The woman's informed consent, too, could and must be obtained.

What of the risks to the cloned embryo itself? Judging by the experience of Wilmut's group in their work on cloning a sheep, the principal risk to the embryos cloned was their failure

successfully to implant, grow, and develop. Comparable risks to cloned human embryos would apparently be their death or destruction long before most people or the law consider them to be persons with moral or legal protections of life. Moreover, artificial reproductive technologies now in use, such as IVF, have a known risk that some embryos will be destroyed or will not successfully implant and will die. It is premature to make a confident assessment of what the risks to human subjects would be of establishing the safety and effectiveness of human cloning procedures, but there are no unavoidable risks apparent at this time that would make the necessary research clearly ethically impermissible.

Could human cloning procedures meet ethical standards of safety and efficacy? Risks to an ovum donor (if any), a nucleus donor, and a woman who receives the embryo for implantation would likely be ethically acceptable with the informed consent of the involved parties. But what of the risks to the human clone if the procedure in some way goes wrong, or unanticipated harms come to the clone? For example, Harold Varmus, director of the National Institutes of Health, has raised the concern that a cell many years old from which a person is cloned could have accumulated genetic mutations during its years in another adult that could give the resulting clone a predisposition to cancer or other diseases of aging (Weiss 1997). Moreover, it is impossible to obtain the informed consent of the clone to his or her own creation, but, of course, no one else is able to give informed consent for their creation, either.

I believe it is too soon to say whether unavoidable risks to the clone would make human cloning unethical. At a minimum, further research on cloning animals, as well as research to better define the potential risks to humans, is needed. For the reasons given above, we should not set aside risks to the clone on the grounds that the clone would not be harmed by them, since its only alternative is not to exist at all; I have suggested that is a bad argument. But we should not insist on a standard that requires risks to be lower than those we accept in sexual reproduction, or in other forms of assisted reproduction. It is not possible now to know when, if ever, human cloning will satisfy an appropriate standard limiting risks to the clone.

Largely Social Harms

3. Human cloning would lessen the worth of individuals and diminish respect for human life.

Unelaborated claims to this effect were common in the media after the announcement of the cloning of Dolly. Ruth Macklin has explored and criticized the claim that human cloning would diminish the value we place on, and our respect for, human life, because it would lead to persons being viewed as replaceable (Macklin 1994). As argued above, only in a confused and indefensible notion of human identity is a person's identity determined solely by his or her genes. Instead, individuals' identities are determined by the interaction of their genes over time with their environments, including the choices the individuals make and the important relations they form with other persons. This means in turn that no individual could be fully replaced by a later clone possessing the same genes. Ordinary people recognize this clearly. For example, parents of a

12-year-old child dying of a fatal disease would consider it insensitive and ludicrous if someone told them they should not grieve for their coming loss because it is possible to replace him by cloning him; it is *their child who is dying*, whom they love and value, and that child and his importance to them could never be replaced by a cloned later twin. Even if they would also come to love and value a later twin as much as their child who is dying, that would be to love and value that *different child* who could never replace the child they lost. Ordinary people are typically quite clear about the importance of the relations they have to distinct, historically situated individuals with whom over time they have shared experiences and their lives, and whose loss to them would therefore be irreplaceable.

A different version of this worry is that human cloning would result in persons' worth or value seeming diminished because we would now see humans as able to be manufactured or "handmade." This demystification of the creation of human life would reduce our appreciation and awe of it and of its natural creation. It would be a mistake, however, to conclude that a human being created by human cloning is of less value or is less worthy of respect than one created by sexual reproduction. It is the nature of a being, not how it is created, that is the source of its value and makes it worthy of respect. Moreover, for many people, gaining a scientific understanding of the extraordinary complexity of human reproduction and development increases, instead of decreases, their awe of the process and its product.

A more subtle route by which the value we place on each individual human life might be diminished could come from the use of human cloning with the aim of creating a child with a particular genome, either the genome of another individual especially meaningful to those doing the cloning or an individual with exceptional talents, abilities, and accomplishments. The child might then be valued only for his or her genome, or at least for his or her genome's expected phenotypic expression, and no longer be recognized as having the intrinsic equal moral value of all persons, simply as persons. For the moral value and respect due all persons to be seen as resting only on the instrumental value of individuals, or of individuals' particular qualities, to others would be to fundamentally change the moral status accorded to persons. Everyone would lose their moral standing as full and equal members of the moral community, replaced by the different instrumental value each of us has to others.

Such a change in the equal moral value and worth accorded to persons should be avoided at all costs, but it is far from clear that such a change would take place from permitting human cloning. Parents, for example, are quite capable of distinguishing their children's intrinsic value, just as individual persons, from their instrumental value based on their particular qualities or properties. The equal moral value and respect due all persons just as persons is not incompatible with the different instrumental value of people's particular qualities or properties. Einstein and an untalented physics graduate student have vastly different value as scientists, but share and are entitled to equal moral value and respect as persons. It would be a mistake and a confusion to conflate the two kinds of value and respect. Making a large number of clones from one original person might be more likely to foster this mistake and confusion in the public. If so, that would be a further reason to limit the number of clones that could be made from one individual.

4. Human cloning would divert resources from other more important social and medical needs (LaBar 1984; Callahan 1993).

As we saw in considering the reasons for, and potential benefits from, human cloning, in only a limited number of uses would it uniquely meet important human needs. There is little doubt that in the United States, and certainly elsewhere, there are more pressing unmet human needs, both medical or health needs and other social or individual needs. This is a reason for not using public funds to support human cloning, at least if the funds actually are redirected to more important ends and needs. It is not a reason, however, either to prohibit other private individuals or institutions from using their own resources for research on human cloning or for human cloning itself, or to prohibit human cloning or research on human cloning.

The other important point about resource use is that it is not now clear how expensive human cloning would ultimately be, for example, in comparison with other means of relieving infertility. The procedure itself is not scientifically or technologically extremely complex and might prove not to require a significant commitment of resources.

5. Human cloning might be used by commercial interests for financial gain.

Both opponents and proponents of human cloning agree that cloned embryos should not be able to be bought and sold. In a science fiction frame of mind, one can imagine commercial interests offering genetically certified and guaranteed embryos for sale, perhaps offering a catalogue of different embryos cloned from individuals with a variety of talents, capacities, and other desirable properties. This would be a fundamental violation of the equal moral respect and dignity owed to all persons, treating them instead as objects to be differentially valued, bought, and sold in the marketplace. Even if embryos are not yet persons at the time they would be purchased or sold, they would be valued, bought, and sold for the persons they will become. The moral consensus against any commercial market in embryos, cloned or otherwise, should be enforced by law, whatever public policy ultimately is created to address human cloning. It has been argued that the law may already forbid markets in embryos on grounds that they would violate the thirteenth amendment prohibiting slavery and involuntary servitude (Turner 1981).

6. Human cloning might be used by governments or other groups for immoral and exploitative purposes.

In *Brave New World*, Aldous Huxley imagined cloning individuals who have been engineered with limited abilities and conditioned to do, and to be happy doing, the menial work that society needed done (Huxley 1932). Selection and control in the creation of people was exercised not in the interests of the persons created, but in the interests of the society and at the expense of the persons created. Any use of human cloning for such purposes would exploit the clones solely as means for the benefit of others, and would violate the equal moral respect and dignity they are owed as full moral persons. If human cloning is permitted to go forward, it should be with regulations that would clearly prohibit such immoral exploitation.

Fiction contains even more disturbing and bizarre uses of human cloning, such as Mengele's creation of many clones of Hitler in Ira Levin's *The Boys from Brazil* (1996), Woody Allen's science fiction cinematic spoof *Sleeper*, in which a dictator's only remaining part, his nose, must be destroyed to keep it from being cloned, and the contemporary science fiction film *Blade Runner* (Levin 1976). Nightmare scenarios like Huxley's or Levin's may be quite improbable, but their impact should not be underestimated on public concern with technologies like human cloning. Regulation of human cloning must assure the public that even such farfetched abuses will not take place.

7. Human cloning used on a very widespread basis would have a disastrous effect on the human gene pool by reducing genetic diversity and our capacity to adapt to new conditions (Eisenberg 1976).

This is not a realistic concern since human cloning would not be used on a wide enough scale, substantially replacing sexual reproduction, to have the feared effect on the gene pool. The vast majority of humans seem quite satisfied with sexual means of reproduction; if anything, from the standpoint of worldwide population, we could do with a bit less enthusiasm for it. Programs of eugenicists like Herman Mueller earlier in the century to impregnate thousands of women with the sperm of exceptional men, as well as the more recent establishment of sperm banks of Nobel laureates, have met with little or no public interest or success (Adams 1990). People prefer sexual means of reproduction, and they prefer to keep their own biological ties to their offspring.

CONCLUSION

Human cloning has until now received little serious and careful ethical attention, because it was typically dismissed as science fiction, and it stirs deep, but difficult to articulate, uneasiness and even revulsion in many people. Any ethical assessment of human cloning at this point must be tentative and provisional. Fortunately, the science and technology of human cloning are not yet in hand, and so a public and professional debate is possible without the need for a hasty, precipitate policy response.

The ethical pros and cons of human cloning, as I see them at this time, are sufficiently balanced and uncertain that there is not an ethically decisive case either for or against permitting it or doing it. Access to human cloning can plausibly be brought within a moral right to reproductive freedom, but the circumstances in which its use would have significant benefits appear at this time to be few and infrequent. It is not a central component of a moral right to reproductive freedom, and it serves no major or pressing individual or social needs. On the other hand, contrary to the pronouncements of many of its opponents, human cloning seems not to be a violation of moral or human rights. But it does risk some significant individual or social harms, although most are based on common public confusions about genetic determinism, human identity, and the effects of human cloning. Because most moral reasons against doing human cloning remain speculative, they seem insufficient to warrant at this time a complete legal prohibition of either research on or later use of human cloning. Legitimate moral concerns about the use and effects of human cloning,

however, underline the need for careful public oversight of research on its development, together with a wider public debate and review before cloning is used on human beings.*

* I want to acknowledge with gratitude the invaluable help of my research assistant, Insoo Hyun, on this paper. He not only made it possible to complete the paper on the NBAC's tight schedule, but also improved it with a number of insightful substantive suggestions.

References

Adams, M., ed., *The Well-Born Science*, Oxford: Oxford University Press, 1990.

Annas, G.J., Regulatory models for human embryo cloning: The free market, Professional guidelines, and government restrictions. *Kennedy Institute of Ethics Journal*, 4(3):235-249, 1994.

Brock, D.W., The non-identity problem and genetic harm, *Bioethics*, 9:269-275, 1995.

———, Reproductive freedom: Its nature, bases and limits, in *Health Care Ethics: Critical Issues for Health Professionals*, D. Thomasma, J. Monagle (eds.), Gaithersburg, MD: Aspen Publishers, 1994.

Callahan, D., Perspective on cloning: A threat to individual uniqueness, *Los Angeles Times*, November 12, 1993, B7.

Chadwick, R.F., Cloning. *Philosophy*, 57:201-209, 1982.

Cohen, J., G. Tomkin, The science fiction, and reality of embryo cloning. *Kennedy Institute of Ethics Journal*, 4:193-204, 1994.

Council of Europe, *Recommendation 1046 (1986) on the Use of Human Embryos and Fetuses for Diagnostic, Therapeutic, Scientific, Industrial and Commercial Purposes*, 1986.

Dworkin, R., *Taking Rights Seriously*, London: Duckworth, 1978.

Eisenberg, L., The outcome as cause: Predestination and human cloning. *J Med Philos*, 1:318-331, 1976.

Feinberg, J., The child's right to an open future, in *Whose Child? Children's Rights, Parental Authority, and State Power*, W. Aiken, H. LaFollette (eds.), Totowa, NJ: Rowman and Littlefield, 1980.

Fletcher, J., *The Ethics of Genetic Control: Ending Reproductive Roulette*, Garden City, NY: Anchor Books, 1974.

Hall, J.L., et al., Experimental Cloning of Human Polypoid Embryos Using an Artificial Zona Pellucida, Abstract 0-001, American Fertility Society jointly with the Canadian Fertility and Andrology Society, Abstracts of the Scientific Oral and Poster Sessions, Program Supplement, 1993, S1.

Harris, J., *Wonderwoman and Superman: The Ethics of Biotechnology*, Oxford: Oxford University Press, 1992.

Huxley, A., *Brave New World*, London: Chalto and Winders, 1932.

Jonas, H., *Philosophical Essays: From Ancient Creed to Technological Man*, Englewood Cliffs, NJ: Prentice-Hall, 1974.

Kahn, C., Can we achieve immortality?, *Free Inquiry*, 9:14-18, 1989.

Kass, L., *Toward a More Natural Science*, New York: The Free Press, 1985.

Kolata, G., The hot debate about cloning human embryo, *New York Times*, October 26, 1993, 1A.

LaBar, M., The pros and cons of human cloning, *Thought*, 57:318-333, 1984.

Lederberg, J., Experimental genetics and human evolution, *The American Naturalist*, 100:519-531, 1966.

Levin, I., *Boys from Brazil*, New York: Random House, 1976.

Macklin, R., Splitting embryos on the slippery slope: Ethics and public policy, *Kennedy Institute of Ethics Journal*, 4:209-226, 1994.

McCormick, R., Should we clone humans?, *Christian Century*, 1148-1149, 1993.

———, *Notes on Moral Theology: 1965 Through 1980*, Washington, DC: University Press of America, 1981.

McKinnell, R., *Cloning: A Biologist Reports*, Minneapolis: University of Minnesota Press, 1979.

Mill, J.S., *On Liberty*, Indianapolis, IN: Bobbs-Merrill Publishing, 1859.

NABER (National Advisory Board on Ethics in Reproduction), Report on human cloning through embryo splitting: An amber light, *Kennedy Institute of Ethics Journal*, 4:251-282, 1994.

Parfit, D., *Reasons and Persons*, Oxford: Oxford University Press, 1984.

Pollack, R., Beyond cloning, *New York Times*, Nov. 17, 1993, A27.

Rainer, J.D. Commentary, *Man and Medicine: The Journal of Values and Ethics in Health Care*, 3:115-117, 1978.

Ramsey, P., *Fabricated Man: The Ethics of Genetic Control*, New Haven, CT: Yale University Press, 1970.

Rhodes, R., Clones, harms, and rights, *Cambridge Quarterly of Healthcare Ethics*, 4:285-290, 1995.

Robertson, J.A., A Ban on Cloning and Cloning Research Is Unjustified, Testimony before the National Bioethics Advisory Commission, March 1997.

———, *Children of Choice: Freedom and the New Reproductive Technologies*, Princeton, NJ: Princeton University Press, 1994a.

———, The question of human cloning, *Hastings Center Report*, 24:6-14, 1994b.

Smith, G.P., Intimations of immortality: Clones, cyrons and the law, *University of New South Wales Law Journal*, 6:119-132, 1983.

Studdard, A. The lone clone, *Man and Medicine: The Journal of Values and Ethics in Health Care*, 3:109-114, 1978.

Thomas, L., Notes of a biology watcher: On cloning a human being, *N Engl J Med*, 291:1296-1297, 1974.

Turner, P.O., Love's labor lost: Legal and ethical implications in artificial human procreation, *University of Detriot Journal of Urban Law*, 58:459-487, 1981.

Verhey, A.D., Cloning: Revisiting an old debate, *Kennedy Institute of Ethics Journal*, 4:227-234, 1994.

Walters, W.A.W., Cloning, ectogenesis, and hybrids: Things to come?, In *Test-Tube Babies*, W.A.W. Walters, P. Singer (eds.), Melbourne: Oxford University Press, 1982.

Watt, H., What moral status has a human clone?, *Bulletin of Medical Ethics*, 93:2, 1993.

Weiss, R., Cloning suddenly has government's attention, *International Herald Tribune*, March 7, 1997, 2, 1997.

WHO (World Health Organization), WHO Director General Condemns Human Cloning, Geneva, Switzerland: World Health Organization Press Office, March 11, 1997.

Wilmut, I., et al., Viable offspring derived from fetal and adult mammalian cells. *Nature*, 385:810-813, 1997.

Wilmut, I., et al., Sheep cloned by nuclear transfer from a cultured cell line. *Nature*, 380:64-66, 1996a.

Wilmut, I., et al., Implications of cloning. *Nature*, 380:383, 1996b.

CLONING HUMAN BEINGS

The Current and Future Legal Status of Cloning

Commissioned Paper
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CONTENTS

PREFACE

> "Perhaps in recognition of the surrealistic circumstances they should have spelled it D-A-L-I, instead of D-O-L-L-Y."[1]

This response is quite representative of how most people reacted to the news that a team of Scottish scientists succeeded in cloning a mammal. On July 5, 1996, a sheep named Dolly was born in Scotland, the result of the transfer of the nucleus of an adult mammary tissue cell to the enucleated egg cell of an unrelated sheep, and gestation in a third, surrogate mother sheep.[2] Although for the past ten years scientists have routinely cloned sheep and cows from embryo cells,[3] this was the first cloning experiment which has succeeded using the nucleus of an adult cell.[4]

Shortly after the report of the sheep cloning was published, President Clinton instituted a ban on federal funding for human cloning.[5] This moratorium provides the opportunity for an analysis of the potential risks and benefits of human cloning, the current legal status of cloning, and the potential constitutional challenges that might be raised if new legislation is put into place to restrict cloning.

With the recent success in cloning an adult mammal, it is reasonable to start thinking about the feasibility and impact of human cloning. Many reproductive and genetic procedures, such as artificial insemination by donor, embryo transfer, in vitro fertilization, and preimplantation screening of embryos, were applied first in animals and then in humans. Animal husbandry is a precursor to clinical reality for humans, with the time of technology transfer to humans ever decreasing. If W. Bruce Currie, biologist at Cornell University, is correct, "[c]loning humans from adults' tissues is likely to be achievable any time from one to ten years from now,"[6] an estimate which was repeated by the journal *Nature*, which published the article about Dolly. Immediately after Dr. Wilmut announced to the world how Dolly was "conceived," Dr. Harold Varmus, the director of the National Institutes of Health, testified before a House subcommittee that the technology involved was "fairly simple."[7] Currie estimates that at least ten fertilization clinics in the United States have the technology which will allow such a feat; he did not, however, name these ten clinics.[8]

The executive summary briefly surveys the current and future legal status of cloning; the rest of this document develops this analysis. The paper then addresses the potential uses that could be made of cloning. The procedures to be used and their purposes are relevant to an analysis of whether human cloning falls within the reach of existing law. Discussion of the potential impact of cloning, which is relevant in determining the need for a legal policy and whether such a policy can be justified as a proper exercise of governmental power, is followed by that of the impact of existing laws on cloning, particularly state bans on embryo research. The next sections describe proposed federal and state laws regarding cloning; analyze whether federal legislation restricting or banning cloning can be challenged as not justified by the federal spending power or the federal power to regulate interstate commerce; analyze whether a ban on human

cloning might be subject to attack as violating scientists' alleged First Amendment right to scientific inquiry; and assess whether a ban on human cloning of complete individuals would violate an individual's or couple's constitutional right to privacy or liberty to make reproductive decisions. The paper then examines constitutional concerns, such as the Thirteenth Amendment prohibition on slavery and the nobility clause, that could restrict certain forms of cloning; analyzes who would be considered to be the legal parent(s) of the resulting child if an individual were cloned; addresses the human research constraints applicable to a child created through cloning; and addresses potential tort claims based on cloning. The final section addresses policy options in this area.

Throughout this paper, two types of cloning research are addressed. The first is research at the genetic, cellular, and tissue level which is not intended to create a cloned individual. Most of the scientists addressing human cloning research focus on this first type of research. The second type is research which is intended to create an individual. The latter type of research might be considered by some to be too remote and speculative to be worthy of serious policy analysis at this time. However, given the fact that much of the public and media discussion has focused on the cloning of whole individuals, a legal policy analysis would be deficient if it did not analyze whether existing and proposed laws would cover the cloning of whole individuals as well.

EXECUTIVE SUMMARY

This section—the executive summary—summarizes the analysis with respect to the most important legal issues that have been raised: Do existing laws ban the procedure? If human cloning were regulated or banned, could that policy be challenged as unconstitutional? If the cloning of a whole individual were allowed, who would be the legal parents?[9]

A. Potential State Restrictions on Cloning

Ten states have laws regulating research and/or experimentation on conceptuses, embryos, fetuses, or unborn children that use broad enough language to include early stage conceptuses.[10] However, several arguments could be made to suggest that most of the statutes should be construed narrowly so as not to apply to cloning. First, an argument can be made that since the experimental procedure is being done on an egg, not an embryo, fetus, or unborn child, the laws should not apply. By the time the embryo is created, the experimental procedure is completed. Second, two of the ten states define the object of protection—the conceptus (Minnesota) or unborn child (Pennsylvania)—as the product of fertilization. If transfer of nucleic material is not considered fertilization, these laws would not apply. Third, the laws of at least eight of the states banning embryo research are sufficiently general that they might be struck down as unconstitutionally vague.[11]

Two statutes have provisions that are particularly likely to be applied to cloning. In New Hampshire, a preembryo may not be allowed to develop beyond 14 days post-fertilization,[12] so cloning research may be permissible within the first 14 days of development. However, "no

preembryo that has been donated for use in research shall be transferred to a uterine cavity."[13] Thus, if a renucleated oocyte is considered to be a preembryo, it would be impermissible in New Hampshire to implant the resulting conceptus to create a child.

In Louisiana, the statute applies to an "in vitro fertilized human ovum . . . composed of one or more living human cells and human genetic material so unified and organized that it will develop in utero into an unborn child."[14] An entity meeting the definition cannot be cultured and farmed solely for research purposes,[15] which would prohibit cloning research to study gene function, cellular development, and so forth. Another provision specifically states that such an entity may be used "solely for the support and contribution of the complete development of human in utero implantation."[16] This creates the anomalous result that researchers could clone a whole individual in Louisiana, but could not do research ex utero on cloned cells.

B. Constitutional Concerns

If the federal government chooses to regulate or even ban cloning, that action might be challenged on a number of constitutional grounds—as not being justified under the commerce clause, as violating scientists' First Amendment freedom of inquiry, or as violating a couple's or individual's constitutional right of privacy or liberty to make reproductive decisions.

1. Reach of the Commerce Clause

Congress has the power to regulate interstate commerce, but states maintain the power to regulate intrastate activities that have little impact on interstate commerce. In 1995, the U.S. Supreme Court held, for the first time in almost 60 years, that Congress had adopted legislation that exceeded its authority under the commerce clause.[17] The facts at issue in that case, however, are distinguishable from the case of cloning. In that case, Congress had banned the possession of a firearm within 1000 feet of a schoolyard. The U.S. Supreme Court held that the law was not a proper exercise of federal power because the activity at issue did not affect interstate commerce, interfered with a traditional state activity (education), and had already been addressed by state laws in most states.[18] There is much more leeway for the federal government to regulate cloning. It is likely that some of the equipment or materials used in the cloning procedure will have moved in interstate commerce,[19] some of the individuals seeking cloning services will have traveled interstate to obtain those services,[20] some funding will have come from out of state,[21] some of the personnel may have been hired from out of state,[22] and some of the researchers may attend related conferences and classes out of state.[23] Moreover, if the federal government were to adopt a law on cloning, Congress could address the commerce clause concerns in the legislative history, which it failed to do in connection with the firearm ban at issue in *Lopez*. Congress' power to regulate cloning under the commerce clause would include a power to ban it.[24]

2. Right to Scientific Inquiry

Certain commentators have speculated that there might be a right of scientific inquiry protected by the First Amendment right to free speech. If the First Amendment protects a marketplace of ideas, it seems likely it would protect the generation of information that would be included in that marketplace. The U.S. Supreme Court has not directly addressed the right of scientific inquiry, but a lower federal court has suggested in *dicta* that scholars have a "right . . . to do research and advance the state of man's knowledge."[25] Other federal courts, however, have refused to recognize a First Amendment right of scientific inquiry.[26] And even if the First Amendment were found to be applicable to scientific inquiry, there is widespread agreement that the method of research could be regulated to prevent harms.

3. Right to Make Reproductive Decisions

The right to make decisions about whether to bear children is constitutionally protected under the constitutional right to privacy[27] and the constitutional right to liberty.[28] The U.S. Supreme Court in 1992 reaffirmed the "recognized protection accorded to liberty relating to intimate relationships, the family, and decisions about whether to bear and beget a child."[29] Early decisions protected married couples' right to privacy to make procreative decisions, but later decisions focused on the individual's rights. The U.S. Supreme Court, in *Eisenstadt v. Baird*,[30] stated, "[i]f 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."[31]

A federal district court has indicated that the right to make procreative decisions encompasses the right of an infertile couple to undergo medically assisted reproduction, including in vitro fertilization and the use of a donated embryo.[32] Some legal analysts have suggested that the constitutional right to make reproductive decisions free from unnecessary governmental intrusion covers the decision of a couple to undergo cloning.[33] However, other legal analysts have noted that the unprecedented step of creating a child with only one genetic progenitor would be such a fundamental change in the way humans "reproduce" that it would not be constitutionally protected.[34]

Even if a restriction on cloning were found to infringe upon an individual's or a couple's right to make reproductive decisions, the government could justify the restriction if it had a compelling state interest and the restriction furthered that interest in the least restrictive manner possible. The potential physical and psychological risks of cloning an entire individual[35] are sufficiently compelling to justify banning the procedure. Moreover, certain uses of cloning—such as creation of a clone as a source of spare organs—would likely be banned by the Thirteenth Amendment prohibition of slavery and involuntary servitude.

The use of cloned cells and tissue for research purposes other than the creation of a child would not be protected by the constitutional rights of privacy and liberty that protect reproductive

decisions. Consequently, a governmental regulation or ban of such research would not have to have such stringent justification. It would be constitutional so long as it was rationally related to an important governmental purpose. Under such an analysis, a court could uphold restrictions that require that sufficient animal research be done in advance. Moreover, it would be permissible to require the scientists proposing the research to have "the burden of proving that the research is vital, cannot be conducted any other way, and is unlikely to produce harm to society."[36]

C. Parenthood Issues

Current state laws addressing parentage, including paternity acts, surrogacy statutes, and egg donation statutes, are not broad enough to address the multitude of parentage issues raised by the process of cloning through nuclear transfer. The process of cloning will result in a child having genetic material from as many as four individuals: the person from whom the cell nucleus was derived, that individual's biological parents, and the woman contributing the enucleated egg cell which contains a small fraction of DNA in the mitochondria.[37] In addition, if the egg with the transferred nucleic material is implanted in a surrogate gestational mother, the child will have two other potential parents—the gestator and, if she is married, her husband. The latter will have rights (even though he has no biological connection to the child) based on the common law presumption that if a woman gives birth within marriage, her husband is the child's legal father, or in some states, based on specific statutes holding that the surrogate and her husband are the legal parents of a child she has gestated, regardless of their genetic contribution.[38] There may also be intended rearing parents unrelated to the individual who is cloned; this may occur when the cloned individual is deceased, a celebrity, or a favorite relative.

Various contributors in the cloning arrangements will have legal rights and responsibilities with respect to the resulting child. Since the clone is a twin to the cloned individual, the latter's parents could be recognized as legal parents. They certainly would be identified as the parents under DNA paternity testing. Yet, given that they will likely have not made the decision to create offspring (in fact, they may be dead at the time their own offspring is cloned), it seems unfair to designate them as the legal parents. It is also not in keeping with a perspective that considers preconception intent as a relevant factor for determining parenthood in the context of assisted reproduction.

In many states, the woman who gives birth is considered to be the legal mother and her husband the legal father of any resulting child. Under statutes in Arizona and Utah, this holds true even when the surrogate is gestating an embryo with no genetic relationship to her. Only in Florida, New Hampshire, North Dakota, and Virginia do court-approved gestational surrogacy arrangements result in the intended parents—not the surrogate—being viewed as the legal parents. However, these four states have leeway for denial of parenthood to people who clone. The laws allow only married individuals to contract with gestational surrogates (thus not applying to the unmarried individual who clones himself or herself). Virginia also allows judges the leeway to deny gestational surrogacy based on psychological examination of the intended parents. Some would argue that the desire to clone oneself is evidence of psychological disturbance.

The person who clones himself or herself could try to establish paternity (or maternity) under the state paternity statute. If such individuals are denied use of the provisions allowing "mothers" and "fathers" (because they do not seem to fit traditional conceptions of that role), they might be able nonetheless to go forward under the provisions in at least 13 states that allow "interested persons" to bring a paternity action.[39] Such an action could be challenged by one of the other rights holders, though, such as the cloned individual's parents or the gestational surrogate.

The state laws for blood testing to prove paternity may or may not be useful to the individual who wishes to prove he or she is the "parent" of his or her clone. The laws provide for a wide range of such tests—from HLA typing to DNA tests. If one of the less precise tests were used, the individual whose nucleic material was used might have a match that makes it appear that he or she is the "parent" and might be declared the legal parent on those grounds. However, if DNA testing were used, the nucleus provider would clearly have the pattern closer to that of a twin (a nearly 100% match) rather than a parent (50% match). It is not clear what a judge would make of such information. The legal standard for paternity is often a particular probability of being a parent. For example, in Mississippi, the blood test must show that there is a statistical probability of paternity of 98% or greater. So, the judge's ideas about paternity and parenthood, rather than the DNA test, would be determinative of whether the nucleus provider was declared the parent of the clone. The nucleus donor's claim to the rights and responsibilities of parenthood would be bolstered under doctrines and cases that give weight to preconception intent in recognizing legal parenthood.[40]

If a couple creates a child who is the clone of a loved one or an unrelated individual chosen for that person's valued traits, parenting rights would also be dispersed across individuals. If the wife carried the clone to term, the couple would be protected by legal presumptions assigning parenthood to the birth mother and her husband. If paternity testing were done, however, the parents of the cloned individual (and maybe the cloned individual himself or herself) might be able to assert rights to the child.

THE GOALS OF CLONING RESEARCH

A. How Is Cloning Performed?

"Cloning" is the manipulation of a cell from an animal or human in such a way that it grows into a copy of that animal with identical nucleic DNA.[41] The clone will not be 100% genetically similar because it will have mitochondrial DNA from the egg donor.[42] In the case of Dolly, an adult mammary cell which contains a copy of every gene needed to make the lamb was extracted and then starved of its nutrients in order for the cell to enter a quiescent state.[43] This cell was then fused with an enucleated egg cell—one in which the nucleus has been extracted—and an electric current was run through the fused cell, activating the dormant cell and causing it to begin to divide. These divided cells were then implanted into a surrogate mother and carried to term.[44]

B. What Are the Uses for Cloning Technology in Animals?

Dolly was not cloned primarily for scientific purposes, but rather for commercial ones. Dr. Wilmut and the Roslin Institute had created a means for sheep to be engineered to express pharmaceutical products in their breast milk. The company that funded the research, PPL Therapeutics, P.L.C. of Edinburgh, applied for a patent on the technique. Dr. Wimut's goal in creating Dolly was to find a method to produce "consistent" transgenic animals.[45] Dr. Wilmut has stated that his idea is to create one transgenically beneficial animal, for whatever scientific or commercial purposes, and then to clone that animal until a small herd is achieved,[46] where reproduction of the animal would be continued by alternative methods to avoid the problem of "species suicide." Cloning animals is seen as beneficial both to the pharmaceutical industry and to agriculture.

This notion of consistent animals is of particular importance to the pharmaceutical industry, where clones may prove to be the most beneficial.[47] Dr. Wilmut has stated that medically useful transgenic sheep and cows would be created, and those animals could then be cloned, thus creating walking biomedical factories.[48] The greatest area of promise in pharmacology seems to be in the area of genetically manipulating animals whose milk will contain useful proteins, such as blood-clotting amino acids to be used in treating hemophilia.[49] Dr. Wilmut states that the Roslin Institute "is confident that it will be possible within two or three years to produce farm animals that will produce in their milk proteins to treat human diseases."[50]

In addition, cloning may provide another method of reproducing cattle and sheep.[51] Increasing the cattle and sheep population could lead to an increase in the world's food supply by producing more milk from smaller herds. For example, cows could produce 30,000 to 40,000 pounds of milk per year as opposed to the average 13,000 pounds per year they now produce.[52] With herd sizes reduced, land which is currently used for cattle and sheep grazing could be devoted to raising grain and other crops.[53]

Another proposed benefit of cloning is the proliferation of champion breeding stock. Champion bulls, dogs, horses, and sheep would all serve to produce either more food and wool or greater contributions to human entertainment.[54] The proposition of cloning existing adults seems advantageous over embryo cloning—twinning—because in twinning, one is not absolutely certain of the sort of animal—or human—the twinned embryos will become. Accordingly, with this new nuclear transplantation technique, it is possible to clone only the "best" existing animals, or those with the most desirable traits. Once the desired animal is created, it is theoretically possible to make as many copies as desired.[55]

C. What Are the Proposed Uses for Cloning Research in Humans?

Many proposed uses of cloning technology in humans have been offered, ranging from the scientifically interesting through the medically useful to the bizarre. Cloning technology may be useful in understanding the mechanisms of disease and in developing treatments; in creating organ and tissue reserves; in creating children for individuals and couples; and in immortalizing oneself,

loved ones, or important individuals. It is likely that one or more of these will be attempted. "In science, the one rule is that what can be done will be done," said Rabbi Moses Tendler, professor of medical ethics at Yeshiva University.[56]

1. Disease Research and Treatment

Dr. Wilmut has stated that his objective in creating Dolly was merely to "build a better glass of milk."[57] However, the implications of his research might possibly benefit humans in additional ways. Cloning research technology could help increase understanding of how genes turn on and off and why cells divide, leading to potential treatments for genetic diseases, cancer, and neurological traumas. It could also help researchers to understand, and potentially reverse, the aging process.

Cloning research might lead to greater understanding of the intricacies of the cellular life cycle, potentially allowing control and manipulation of this cycle.[58] Cloning research, specifically nuclear transplantation, promises scientists the opportunity to learn how to "starve" mature, differentiated cells and reactivate their DNA, thus causing differentiated cells' genes to revert to their most primitive state.[59] By redirecting cells to act as they do in their embryological state, scientists can learn how to direct, or grow, these cells in the manner they wish, ultimately leading to control of the development of normal and abnormal cells.[60] Thus, cloning technology may lead scientists to discover why cancerous cells mutate, revert to an embryonic stage, and then uncontrollably divide.[61] Such technology might also allow researchers to go one step further and take differentiated cells from anywhere in a patient's body and redirect the cells into other sorts of cells, such as brain cells to treat Parkinson's disease or lung cells to treat cystic fibrosis.[62]

Cloning research might possibly lead to enhanced understanding of how genes operate and how they can be manipulated to cure and prevent diseases.[63] Neuroscience may also benefit from cloning techniques by enhancing understanding of why spinal cord tissue, brain tissue, and heart muscle do not regenerate after injury.[64]

Many of the questions that cloning research would address could also be addressed in other ways, however, so it is not known whether human cloning is necessary to provide these benefits.[65] One researcher has speculated, for example, that cloning research will have only a "modest role" in the field of developmental biology.[66]

2. Reproductive Technology

Cloning research may lead to greater insights into the mechanisms of human reproduction—for example, by enhancing understanding of the high rate of spontaneous abortions in natural situations.[67] Such research could lead to infertility treatments.

Beyond scientific research in cloned tissue, the cloning of complete individuals raises the potential for individuals to create children. Numerous forms of noncoital reproduction have

developed over the past two decades, including in vitro fertilization, egg donation, embryo donation, and surrogate motherhood. Some of the individuals who currently provide assisted reproductive services envision a role for cloning as well.

If both members of a couple are infertile, they may wish to clone one or the other of themselves.[68] If one member of the couple has a genetic disorder that the couple does not wish to pass on to a child, the unaffected member of the couple could be cloned. In addition, if both husband and wife are carriers of a debilitating recessive genetic disease and are unwilling to run the 25% risk of bearing a child with the disorder, they may seek to clone one or the other of them.[69] This may be the only way in which the couple will be willing to have a child that will carry on their genetic line. In the future, these couples might also wish to avail themselves of gene therapy on the resulting embryos, which is not currently possible, to eliminate undesirable hereditary genetic traits in their cloned children.[70] This combination of techniques would be similar to the ones that led ultimately to the creation of Dolly.

Charles Strom, director of genetics and the DNA laboratory at Illinois Masonic Medical Center, argues that the high rate of embryo death that has occurred in animal cloning should not dissuade people from considering cloning as a legitimate reproductive technique.[71] Strom points out that all new reproductive technologies have been marred by high failure rates, and that it is just a matter of time before cloning could be as economically efficient as any other form of artificial reproduction.[72]

Even people who could reproduce coitally may desire to clone for a variety of reasons. People may want to clone themselves, deceased or living loved ones, or individuals with favored traits. A wealthy childless individual may wish to clone himself or herself to have an heir or to continue to control a family business. Parents who are unable to have another child may want to clone their dying child.[73] This is not unlike the current situation in which a couple whose daughter died is making arrangements to have her cryopreserved in vitro embryo implanted in a surrogate mother in an attempt to recreate the daughter.[74]

Additionally, a person with favored traits could be cloned. Respected world figures and celebrities such as Mother Teresa, Michael Jordan, and Michelle Pfeiffer have been suggested as candidates for cloning. Less well-known individuals could also be cloned for specific traits. For example, people with a high pain threshold or resistance to radiation could be cloned.[75] People who can perform a particular job well, such as soldiers, might be cloned.[76] One biologist suggested cloning legless men for the low gravitational field and cramped quarters of a space ship.[77]

Others worry that immortalizing people will lead to an inherently discriminatory practice of selecting only the "best" to be immortalized.[78] For many people, the notion of cloning superior or important historical figures is simply too closely related to the practice of eugenics. Also, some believe that no one should be deciding which humans are worthy of cloning.[79] Would it be the scientists themselves,[80] or should government officials decide? Arthur Caplan, director of the

Center for Bioethics at the University of Pennsylvania, stated that history has taught us frightening lessons "from Nazi Germany to Bosnia, of the evils humans can do when they set values on one another according to biological or inherited traits."[81]

3. Organ and Tissue Reserve

Human cloning research might provide insights that could be valuable in the field of organ transplantation. National Institutes of Health director Dr. Harold Varmus stated that possibly one area of cloning research might provide methods of growing skin, which could then be used in grafting for burn victims and patients with skin-destroying diseases.[82] He explained that nuclear transplantation cloning technology, by enhancing an "understanding of how genes are turned off and on and how we can make different kinds of cell types, not whole human beings, but different kinds of human tissues for transplantation and for treatment of disease, offers tremendous prospects."[83]

Beyond basic scientific research and the development of a technology to create organs in vitro, it has been suggested that clones could be created to donate non-essential organs like kidneys and blood.[84] John Fletcher, former bioethicist from the National Institutes of Health, stated that "[i]t is hard to argue against the idea of a family's loving a child so much that it will happily raise another, identical child so that one of its kidneys or a bit of its marrow might allow the first to live. . . . The reasons for opposing this are not easy to argue."[85] More generally, John Robertson advocates cloning a "backup supply of embryos from which tissue or organs could be obtained if a tragedy befell a first child."[86]

It has been suggested that a person suffering from leukemia could be cloned, the resulting fetus's marrow could be extracted in utero, and then the cloned fetus could be aborted in utero, thus avoiding some of the fears that clones would be treated as second-class citizens.[87] Jeffrey Kluger argues that cloned organ banking is the ultimate realism of the Maoist Chinese belief that individuals are "uberorganistic," or a collection of multicellular parts to be die-cast as needed.[88] Cloning a person for an organ reserve would be futile if the resulting individual had the same diseased organ, however. But situations may arise in which an organ transplant may be needed as the result of injury or nongenetic illness.

Ursula Goodenough, a cell biologist from Washington University, raised an additional application of cloning—to allow reproduction without men.[89] If females cloned themselves, men would be "superfluous" in reproduction, leading to a world where men may eventually be phased out entirely—the ultimate "feminist utopia."[90] From the beginning of Wilmut's announcement of Dolly, commentators have discussed the implications of "virgin birth," or of a woman giving birth to her twin.[91] Ann Northrop, a columnist for the New York gay newspaper *LGNY*, says that nuclear transplantation is enticing to gays and lesbians because it offers them a means of reproduction and "has the potential of giving women complete control over reproduction."[92] "This is sort of the final nail in men's coffins. Men are going to have a very hard time justifying

their existence on this planet, I think. Maybe women may not let men reproduce," said Northrop.[93]

Also, Clone Rights United Front, a group of gay activists based in New York, have been demonstrating against the proposed New York legislation which would ban nuclear transplantation research and human cloning. They oppose such a ban because they see human cloning as a significant means of legitimizing "same-sex reproduction."[94] Randolfe Wicker founded the Clone Rights United Front in order to pressure legislators not to ban human cloning research, because he sees nuclear transplantation cloning as an inalienable reproductive right.[95] Wicker stated, "We're fighting for research, and we're defending people's reproductive rights. . . . I realize my clone would be my identical twin, and my identical twin has a right to be born."[96]

THE POTENTIAL IMPACTS OF CLONING

A. Problems in Application to Humans

There is widespread consensus that human cloning research should not be undertaken at this time. Before such a step is undertaken, further animal research is necessary. Princeton University biologist Dr. Shirley Tilghman has indicated that it is a long-term project to determine the risks in animals.[97]

There are many concerns about the potential danger of treatments based on cloning techniques and risks of cloning whole individuals. The high rate of laboratory deaths may suggest that cloning in fact damages the DNA of a cell, and scientists urge that Dolly should be closely monitored for abnormal genetic anomalies which did not kill her as a fetus but may have long-term harmful effects.[98] Dr. Wilmut warns that when thinking of applying nuclear transplantation as a means of human reproduction, one "shouldn't underestimate the difficulties of this [nuclear transplantation] research."[99]

It is unclear whether the animal research could be successfully generalized to humans. For example, all of the initial frog cloning experiments succeeded only to the point of the amphibian's tadpole stage.[100] In addition, some of the tadpoles were grossly malformed.[101] Thus, there is fear that initial trials in human nuclear transplantation would also meet with disastrous results.[102] Drs. Wilmut and Varmus, testifying before Congress, specifically raised the concern that animal-cloning technology is not scientifically ready to be applied to human cloning research, even if it were permitted, because there are technical questions which can be answered only by continued animal research.[103] Dr. Wilmut is specifically concerned with the ethical issue which would be raised by any "defective births" which may be likely to occur if nuclear transplantation is attempted with humans.[104]

In addition, if all the genes in the adult DNA are not properly reactivated, there might be a problem at a later developmental stage in the resulting clone.[105] Some differentiated cells

rearrange a subset of their genes. For example, immune cells rearrange some of their genes to make surface molecules.[106] That rearrangement could cause a problem for the resulting clone.

Moreover, human cloning research may not lead readily to treatments. In sheep embryos, the genes from the donor cell do not turn on until the egg has divided three or four times. In humans, by contrast, the genes turn on after two divisions. Although the difference may seem insignificant, Colin Stewart, from the National Cancer Institute, warns that the problem may lie in the fact that this rapid "turn-on time" may make it impossible to act quickly enough to catch the disease where its cancerous cells could be effectively and adequately quashed.[107] Additionally, for cancers which appear to be inheritable, such as the BRCA-1 mutation, there is no reason to assume that the cells will not mutate into other cancers or that the manipulation of the cancerous cells by these techniques will not further irritate the cells and worsen the original condition.[108]

Also, because scientists do not fully understand the cellular aging process, scientists do not know what "age" or "genetic clock" Dolly inherited.[109] On a cellular level, is she now a normal seven-month-old lamb, or is she six years old (the age of the mammary donor cell)?[110] Colin Stewart believes that Dolly's cells most likely are set to the genetic clock of the nucleus donor, and therefore are comparable to those of her six-year-old progenitor.[111] One commentator stated that if the hypotheses of a cellular, self-regulating genetic clock are correct, clones would be cellularly programmed to have much shorter life spans than the "original," which would seriously undermine many of the benefits which have been set forth in support of cloning—mostly agricultural justifications—and would psychologically lead people to view cloned animals and humans as short-lived, disposable copies.[112] This concern for premature aging has lead Dr. Sherman Elias, geneticist and obstetrician at the Baylor College of Medicine, to call for further animal testing of nuclear transplantation as a safeguard against subjecting human clones to premature aging and the potential harms associated with aged cells.[113]

The hidden mutations that may be passed on by using an adult cell raise concerns as well. "[Mutations are] a problem with every cell, and you don't even know where to check for them," writes Ralph Brinster of the University of Pennsylvania.[114] "If a brain cell is infected with a mutant skin cell, you would not know because it would not affect the way the cell develops because it is inactive. If you chose the wrong cell, then mutations would become apparent."[115]

Moreover, even if cloning were successful, it could lead to physical harm to the individual created, such as when the latter individual is subjected to physically invasive procedures to supply organs for transplants. Father Richard McCormick has said that to use a clone as a bank of potential organs and blood for donation is wrong; and one writer, Kenneth L. Woodward, called the practice an "inherently evil, morally unjustifiable intrusion into the human life."[116] Many feel that the manner in which a clone comes into existence should not affect the dignity or the rights the clone is granted. Therefore, notes Leon Kass, the clone should be treated as other humans are, and the notion of setting up a reserve of organs would be akin to slavery.[117]

B. Potential Psychological Impacts of Cloning Whole Individuals

There are concerns about the psychological impacts of cloning, both on the person whose DNA is used to create the clone and the resulting offspring. Psychologists worry that the mental health of the original may suffer from seeing himself or herself cloned. Many originals may feel that a clone would give them a second chance at life or an opportunity to change their own fate.[118] However, it could be too psychologically confusing and distressing for the originals to see themselves as children if they are not pleased about aging. Similarly, if the original sees the clone as a chance to correct fate, then the pressure placed on the clone would harm both the original and the clone.[119]

Mixing parental and twin roles could be psychologically harmful to the parent and the clone. "For the clonant to have as his parent the foreknower and creator of every one of his genetic predispositions might well make child adjustment exponentially more difficult," argues Francis Pizzulli.[120]

Thomas Murray worries about the self-identity of the clone when the clone finds out how he or she was conceived: "[H]uman beings tend to insist on finding meanings in relationships that it's not clear animals do."[121] Murray points out that an animal probably does not care about its conception, while a human does. It is often observed that adopted children feel a psychological compulsion to find their biological parents, for a number of reasons, including simple curiosity about their "genetic roots." Therefore, it is likely that human clones would experience the same compulsion to find the "original" from whom they were created. Just as "illegitimate children" historically were psychologically harmed and socially discriminated against, the children created by cloning might have problems, particularly where the replicant is ethically or religiously opposed to nuclear transplantation cloning. Similarly, in situations where a clone is created without the consent of the original, the potential rejection and hostility which the original may feel toward his or her cloned twin would be undeniably harmful to the clone's psyche.

Cloning could undermine human dignity by threatening the replicant's sense of self and sense of autonomy. Cloning represents the potential for "[a]buses of the power to control another person's destiny—both psychological and physical—of an unprecedented order. . . ."[122] Pizzulli points out that legal discussions of whether the replicant is the property of the cloned individual, the same person as the cloned individual, or a resource for organs all show how easily the replicant's own autonomy can be swept aside.[123]

Unlike a naturally occurring twin, the replicant "is *deliberately* infused with a *predetermined* genetic identity."[124] He is "saddled with a genotype that has already lived."[125] Pizzulli notes that "a clonant's genetic identity not only deprives him of a unique genotype but also has a detrimental impact upon his ability to experience a unique 'social environment' (i.e., physical and psychological stimuli that interact with his genotype subsequent to conception)."[126] Cloning, notes Pizzulli, "raises issues that go to the very nature of the individuality which is implicit in any legal order."[127] He points out, "[a]rguably a person cloned from a departed loved one has less chance of being loved solely for his own intrinsic worth."[128]

Another problem is that the clone has lost the ability to control disclosure of intimate personal information.[129] This may threaten the individual's self-image.[130] Studies of people's responses to genetic testing information show that learning genetic information about oneself (whether it is positive or negative information) can harm one's self-image.[131] The replicant individual may be made to feel that he or she is less of a free agent. Laurence Tribe argues that if one's genetic makeup is subject to prior determination, "one's ability to conceive of oneself as a free and rational being entitled to resist various social claims may gradually weaken and might finally disappear altogether."[132] Under such an analysis, it does not matter whether or not genetics actually determines a person's characteristics. Having a predetermined genetic makeup can be limiting if the person rearing the replicant, and/or the replicant, believes in genetic determinism.[133]

C. Potential Social Impacts of Cloning

Concerns have also been raised about the overall social impact of allowing people to create children through cloning. A general argument is made against cloning on the grounds that it is unnatural, but what is natural is historically bound and changes as technology becomes available. Contraception changed the natural assumption of the link between sex and procreation. Artificial insemination and in vitro fertilization further changed this assumption by showing that it was possible to procreate without sex. Joshua Lederberg argues that artificial reproduction is only as bizarre and new as sexual reproduction was at an earlier stage in evolution.[134] In addition, Joseph Fletcher has argued that the "natural" should not be privileged. He states:

> [L]aboratory reproduction is radically human compared to conception by . . . heterosexual intercourse. It is willed, chosen, proposed and controlled, and surely these are among the traits that distinguish *Homo sapiens* from others in the animal genus. . . . Coital reproduction is, therefore, less human than laboratory reproduction . . . with our separation of baby making from lovemaking both become more human because they are matters of choice, and not chance. This is . . . essentially the case for planned parenthood. I cannot see how either humanity or morality are served by genetic roulette.[135]

Even though labeling cloning as unnatural may not provide an appropriate policy reason to ban it, the social impacts of such a departure from the usual means of creating children must be factored into the policy analysis. There is concern that cloning will interfere with evolution. Because cloning promotes genetic uniformity, cloning increases the danger that a disease might arise in the future to which the resulting clones have no resistance.[136] George Johnson, professor of biology at Washington University, an evolutionist, opposes cloning because "genetic variation is the chief defense our species has against an uncertain future. If we strip ourselves of it, even partially, is to endanger our species."[137] What has allowed the human species to survive is genetic adaptation, and producing genetically identical humans would therefore be threatening to the species.[138] Also, it is not clear yet whether all or a high proportion of children created through nuclear transplantation will be sterile, which may affect the potential for humans to procreate in the traditional manner.[139] However, some commentators argue that if human cloning is restricted

to only very rare cases, then the evolution of the human species should not be stunted nor the human gene pool disturbed any more than the gene pool is currently affected by naturally occurring identical twins.[140]

Philippe Stroot, a spokesperson for World Health Organization, condemned human cloning as "ethically unacceptable"[141] because it threatens human evolution not only by destroying genetic diversity, but also by posing risks of transmitting diseases from the original to the clone, and, if transgenic manipulation is allowed, by transmitting diseases from animal species to humans.[142] Stroot stated that there are always concerns associated with medical technologies which involve the introduction of interspecies cells into one another, and that the potential for harm created by transgenic animals and humans must be closely monitored.[143] Future generations may be harmed if cloning is used extensively, since they would be limited only to the narrow range of acceptable genotypes left after a particular generation has instituted a cloning program.[144]

There are also concerns about the changes that cloning could bring to the institution of the family. Boston College theologian Lisa Sowhill Cahill is concerned with the commodification of human beings and their genes and the manipulation of human genetics to achieve more socially desirable children.[145] Allen Verhey, a Protestant ethicist at Hope College in Holland, Michigan, warns that cloning would desensitize society into regarding all children, particularly cloned children, as "products."[146]

A wide range of opponents—from Pope John Paul[147] to Senator Connie Mack to health law expert George Annas to Dr. Wilmut[148]—feel that nuclear transplantation cheapens not only the life of the clone but that of all humanity.[149] Opponents envision a world where clones are "cannibalized for spare parts,"[150] or are made solely for medical purposes, asked to donate their organs, and are then forever treated "like second class citizens."[151]

Cloning may also have negative impacts on legal concepts. Pizzulli points out that "(a) privacy and autonomy might be severely attenuated in one known by himself or others to have a predetermined genetic identity; and (b) irrespective of personal and/or public knowledge of one's clonal origins, the technology of cloning might have macro-effects upon society by eroding the concept of individuality which is at the core of our notions of privacy and autonomy."[152] In addition to weakening an individual's sense of free will, cloning would "weaken the social constructs and political institutions that serve to foster the exercise of individual autonomy and to inhibit the coercive manipulation of individuals."[153]

There have been religious arguments against cloning as well. Within the week after Dolly's story became public, the Vatican called for a global ban on cloning.[154] According to the Pontiff, the creation of life outside of marriage goes against God's plan. Additionally, according to the Pontiff, out of respect for animals, all cloning of animals should be abandoned as well.[155]

EXISTING LAWS THAT COULD RESTRICT CLONING

Are there existing state laws that would ban human cloning as either a scientific research technique to study cells and tissue or as a new means to create whole persons? The only existing legal regulation that speaks directly to cloning is the federal ban on cloning using federal funds. Proposed laws on the subject are under consideration,[156] but until they are passed, the analysis of whether a particular state restricts cloning requires scrutiny of statutes which were adopted for other purposes. In addition to the statutory precedents, criminal and tort law precedents in many states create an obligation on the part of scientists and clinicians to exercise due care when they undertake research or innovative therapy with respect to embryos and fetuses.[157] Moreover, constitutional principles must be considered in determining whether the application of such precedents to cloning is appropriate.[158]

A. State Statutes Governing Research on Embryos

There are ten states which have laws regulating research and/or experimentation on embryos, preembryos, fetuses, conceptuses, or unborn children which arguably may apply to cloning research.[159] The difficulty in discerning whether any of the states' regulations could reach cloning is primarily definitional. Each statute approaches the prohibited activities in a slightly different way, and thus a close analysis is necessary to determine whether cloning is within a particular statute's reach. Among the questions to be addressed are whether the cloning technique fits the definition of "research" or "experimentation"; whether the entity being researched upon fits the definition of Alive" and, depending on the state, "preembryo," "embryo," "fetus," "conceptus," or "unborn child"; and whether nucleic transfer can be considered to involve "fertilization."

Eight of the states prohibit some form of research on some product of conception, referred to in the statutes as a conceptus,[160] embryo,[161] fetus,[162] or unborn child.[163] An argument could be made that the experimentation is being done on an *egg*, not the product of conception, and thus these statutes should not apply. By the time the egg is renucleated, the experiment or research (which is prohibited) has already been completed. Since the statutes would not apply until after the cloning procedure is completed, it could be argued that the most protection these statutes supply would be protection from experimentation after the renucleation; it would not prevent the cloning itself.

The statutes are ambiguous. On the one hand, it could be argued that the statutes should not cover cloning, particularly since it was not within the original contemplation of the laws' drafters. On the other hand, it could be argued that the spirit of the legislation is to protect the beginning of human life and so the statutes would apply.[164]

The analysis is further complicated in states that define the term conceptus or unborn child as the product of "fertilization." Whether Minnesota's and Pennsylvania's statutes would apply to cloning turns on whether the term "fertilization" includes cloning. Minnesota's statute bans research on a "living conceptus," created in utero or ex utero, "from fertilization through 265

days thereafter."[165] Since fertilization is not defined, a court might turn to a dictionary definition: "the process of union of two germ cells whereby the somatic chromosome number is restored and the development of a new individual is initiated . . . ."[166] Cloning is not the union of two germ cells, but this process *does* restore the somatic chromosome number, *and* the development of a new individual is initiated. The two most important elements of fertilization are satisfied, and the third merely explains the only way previously known to accomplish the first two. Thus fertilization could be interpreted to include cloning. The 265-day period of coverage in the Minnesota statute potentially creates a loophole, though. If an embryo is created through cloning, it could be argued that if it is cryopreserved for 265 days after "fertilization," it could be experimented upon thereafter.

Pennsylvania prohibits nontherapeutic experimentation and nontherapeutic medical procedures on an "unborn child,"[167] which is defined as being an organism of the species of homo sapiens from fertilization to live birth.[168] Fertilization, in turn, is defined as the fusion of a human spermatozoa with a human ovum. Like Minnesota, then, the reach of the statute would depend in part on whether the definition of fertilization was stretched to cover nucleic transfer. Pennsylvania's law is open to an additional challenge. The statute's use of the term "unborn child" might allow for an argument that it should not be interpreted to cover cloning research which is not intended to lead to birth.

A further complication is presented by the fact that six of the statutes apply to "live" fetuses only.[169] Two of the statutes—Florida[170] and Maine[171]—do not define "live" but it is likely that a court would determine that the product of cloning research was live.

In the other four states that provide protection for "live fetuses," a fetus is defined as being "live" at that time when "in the best medical judgment of a physician, it shows evidence of life as determined by the same medical standards as are used in determining evidence of life in a spontaneously aborted fetus at approximately the same stage of gestational development."[172] Whether these statutes would apply to the new cloning technique is a medical determination. If they are to apply, Massachusetts, North Dakota, and Rhode Island would prohibit all research or experimentation,[173] while Michigan would prohibit only non-therapeutic research and experimentation.[174]

Some of the states that ban research and/or experimentation on fetuses have exceptions if the activity is necessary to preserve the life or health of the fetus.[175] An argument could be made that these statutes might create an exception for cloning whole individuals, because without the very procedure the statute would regulate, the fetus would not *be* alive to preserve. John Robertson argues that, in cloning, "the intent there is actually to benefit that child by bringing it into being so if one views it somehow as experimentation on the expected child I would think it should be classified as experimentation for its benefit and thus would fall within recognized exceptions when experimentation can occur."[176] However, a court would be unlikely to find such an argument persuasive; a court is likely to hold that the procedure needs to be therapeutic to an already existing fetus.

Two statutes have provisions that are particularly likely to be applied to cloning. The New Hampshire law does not allow a preembryo to develop ex utero past 14 days after fertilization, which would appear to allow cellular-level and genetic-level cloning research during that period. However, New Hampshire's statute prevents a "preembryo" that has been used for research from being transferred to a uterine cavity.[177] The statute's concern is clearly to prevent the birth of a researched-upon individual. New Hampshire's statute would completely ban cloning research that leads to a birth (until such time as there is an artificial womb perfected,[178] since the statute only prohibits implantation into a uterine cavity).

Louisiana has the most far-reaching statute. Louisiana's statute protects an "in vitro fertilized human ovum . . . composed of one or more living human cells and human genetic material so unified and organized that it will develop in utero into an unborn child."[179] Although the same arguments as above may be made about the definition of fertilization, they seem unnecessary because the definition of "in vitro fertilized ovum" is broad enough to include any human cells destined to become children. Accepting this interpretation, the entire statute applies to cloning. A renucleated oocyte is certainly one human cell and human genetic material, presumably alive, and so unified that it will develop into an unborn child. The Louisiana statute would bestow various rights upon the clone. Under the Louisiana statute, the resulting in vitro fertilized ovum can be used only for support and contribution of the complete development of human in utero implantation;[180] it cannot be cultured or farmed solely for research,[181] is deemed a juridical person,[182] must be given an identity,[183] can sue and be sued,[184] has a right to confidentiality,[185] is a biological human being which is not property,[186] may not be destroyed,[187] and is owed a high duty of care;[188] and all disputes regarding the in vitro fertilized human ovum shall be resolved in the best interest of the in vitro fertilized human ovum.[189]

The Louisiana statute specifies the relation of the resulting embryo to other persons and the duties owed by others to it. An in vitro embryo is not property.[190] If parents reveal their identities, their rights as parents of the fertilized ovum are preserved; otherwise, the physician or a court-appointed curator is its guardian.[191] The gamete donors owe the in vitro embryo a "high duty of care and prudent administration."[192] The donors may renounce their rights generally, in which case the embryo is placed for "adoptive implantationy," or in favor of a couple willing and able to accept the embryo.[193] Neither couple may pay or receive compensation to renounce parental rights.[194] Disputes involving the embryo are to be determined in the embryo's best interests.[195]

The physician who caused the in vitro fertilization is directly responsible for the embryo's safekeeping in vitro.[196] The physician, hospital, and clinic are not strictly liable for any screening, collection, conservation, preparation, transfer, or cryopreservation procedure undertaken in good faith. This immunity, however, appears to only apply to actions brought on behalf of an in vitro embryo as a juridical person.[197]

The Louisiana statuteq would severely limit or prevent some of the uses that have been suggested for cloning, such as cloning for body parts, and would settle the question of whether a clone is a

separate person or an extension of the original. It creates an anomalous situation, however, where research would be prohibited on cloned cells but there would be no specific ban on cloning a whole individual. The latter activity would seem to be permissible under the provision saying that an in vitro fertilized ovum may be used "solely for the support and contribution of the complete development of human in utero implantation."[198]

The states vary in the type of penalties they impose for violation of the fetal research laws. In some states, violation of the fetal research law is considered to be unprofessional conduct,[199] creating the potential for a physician/researcher who violates the law to lose his or her license to practice medicine. In other jurisdictions, the violation of such laws can subject the researcher to a fine and imprisonment.[200]

The Massachusetts statute creates an elaborate regulatory mechanism providing for public and private actions to enforce the law. When a proposal for research on fetuses is approved, the written approval by the Institutional Review Board must be filed with the local District Attorney.[201] The approval is open for public inspection. If the District Attorney believes that the proposed procedure is prohibited, he or she shall file a complaint, giving notice to the Commissioner of Public Health, who in turn gives notice to all licensed medical schools and other institutions in the state that may be affected by a judgment in the case.[202] The statute authorizes a broad class of people or institutions potentially affected by the judgment to intervene in the case.[203] The trial on the merits must be without a jury,[204] and any judgment must be published in newspapers and sent to licensed hospitals and medical schools.[205] There is also a procedure for researchers to bring a declaratory judgment action to determine whether a proposed procedure violates the provisions of the statute.[206]

In addition to questions of statutory interpretation, the state laws that have general bans on embryo research or experimentation may be challenged as unconstitutional for being impermissibly vague. Such laws have already been struck down in three states on those grounds. In *Lifchez v. Hartigan*, the ban on experimentation on embryos was unconstitutionally vague because it failed to define the terms "experimentation" and Atherapeutic."[207] The court pointed out that there are multiple meanings of the term "experimentation."[208] It could mean pure research, with no direct benefit to the subject. It could mean a procedure that is not sufficiently tested so that the outcome is predictable, or that departs from present-day practice. It could mean a procedure performed by a practitioner or clinic for the first time. Or it could mean routine treatment on a new patient. Since the statute did not define the term, it violated researchers' and clinicians' due process rights under the Fifth Amendment since it forced them to guess whether their conduct was unlawful.[209]

A similar result was reached by a federal appellate court assessing the constitutionality of a Louisiana law prohibiting nontherapeutic experimentation on fetuses in *Margaret S. v. Edwards*.[210] The appeals court declared the law unconstitutional because the term "experimentation" was so vague it did not give researchers adequate notice about what type of conduct was banned.[211] The court said that the term "experimentation" was impermissibly

vague[212] since physicians do not and cannot distinguish clearly between medical experimentation and medical tests.[213] The court noted that "even medical treatment can be reasonably described as both a test and an experiment."[214] This is the case, for example, " whenever the results of the treatment are observed, recorded, and introduced into the data base that one or more physicians use in seeking better therapeutic methods."[215]

A third case struck down as vague the Utah statute that provided that "live unborn children may not be used for experimentation, but when advisable, in the best medical judgment of the physician, may be tested for genetic defects."[216] The Tenth Circuit held that "[b]ecause there are several competing and equally viable definitions, the term 'experimentation' does not place health care providers on adequate notice of the legality of their conduct."[217] A petition for certiorari was filed in the U.S. Supreme Court in this case on March 18, 1997.

It should be noted, however, that the vagueness claim could be avoided if the state or federal government ban included more explicit language. For example, the proposed federal cloning ban, S. 368, would not be unconstitutionally vague. It prohibits "the replication of a human individual by the taking of a cell with genetic material and the cultivation of the cell through the egg, embryo, fetal and newborn stages into a new human individual."[218]

B. The Reach of Laws Governing In Vitro Fertilization and Assisted Reproductive Technology

Cloning procedures for reproductive purposes would be subject to the Fertility Clinic Success Rate and Certification Act of 1992,[219] which regulates assisted reproductive technology programs—defined as "all treatments or procedures which include the handling of human oocytes or embryos,"[220] and embryo laboratories—defined as facilities in which "human oocytes are subject to assisted reproductive technology treatment or procedures based on manipulation of oocytes or embryos which are subject to implantation."[221] The Act requires assisted reproductive technology programs to report their pregnancy success rates to the Secretary of Health and Human Services[222] for publication in an annual consumer guide.[223] In addition, the Act requires that assisted reproductive technology programs identify the embryo laboratories that they rely on for lab work[224] for publication in the consumer guide.[225] Finally, the Act requires the Secretary of Health and Human Services to develop a model program for the inspection and certification of embryo labs to be implemented by the states.[226]

If cloning is considered to be a form of fertilization, questions arise regarding whether state laws setting standards for who may perform in vitro fertilization will cover the practice. There are fewer state laws specifically addressing the conduct of in vitro fertilization than addressing the conduct of fetal research. Although the impetus behind the in vitro fertilization laws was, for the most part, the regulation of the clinical practice of in vitro fertilization, the provisions are sometimes broad enough to regulate cloning researchers. Certain laws governing reporting, the qualifications of personnel, and so forth, will be applicable to researchers. A New Hampshire law requires counseling in advance of in vitro fertilization and limits the procedure to

participants over age 21[227] (which, if applied to cloning could prohibit the use of DNA from a minor child). Pennsylvania has a reporting requirement which mandates that anyone performing in vitro fertilization file quarterly reports with the Department of Health describing such facts as the number of embryos destroyed and discarded and the number of women in whom embryos are implanted.[228] Louisiana's law requires that in vitro fertilization shall only be undertaken by practitioners and facilities meeting the standards of the American College of Obstetricians and Gynecologists (ACOG) and the American Fertility Society (AFS) (currently the American Society for Reproductive Medicine).[229] Some states have statutes dealing with insurance reimbursement of in vitro fertilization for infertility. A few of those states mandate that, to be reimbursed, the in vitro fertilization procedure must be performed in facilities that meet the ACOG and AFS standards.[230] The insurance-related provisions are unlikely to be applicable to cloning, since cloning will be denied coverage as being too experimental.

PROPOSED FEDERAL AND STATE STATUTES REGARDING CLONING

The announcement of Dr. Ian Wilmut's experiment led to the immediate introduction of federal and state bills to ban the practice of human cloning. Most do not suffer from the problem of unconstitutional vagueness, since the particular activity they ban—cloning—is explicitly described. However, it is described in different ways in the various bills, which could lead to definitional problems similar to those encountered in the fetal research laws as new variations of the technology are developed that may not exactly fit into the current cloning definition.

Federal legislation has been introduced, and bills have been proposed in at least 11 states (Alabama, California, Florida, Illinois, Maryland, Missouri, New York, New Jersey, Oregon, South Carolina, and West Virginia). The federal bill and two states' bills ban the use of governmental funds for cloning an entire individual.[231] The other nine states' bills ban cloning of an entire individual, no matter what the funding source. Only a few states' bills conceivably apply to cloning research not intended to create an entire individual. One bans research using cloned cells or tissue.[232] In addition, two other statutes might unintentionally ban such research. The South Carolina statute defines cloning as the creation of a human being and then bans the steps leading to it. It prohibits cloning by extracting the nucleus from any unfertilized egg and infusing into it DNA from any other cell.[233] Such a provision may restrict cellular research using cloning techniques because it might be difficult for a scientist to convincingly prove that he or she was not doing it to create an individual. West Virginia bans creation of a human "organism" through cloning, which might be interpreted to ban creation of tissue or an organ through cloning techniques.

Moreover, some of the statutes have loopholes since they only ban the creation of a "genetically identical" individual.[234] Since a donated egg is used to create the clone, the resulting individual will have some mitochondrial DNA that is not identical to that of the original individual. Thus, an argument could be made that the law would not apply because it does not create a "genetically identical" individual.

A. Federal Action

At the federal level, Senator Christopher Bond of Missouri introduced S. 368, a bill to ban the use of federal funds for research with respect to the cloning of a human individual. His bill defines cloning as "the replication of a human individual by the taking of a cell with genetic material and the cultivation of the cell through the egg, embryo, fetal, and newborn stages into a new human individual."[235] Thus, Senator Bond's bill would not prohibit federal funding of cloning research that did not result in a live birth. Researchers could clone human cells and allow the resulting entity to proceed through cell divisions to determine what influenced the turning on and off of certain genes. They apparently could also undertake cloning research to create human organs for transplant in the laboratory, so long as no new humans are born.

In addition, Representative Vernon Ehlers, on March 5, 1997, introduced H.R. 922 and 923. H.R. 922 provides that "[n]one of the funds made available in any Federal law may be expended to conduct or support any project of research that involves the use of a human somatic cell for the process of producing a human clone." H.R. 923 provides that "it shall be unlawful for any human person to use a human somatic cell for the process of producing a human clone." The latter bill has a civil penalty of $5,000, which, given the overall cost of cloning and the incentive to undertake the procedure for scientific and personal reasons, would probably not be enough to deter someone from cloning a person.

B. Alabama

State Senator John Amari of Alabama introduced S.B. 511, which prohibits the cloning of human beings.[236] Again, the definition of cloning is broad: "reproducing a being of like genetic constitution from a single somatic cell by repeated cell division."[237] Amari also introduced Senate Joint Resolution 58 requesting the U.S. Congress to prohibit cloning and urging other countries to prohibit the practice. The preamble of the joint resolution gave several reasons for the prohibition.

> "The creation of a human being is sacred and every person has the right to be born as the result of human reproduction."
>
> "The cloning of human beings could irreparably harm the dignity of human life and show an appalling lack of respect for human life."
>
> "The cloning of human beings could result in dangerous experiments with unfathomable consequences."

C. California

A bill was introduced in California by State Senator Johnston amending the human experimentation law to ban the cloning of a human being.[238] In addition, California State Senator

Dave Kelley introduced a Senate Joint Resolution[239] requesting the President and Congress "to act immediately and swiftly to ban, outlaw, and take all necessary means to prevent the cloning of human beings." The resolution points out that cloning human beings raises serious moral, ethical, legal, and other questions and that other countries ban cloning. The resolution also indicates that State Senator Kelley plans to introduce a bill banning cloning in California in the next legislative session.

D. Florida

Florida State Representative Villalobos introduced a bill to make it unlawful "to clone or attempt to clone the DNA of any human being."[240] This law would not just limit the cloning of a whole human being, or research involving nuclear transfer, but would restrict much existing scientific research in which cells are "cloned" or replicated through techniques that involve cell division.

E. Illinois

An Illinois bill, introduced by House Member Carolyn Krause, defines cloning as "the intentional manipulation of a human egg cell to make it genetically identical to another human being, living or dead."[241] The bill prohibits both human cloning and the use of public funds or property for human cloning.[242] It has an exception for in vitro fertilization, use of fertility-enhancing drugs, and certain other medical procedures that are not intended to create a genetically identical being.[243]

F. Maryland

In Maryland, State Representative Valderrama introduced a House Joint Resolution to ban state funding of cloning or cloning research that would "replicate a human being."[244] The resolution preamble asserts:

> The principles of industrial production and design, such as quality control, predictability, profitability, and efficiency, should never be allowed to apply to the production of humans.
>
> Social, ethical, and moral values should not be sacrificed in favor of the dubious potential benefits of scientific experimentation in human cloning.
>
> Cloning would tend to devalue human life or dehumanize mankind.

The resolution also points out that in a recently published poll, 90% of respondents favored prohibiting cloning by law.

G. Missouri

Representative Edwards-Pavia of Missouri introduced a bill forbidding the use of state funds for "the replication of a human person taking a cell with genetic material and cultivating such cell

through the egg, embryo, fetal and newborn stages of development into a new human being."[245] In addition to the limitations of coverage (it would not apply to cloning with private funds), it is ambiguous since it does not define "replication." It might be considered unconstitutionally vague since so many forms of reproduction (including coital) start with one cell (in most instances, the fertilized egg) and proceed through those stages of development.

H. New Jersey

The New Jersey bill, introduced by Assemblywoman Gell and Assemblyman Doria, takes an interesting approach and includes cloning within a broader bill regulating genetics. The bill makes it criminal to knowingly engage or assist, directly or indirectly, in the cloning of a human being, which is defined as "the replication of a human individual by cultivating a cell with genetic material through the egg, embryo, fetal and newborn stages into a new human individual."[246] (This again would create a problem with the definition of replication). The New Jersey bill also includes a number of provisions that would prevent an individual from being cloned without his or her consent. These provisions provide that, except in limited circumstances, an individual's DNA sample which has been used shall be destroyed upon the individual's request[247] and an individual's DNA sample used in research shall be destroyed upon completion of the project or withdrawal of the individual, unless the individual directs otherwise.[248]

I. New York

New York State Senator John Marchi has introduced a bill, S.B. 2877,[249] to criminalize human cloning and conspiracy to clone. Cloning is defined as "the growing or creation of a human being from a single cell or cells of a genetically identical human being through asexual reproduction."[250] The substantive provision prohibits cloning "by extracting the nucleus from any unfertilized human egg and infusing into such egg deoxyribonucleic acid from any other cell; or cloning a human being by any other measure or method."[251] The bill also provides that "[a] person is guilty of conspiring to clone when, the intentional conduct would result in the cloning of a human being, such person agrees with one or more persons to engage in or cause the cloning of a human being."[252] The Commissioner of Public Health or a departmental representative can enter into any workplace at a reasonable hour if there is reason to believe cloning is being conducted.[253] A parallel bill was introduced in the New York Assembly by Member of the Assembly Connelly.[254] Yet both bills may be problematic because of the language about a "genetically identical" individual.

J. Oregon

The Oregon proposal, sponsored by State Senator Lim, makes it "unlawful for any person to create a clone from a cell derived from a human being, including a fetus, embryo, or other product of conception."[255] The bill defines a clone as "an individual grown from a single somatic cell of its parent and genetically identical to the parent."[256]

K. South Carolina

State Representative Mason of South Carolina has introduced a bill that bans cloning and conspiracy to clone. The definition of cloning, though, has the same problem as the one in New York. Cloning is defined as "the growing or creation of a human being from a single cell or cells of a genetically identical human being through asexual reproduction."[257]

L. West Virginia

The West Virginia bill, introduced by State Senator Bailey, makes it "unlawful to use recombinant deoxyribonucleic acid (DNA) or recombinant ribonucleic acid (RNA) research and cell fusion, or other such genetic engineering technology, to engage in the manipulation or alteration of a human organism's genetic material to produce another human organism from that genetic material, more commonly referred to as cloning." The use of the term human organism, however, might be interpreted to include the creation of human tissue or organs, not just the creation of a whole individual.[258]

THE FEDERAL ROLE IN REGULATING CLONING

Because both President Clinton and various members of Congress have expressed concerns about human cloning of individuals—as have a majority of members of the public—federal action is being considered to ban the practice. Such an action would raise important questions of federalism and might be challenged as exceeding the federal government's authority. However, a close analysis of U.S. Supreme Court cases regarding federal powers provides justification for federal action in this area.

The states have traditionally regulated issues related to health care. For example, physicians and hospitals are licensed and regulated by state boards of medical examiners. Thus, at first glance, it would seem that cloning would be more appropriately regulated at the state level. However, despite this tradition of decentralization, the federal government may justify regulation of human cloning by linking such regulation to its spending power[259] and/or its power to regulate interstate commerce.[260]

The federal government currently regulates a variety of medical and scientific activities which are linked to government funding. In conjunction with its provision of Medicare funds, the federal government has required physicians to abide by certain regulations, such as by prohibiting certain forms of fraud and abuse.[261] Similarly, as a condition of receiving federal funds for scientific research, scientists must comply with federal regulations governing research.[262] Consequently, a federal ban on human cloning research with federal funds, as the President has currently promulgated, would be a permissible exercise of federal power.[263] However, regulation based on the spending power is insufficient to regulate research in the private sector, conducted with non-governmental funds. To be permissible, federal regulation of private research must be justified under the commerce clause.

The U.S. Constitution provides that Congress has the authority "to regulate commerce . . . among the several States. . . . [264] Court cases have held that the federal government has the power to regulate economic activities that substantially affect interstate commerce.[265] When Congress regulates medical and scientific activities pursuant to its commerce clause power, it often includes a jurisdictional element—a provision in the statute which indicates that it applies only to activities involving interstate commerce. One example is the National Organ Transplant Act, which provides, in part, that "[i]t shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation if the transfer affects interstate commerce."[266] Even the proposed Human Research Subject Protections Act of 1997 contains a jurisdictional element in its definition of research facility: "any public or private entity, agency . . . or person that uses human subjects in research involving interstate commerce."[267]

Until recently, the Supreme Court endorsed a broad construction of the commerce clause. However, in 1995, for the first time in close to 60 years,[268] the Supreme Court held that Congress had passed a law that exceeded its authority under the commerce clause.[269] In *U.S. v. Lopez*, the Supreme Court held that the Gun-Free School Zones Act of 1990, prohibiting the possession of a firearm "at a place that the individual knows or has reason to believe, is a school zone,"[270] neither "regulate[d] commercial activity nor containe[d] a requirement that possession be connected in any way to interstate commerce."[271] Consequently, the law was struck down as exceeding the federal power to regulate.

Commerce clause case law concerns the basic principle that the Constitution creates a Federal Government of enumerated powers.[272] As James Madison wrote, "[t]he powers delegated by the proposed Constitution to the federal government are few and defined. Those which are to remain in the State governments are numerous and indefinite."[273] Federalism is central to our form of government. As the U.S. Supreme Court has pointed out, "[a] healthy balance of power between the States and the Federal Government will reduce the risk of tyranny and abuse from either front."[274] The nature of Congress' commerce power was first defined in *Gibbons v. Ogden*.[275] The commerce power "is the power to regulate; that is, to prescribe the rule by which commerce is to be governed. This power, like all others vested in Congress, is complete in itself, may be exercised to its utmost extent, and acknowledges no limitations other than are prescribed in the Constitution."[276]

In the "watershed"[277] case *NLRB v. Jones & Laughlin Steel Corp.*,[278] the Court sustained the directive of the National Labor Relations Board, issued pursuant to the National Labor Relations Act of 1935, that the defendant steel company desist from discriminating against employees on the basis of union membership and in other respects interfering with attempts to organize the company's employees. The Court held that intrastate activities that "have such a close and substantial relation to interstate commerce that their control is essential or appropriate to protect their commerce from burden and obstructions" are within Congress' power to regulate.[279] Subsequent decisions, recognizing the great changes that had occurred in the way business was carried on, indicate that Congress did not have to show that each transaction it

regulates has a substantial impact on commerce: "[w]here a general regulatory statute bears a substantial relation to commerce, the *de minimis* character of the individual instances arising under that statute is of no consequence."[280]

For example, in *U.S. v. Darby*,[281] the Court upheld the Fair Labor Standards Act stating:

> The power of Congress over interstate commerce is not confined to the regulation of commerce among the states. It extends to those activities intrastate which so affect interstate commerce or the exercise of the power of Congress over it as to make regulation of them appropriate means to the attainment of a legitimate end, the exercise of the granted power of Congress to regulate interstate commerce.[282]

Under this approach, intrastate activities were reached in *Hodel v. Virginia Surface Mining & Reclamation Assn.*,[283] *Perez v. U.S.*,[284] *Katzenbach v. McClung*,[285] and *Heart of Atlanta Hotel, Inc. v. U.S.*[286] At issue in those cases were the regulation of intrastate coal mining, intrastate extortionate credit transactions, restaurants utilizing substantial interstate supplies, and inns and hotels.

In some instances, the federal government was found to have power to regulate because of supplies which moved in interstate commerce.[287] In other instances, the key was that customers came from out of state. The Supreme Court has upheld the constitutionality of the Civil Rights Act of 1964[288] as applied to hotels[289] of seemingly "purely local character."[290] In holding that "the power of Congress to promote interstate commerce also includes the power to regulate the incidents thereof, including local activities . . . which might have a substantial effect upon . . . commerce,"[291] the Court reasoned that racial discrimination would burden interstate travel.[292]

In light of the contours of the federal commerce power as outlined by case law, the *Lopez* court affirmed three broad categories of legislation authorized by the commerce clause: (1) statutes regulating the use of the channels of interstate commerce; (2) laws governing "the instrumentalities of interstate commerce, or persons or things in interstate commerce, even though the threat may come only from intrastate activities"; and (3) statutes regulating activities "that substantially affect interstate commerce."[293]

In holding that "possession of a gun in a local school zone is in no sense an economic activity that might, through repetition elsewhere, substantially affect any sort of interstate commerce,"[294] the Court relied on a number of factors. First, the majority opinion repeatedly noted that the Gun-Free School Zones Act did not regulate any "commercial transaction or economic activity."[295] In *Lopez*, "neither the actors nor their conduct have a commercial character and neither the purpose nor the design of the statute have an evident commercial nexus."[296] Rather, the Gun-Free School Zones Act was "a criminal statute that by its terms had nothing to do with 'commerce' or any sort of economic enterprise."[297]

Second, the Gun-Free School Zones Act contained "no jurisdictional element which would ensure, through case-by-case inquiry, that the firearm possession in question affects interstate commerce."[298] Professor Deborah Merritt suggests that a jurisdictional element would have signaled that Congress was aware of its limits under the Commerce Clause and took those limits seriously.[299] The jurisdictional clause would have slightly narrowed the scope of federal prosecutions, making the federal interest more apparent.[300] By failing to include a jurisdictional element, "Congress almost dared the Court to find the statute unconstitutional."[301]

Third, the Court was influenced by the lack of express findings or legislative history. In fact, the Government conceded that "neither the statute nor its legislative history contains express congressional findings regarding the effects upon interstate commerce of gun possession in a school zone."[302] Although congressional findings or a legislative history are not prerequisites to sustaining a statute under the commerce clause, the majority noted that such findings or history would have enabled them "to evaluate the legislative judgment that the activity in question substantially affected interstate commerce, even though no such substantial effect was visible to the naked eye. . . ."[303] The Court wanted either Congress or the Solicitor General's office to articulate a rationale for the exercise of congressional power at issue.[304]

Fourth, the statute's link to education, an area traditionally regulated by the States,[305] was also significant. The Government argued that "the presence of guns in school poses a substantial threat to the education process by threatening the learning environment. A handicapped educational process, in turn, will result in a less productive citizenry. That, in turn, would have an adverse effect on the Nation's economic well-being."[306] The Court was troubled by this argument, which was based on a tenuous link between the presence of guns in schools and the Nation's economy. Acceptance of such an argument would imply that Congress could regulate almost all aspects of education.

Fifth, the statute's focus on gun possession also affected the Court's decision. The statute at issue was broadly drawn. As a result, it included some forms of gun possession that posed little, if any threat to school children.[307] A hypothetical situation posed by the Fifth Circuit which would fall under the prohibitions of the statute involved carrying an unloaded shotgun "in an unlocked pickup truck gun rack, while driving on a country road that at one turn happens to come within 950 feet of the boundary of the grounds of a one-room church kindergarten located on the other side of a river, even during the summer when the kindergarten is not in session."[308]

Furthermore, gun possession on school premises lacked the "aura of national urgency"[309] present in earlier cases endorsing a broad construction of the commerce clause.[310] Most states had already outlawed the possession of guns on school premises, and there were no findings, nor did the Government argue, that state and local officials were unable to enforce those laws.

Finally, the *Lopez* Court might have believed that in response to the Government's arguments, it simply had to set some limit to Congress' authority. The Government argued that violent acts affect the national economy by raising insurance rates; violent crimes affect the

economy by discouraging interstate travel; and guns disrupt education, reducing workforce skills and ultimately diminishing productivity.[311] In considering these arguments, the Court pointed out that if it were to accept them, it would be "hard pressed to posit any activity by an individual that Congress is without power to regulate."[312] Under the "costs of crime" reasoning, "Congress could regulate not only all violent crime, but all activities that might lead to violent crime, regardless of how tenuously they relate to interstate commerce."[313] Under the "national productivity" reasoning, "Congress could regulate any activity that it found was related to the economic productivity of individual citizens: family law (including marriage, divorce, and child custody), for example."[314] Under these arguments, it would be "difficult to perceive any limitation on federal power."[315]

Although *Lopez* reminds us that Congressional authority to regulate under the commerce power is limited, commentators suggest that the unique combination of factors at play in that case will readily distinguish it from future challenges. Nonetheless, it does raise a number of factors to be considered in determining whether Congress' commerce power extends to the regulation of cloning.

The first question is whether cloning is, in fact, commerce. Medicine initially was viewed as an altruistic, non-commercial endeavor. Hospitals were charitable institutions for the poor and were exempt from various rules that governed businesses. For example, tort suits against hospitals were prohibited on the ground of charitable immunity.[316] In recent years, hospitals have taken on more of the characteristics of business, characterized by revenues and expenditures in the millions of dollars.[317] The characterization of hospitals as businesses has justified the extension of such federal regulatory schemes as the Fair Labor Standards Act,[318] the National Labor Relations Act,[319] and the Sherman Act[320] to hospitals. Each of those acts specifically state that they apply only to interstate commerce.[321] Cases upholding the application of these regulatory schemes to hospitals reason that the purchase of medicine and supplies from out-of-state sources and reimbursement from out-of-state insurance companies and the federal government are sufficient to establish a substantial effect on interstate commerce.[322]

Providers challenging the federal regulation of cloning may argue that they provide their services for purely altruistic purposes—creation of organs, reproductive options—rather than economic gain. What if cloning were provided without charge? Sperm is provided without charge at the Repository for Germinal Choice in Escondido, California (the Nobel Prize Sperm Bank) due to the owner's interest in attempting to upgrade the intelligence of the next generation. A similar entity could be established to allow people to raise clones of talented individuals. Nevertheless, an organization does not have to be a commercial enterprise to affect interstate commerce.[323]

What if it were alleged that cloning did not have a *substantial* impact on interstate commerce? Such an argument has already been made in the medical setting, when individual dentists challenged the application of Title III of the Americans with Disabilities Act to their practices as unconstitutional under the commerce clause.[324] Title III prohibits discrimination on

the "basis of disability . . . by any person who owns, leases, . . . or operates a place of public accommodation."[325] Private entities are considered public accommodations "if the operation of such entities affect commerce."[326] In *Abbott v. Bragdon*,[327] the defendant argued that because the practice of dental medicine occurs purely intrastate, it did not substantially affect commerce and thus was beyond Congress' regulatory authority under the commerce clause.[328] The court found that

> if the Defendant's purchase of supplies and equipment from out of state, receipt of payments from out of state insurers and credit card companies, and attendance of classes and conferences out of state by themselves do not substantially affect interstate commerce . . . those commercial activities taken together with the activities of other dentists similarly situated, have an effect on interstate commerce substantial to fall within the reach of congressional authority under the Commerce Clause.[329]

The court concluded that an "economic enterprise that trades in interstate commerce, even one centered on filling cavities," is sufficiently tied to commercial activity.[330] In fact today "[t]here is little doubt that health care providers are subject to the congressional commerce authority and, therefore, the Congress can opt to impose regulatory controls or federal policy conditions on the activities of those providers. . . ."[331]

The Food and Drug Administration (FDA) under the Food, Drug, and Cosmetic Act,[332] which regulates drugs and medical devices, also provides a precedent for considering cloning to involve interstate commerce. The Food, Drug, and Cosmetic Act prohibits:

(a) The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.

(b) The adulteration or misbranding of any food, drug, device, or cosmetic in interstate commerce.

(c) The receipt in interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise.[333]

Although "it is well settled that Congress has the power, under the commerce clause of the Federal Constitution, to condemn the interstate transportation"[334] of drugs and devices that violate the Act, manufacturers continue to challenge this authority,[335] and the power of the FDA is continually upheld. This is because it can generally be shown that some part of the drug or device—an ingredient, a container, or a package—has passed in interstate commerce. Along those lines, *U.S. v. 39 Cases*,[336] held that a drug manufactured in one state for distribution in the same state was subject to the provisions of the Act because component ingredients were shipped in interstate commerce to the manufacturer. The court reasoned that "it would be a strained

interpretation to say that each 'drug' component falls within the jurisdiction of the Act, being shipped in interstate commerce, but, when compounded together to form another 'drug,' the finished product is not being held for sale after shipment in interstate commerce."[337] To so interpret the Act would create a loophole at the expense of public protection.[338]

In 1980, Congress passed a law regulating the interstate sale, barter, or exchange of blood, blood components, or blood derivatives, unless "such . . . blood, blood component or derivative . . . has been propagated or manufactured and prepared at an establishment holding an unsuspended and unrevoked license issued by the Secretary [of Health and Human Services] to propagate or manufacture, and prepare such . . . blood, blood component or derivative. . . ."[339] The regulation of the biological components involved in cloning would be a logical expansion of this power.[340] In fact, if the cloning was done with DNA from blood, it would have to comply with this law.

If an entity that undertook cloning claimed that it operated exclusively intrastate, using supplies, equipment, and personnel from the state, it might claim to be exempt from the reach of federal law. This is similar to the claim of researchers in California working under the California AIDS Vaccine Research and Development Grant Program,[341] which provides funds to the private sector for the development of an AIDS vaccine "until the Federal Food and Drug Administration (FDA) approves the clinical testing of an AIDS vaccine on humans."[342] In establishing this program, the California legislature permitted AIDS vaccines to be tested in the state without being subject to FDA requirements. Under the program, the vaccine is manufactured by a California company for use in California on California residents. Despite this justification, it is not likely that the regulation of an AIDS vaccine and its clinical trial would be viewed by courts as an intrastate activity and therefore beyond Congress' reach. Rather, the federal government has probably not decided to step in and regulate the program under the federal Food and Drug Act because, as one commentator suggests, that opposition to the program would be "akin to political suicide."[343] Given the pervasive and immediate threat AIDS poses to the public health of our nation, no politician would "want to appear to be standing in the way of people receiving experimental treatments, even if unproven and unsafe."[344]

Cloning research and services do not evoke the same policy justifications as does access to an AIDS vaccine. Although cloning research could provide bone marrow, organs, and even children to infertile couples, those concerns are not as pervasive as is the threat of AIDS. Furthermore, there are alternatives to cloning for obtaining organs and for treating infertility.

Post-*Lopez* cases challenging the constitutionality of the Freedom of Access to Clinic Entrances Act (FACE)[345] may provide guidance in determining whether federal regulation of human cloning would survive similar constitutional challenges. FACE prohibits the physical obstruction, injury, or interference "with any person because that person is or has been . . . obtaining or providing reproductive services;"[346] the physical obstruction, injury, or interference "with any person lawfully exercising or seeking to exercise the First Amendment right of religious freedom at a place of worship;"[347] and the intentional destruction of a reproductive health services

facility or a place of worship.[348] Congress derived its authority to enact FACE from its authority to regulate activities that substantially affect interstate commerce.[349] Cases sustaining the constitutionality of the Act under the commerce clause hold that unlike the Gun-Free School Zones Act at issue in *Lopez*, FACE regulates commercial activity—the provision of reproductive health services.[350] Furthermore, such cases hold that the provision of reproductive health services substantially affects interstate commerce based on the following congressional findings: (1) reproductive health facilities acquire equipment, medicine, medical supplies, surgical instruments and other necessary medical products from other states;[351] (2) "individuals travel interstate to obtain and provide reproductive services;"[352] (3) "obstruction of facilities decreases the overall availability of reproductive health services nationwide;"[353] and (4) "obstruction of facilities is a nationwide problem that is beyond the control of individual states."[354] Because FACE regulates a commercial activity that substantially affects interstate commerce, as supported by congressional findings, it is a legitimate exercise of Congress' commerce power.

Congressional findings similarly justify the enactment of the Fertility Clinic Success Rate and Certification Act of 1992,[355] which requires that assisted reproductive technology programs report their pregnancy success rates to the Secretary of Health and Human Services for publication in an annual consumer guide and that the Secretary develop a model program for the certification of embryo laboratories to be implemented by the states. This legislation arose in response to the absence of regulation in "one of the fastest growing areas of health care."[356] The drafters sought to protect "vulnerable" couples from a field "ripe for exploitation."[357] In addition, the legislative history points out that the government had to "step in" because the regulation of clinics could not be left to voluntary guidelines created by professional societies such as the American Society for Reproductive Medicine, since those clinics causing the most problems were unlikely to comply with voluntary programs. The Fertility Clinic Success Rate and Certification Act does not adopt substantive provisions directly regulating clinics, but rather calls for the secretary to develop model guidelines for states to adopt, if they desire.[358] This form of implementation suggests that Congress contemplated commerce clause concerns in the direct regulation of in vitro fertilization (IVF) laboratories.

However, under case law addressing the constitutionality of FACE, it is likely that Congress could directly regulate those facilities that provide cloning as a reproductive service. First, the provision of reproductive health services is a commercial activity.[359] The test that will be used to determine whether Congress has the authority to regulate cloning performed with private funds is "whether a rational basis existed for concluding that [the] regulated activity sufficiently affected interstate commerce."[360] Second, cloning facilities are likely to substantially affect interstate commerce in some of the same ways that the facilities at issue in the FACE cases do. For example, cloning facilities are likely to acquire equipment, medicine, medical supplies, surgical instruments, and other necessary medical products from other states. *U.S. v. Dinwiddie* points out that the commerce clause allows regulation of a health care facility if its patients are "in interstate commerce."[361] It is likely that some of the patients coming to cloning clinics will travel interstate. By one estimate, there are 10 clinics in the United States that may be able to provide

these services,[362] and, consequently, people in other states would have to cross state lines to obtain the services.

Having out-of-state employees and purchasing out-of-state equipment also makes a business subject to the commerce clause.[363] In addition, cloning providers will share information and research findings in a national arena, requiring attendance at national classes and conferences. Under *Abbott*, traveling to and attendance at national conferences may be sufficient to satisfy the "substantially affects" requirement.[364] Furthermore, those human beings who result from cloning will have the right to travel. Finally, cloning is an issue of national concern. Like IVF, cloning is "ripe for exploitation" (often with the same potential consumers—infertile couples). The legal, physical, psychological, and sociological issues implicated by cloning are even less familiar to the public than those raised by IVF.

The activity of cloning is further distinguishable from the activities at issue in *Lopez* because it does not affect an area where there is a history of state regulation and where states have regulated extensively. Unlike lower school education, which is provided at a local level, cloning would generally be provided by a limited number of facilities around the country that draw personnel and patients from a national market. In addition, few states have regulated the conduct of human research.[365] Such research has primarily been funded and regulated at the federal level. In *Lopez*, 40 states had already acted to ban the possession of guns near schoolyards.[366] With respect to cloning, states do not yet have a legal scheme in place to deal with the issue.[367] In fact, state legislatures have introduced bills calling on the federal government to address the issue.[368]

Cloning research which does not create full human beings may not "substantially affect" interstate commerce in the same way as reproductive cloning. However, the research facilities are likely to participate in an interstate market of supplies, scientists, and information, and thus be within the reach of federal law.

If a federal law were adopted, it would be important to provide a sufficient legislative history to indicate how cloning would affect interstate commerce, to establish why cloning is of national importance, and to document state legislative actions specifically asking for the federal government to intervene in this area.

IS THERE A RIGHT OF SCIENTIFIC INQUIRY?

If Congress (or a state) were to adopt a ban on human cloning, questions would arise as to its constitutionality. Specifically, a question would arise regarding whether scientists have a constitutional right of inquiry that could serve as the basis of a constitutional challenge to such a restriction.

There is no doubt that scientific inquiry has been an enduring American value. The framers of the Constitution discussed the sacred nature of scientific inquiry.[369] The Constitution established a system of patents to promote scientific invention.[370] Historically, scientific theories

have been protected because of the great social import the United States places on the "sanctity of knowledge and the value of intellectual freedom."[371]

In fact, Senator Tom Harkin has defended cloning research by explicitly stating that scientists have the right to research and that there are not "any appropriate limits to human knowledge. None, whatsoever. . . . To my friends Senator Bond and President Clinton who are saying 'Stop, we can't play God,' I say 'Fine. Take your ranks alongside Pope Paul V who in 1616 tried to stop Galileo.'"[372] Senator Harkin argues that any government ban or limitation on human cloning research is essentially an "attempt to limit human knowledge [which is] demeaning to human nature."[373] Harkin also stated that human cloning "is right and proper . . . [because] it holds untold benefits for humankind in the future."[374]

Although there is no specifically enumerated right to research in the U.S. Constitution, certain commentators argue that support for such a right could be derived from the Fourteenth Amendment right to personal liberty[375] and the First Amendment right to free speech.[376] This right to research consists of the freedom to pursue knowledge.[377] The strongest claims have been made for a First Amendment right of scientific inquiry. The U.S. Supreme Court in *Branzburg v. Hayes* specifically analogized the information function performed by academic researchers to that performed by the press.[378] If the First Amendment protects a marketplace of ideas, it seems likely that it would protect the generation of information that will be included in the marketplace. The U.S. Supreme Court has protected the precursors to speech in a variety of settings,[379] such as extending First Amendment protection to the financing of speech[380] and the gathering of news[381] as necessary precursors to speech itself.

There is extensive discussion *in dicta* of a right of inquiry. The Supreme Court stated in *Meyer v. Nebraska*[382] that the right to liberty guaranteed by the Fourteenth Amendment encompassed freedom to "acquire useful knowledge . . . and generally to enjoy those privileges long recognized at common law as essential to the orderly pursuit of happiness by free men."[383] A federal district court similarly suggested that scholars have a "right . . . to do research and advance the state of man's knowledge."[384] But what does that "right" consist of? It is clear that the right of scientific inquiry protects access to existing information. For example, that federal court opined *in dicta* that obscenity laws could not be applied to prohibit the Kinsey Institute from studying obscene materials.[385] However, other court cases specifically reject the idea that a fundamental right of scientific inquiry exists.[386] These cases are relevant because they held that there is no fundamental right of medical researchers to conduct medical research on fetuses.

Even if scientific inquiry were found to be protected by the Constitution, certain restrictions would be permissible. Regulation would not be permissible if it were solely undertaken to restrict the generation of new knowledge. However, the government could regulate to protect against compelling harms (such as the psychological, physical, and social risks of cloning of whole individuals), so long as the regulation is no more restrictive on speech than is necessary to further that interest.

The freedom to pursue knowledge is distinguishable from the right to choose the method for achieving that knowledge, since the method itself may permissibly be regulated.[387] Although the government may not prohibit research in an attempt to prevent the development of new knowledge, it may restrict or prohibit the means used by researchers which intrude on interests in which the state has a legitimate concern.[388]

Therefore, both the federal government and the states may regulate the researcher's methods in order to protect the rights of research subjects and community safety.[389] Research may be restricted, for example, to protect the subject's right to autonomy and welfare by requiring informed, free, and competent consent.[390] This is in keeping with other permissible restrictions under the First Amendment. In cases where "speech" and "nonspeech" elements are inextricably bound up in the conduct, "a sufficiently important governmental interest in regulating the nonspeech element can justify incidental limitations on First Amendment freedoms."[391] Thus, where the government can prove that restrictions on cloning and cloning technology are sufficiently important to the general well-being of individuals or society, such restrictions are likely to be upheld as legitimate, constitutional governmental actions, even if scientists were held to have a First Amendment right of scientific inquiry.[392]

THE RIGHT TO MAKE REPRODUCTIVE DECISIONS

The right to make decisions about whether or not to bear children is constitutionally protected under the constitutional right to privacy[393] and the constitutional right to liberty.[394] The U.S. Supreme Court in 1992 reaffirmed the "recognized protection accorded to liberty relating to intimate relationships, the family, and decisions about whether to bear and beget a child."[395]

Early decisions protected married couples' right to privacy to make procreative decisions, but later decisions focused on individuals' rights as well. The U.S. Supreme Court, in *Eisenstadt v. Baird*,[396] stated, "[i]f 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."[397]

A federal district court has indicated that the right to make procreative decisions encompasses the right of an infertile couple to undergo medically-assisted reproduction, including in vitro fertilization and the use of a donated embryo.[398] *Lifchez v. Hartigan*[399] held that a ban on research on conceptuses was unconstitutional because it impermissibly infringed upon a woman's fundamental right to privacy. Although the Illinois statute banning embryo and fetal research at issue in the case permitted in vitro fertilization, it did not allow embryo donation, embryo freezing, or experimental prenatal diagnostic procedures. The court stated:

> It 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. Chorionic villi sampling is similarly protected. The cluster of constitutional choices that includes the right to

> abort a fetus within the first trimester must also include the right to submit to a procedure designed to give information about that fetus which can then lead to a decision to abort.[400]

Some commentators argue that the Constitution similarly protects the right to create a child through cloning. As Pizzulli points out, "[i]n 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."[401]

John Robertson argues that cloning is not qualitatively different from the practice of medically assisted reproduction and genetic selection that is currently occurring.[402] Consequently, he argues that "cloning . . . would appear to fall within the fundamental freedom of married couples, including infertile married couples to have biologically related offspring."[403] Similarly, June Coleman argues that the right to make reproductive decisions includes the right to decide in what manner to reproduce, including reproduction through, or made possible by, embryo cryopreservation and twinning.[404] This argument could also be applied to nuclear transplantation by saying that a ban on cloning as a method of reproduction is tantamount to the state denying one's right to reproductive freedom.

In contrast, George Annas argues that cloning does not fall within the constitutional protection of reproductive decisions. "Cloning is replication, not reproduction, and represents a difference in kind, not in degree in the way humans continue the species."[405] He explains that "[t]his change in kind in the fundamental way in which humans can 'reproduce' represents such a challenge to human dignity and the potential devaluation of human life (even comparing the 'original' to the 'copy' in terms of which is to be more valued) that even the search for an analogy has come up empty handed."[406]

If a constitutional right to clone was recognized, any legislation which would infringe unduly upon this fundamental right would be subject to a "strict standard" of judicial review.[407] Legislation prohibiting the ability to clone or prohibiting research would have to further a compelling interest in the least restrictive manner possible in order to survive this standard of review.[408]

The potential physical and psychological risks of cloning an entire individual[409] are sufficiently compelling to justify banning the procedure. The notion of replicating existing humans seems to fundamentally conflict with our legal system, which emphatically protects individuality and uniqueness.[410] Banning procreation through nuclear transplantation is justifiable in light of the sanctity of the individual and personal privacy notions that are found in different constitutional amendments and protected by the Fourteenth Amendment.[411]

One could argue that a ban on cloning would "preserve the uniqueness of man's personality and thus safeguard the islands of privacy which surround individuality."[412] These privacy rights are implicated through a clone's right to "retain and control the disclosure of

personal information—foreknowledge of the clonant's genetic predispositions."[413] Catherine Valerio Barrad argues that courts should recognize a privacy interest in one's DNA because science is increasingly able to decipher and gather personal information from one's genetic code.[414] The fear that potential employers and health insurers may use private genetic information discriminatorily is not only a breach of privacy of the original DNA possessor, but any clone "made" from that individual.[415] Even in cases where the donor waives his privacy rights and releases genetic information about himself, the privacy rights of the clone are necessarily implicated due to the fact that the clone possesses the exact same genetic code.[416] Thus, the legal system would have to devise strategies to deal with the privacy issues of donors and clones.[417] In particular, laws would need to be created to effectively deal with situations where either the original's or the clone's genetic information is released without the prior consent of the other individual sharing that genetic code. This argument also evokes the Fifth Amendment's protection of a "person's ability to regulate the disclosure of information about himself."[418]

The government could also assert a compelling interest in protecting against social harms. For example, the government could assert an interest in preserving evolution and forbid cloning because it could lessen diversity in society.[419] The government may also assert an interest in diversity as a cultural good independent of its value for evolution.[420]

The use of cloned cells and tissue for research purposes other than the creation of a child would not be protected by the constitutional rights of privacy and liberty that protect reproductive decisions. Consequently, a governmental regulation or ban of such research would not have to have such stringent justification. It would be constitutional so long as it was rationally related to an important governmental purpose.

CONSTITUTIONAL LIMITS TO CLONING

While a First Amendment right of scientific inquiry or a constitutional liberty or privacy argument might be seen as protecting cloning, other constitutional provisions may limit the use of cloning.

A. Thirteenth Amendment Concerns

Cloning a whole individual whose genetic constitution is known in advance may create a form of "genetic bondage"[421] that runs afoul of the U.S. Constitution's Thirteenth Amendment prohibition on slavery.[422] To the extent that a cloned individual would be limited in his or her freedom based on expectations about his or her genetic makeup, being a clone can be seen as creating a badge of slavery. A clone's autonomy might be limited where his or her genetic traits and predispositions are already known.[423] Intentionally producing people whose genetic predispositions are known undermines the theory of free will, and courts have held that infringement on free will and civil liberty may be prohibited by the Thirteenth Amendment.[424] Bans or restrictions on cloning would be justifiable where the government could prove that cloning is inconsistent with the notion of free will, and that such an erosion of the free will would result in grave societal harms.[425]

Laurence Tribe has noted that cloning "will profoundly affect what it means to be a human being and will do so in ways that matter whether or not particular 'abuses' ever take place."[426] Francis Pizzulli points out that a ban on cloning individuals would likely be constitutional since it is not based on a religious rationale but on "the valid secular purpose of safeguarding a normative view of human identity," resting upon the personal privacy and individual autonomy values of the Thirteenth and Fourteenth Amendments.[427] "Implicit in the prohibition of clonal humans is the rationale that certain types of humans ought not to exist, either because they have inalienable rights to nonexistence or because their presence would erode important social values."[428]

Additionally, the creation of persons to be used as "spare" parts for transplantation would not only be socially repugnant,[429] but be violative of the clone's Thirteenth Amendment rights against involuntary servitude.[430] The clone's right to bodily integrity and personal property rights are also violated by the notion of spare organ-part banking.[431]

B. Nobility Clause

The United States was formed with a rejection of British values that certain special privileges should attach based on one's blood lines. To that end, the U.S. Constitution, art. I, § 9, cl. 8 states, "No title of nobility shall be granted by the United States." State constitutions, too, have such provisions. The Alabama constitution provides, "No title of nobility, or hereditary distinction, privilege, honor, or emolument, shall ever be granted or conferred in this State." An 1872 Alabama case interpreted this provision in the following way:

> To confer a title of nobility, is to nominate to an order of persons to whom privileges are granted at the expense of the rest of the people. It is not necessarily hereditary, and the objection to it arises more from the privileges supposed to be attached, than to the otherwise empty title or order. These components are forbidden separately in the terms "privilege," "honor," and "emolument," as they are collectively in the term "title of nobility." The prohibition is not affected by any consideration paid or rendered for the grant. Its purpose is to preserve the equality of the citizens in respect to their public and private rights.[432]

In an innovative legal analysis, Francis Pizzulli suggests that the values underlying the nobility clause could render unconstitutional a positive eugenics program.[433] If certain individuals are given the right by the government to clone based on their genetic makeup (such as top scientists, political leaders, musicians, or athletes), it might be viewed as creating a class of nobility.[434] At the very least, letting only certain individuals have access to cloning due to their purported genetic distinction would violate the idea of "equality of citizens in respect to their . . . private rights."[435]

Even if the nobility provisions of the federal and state constitutions do not directly apply,[436] they signal an important set of values against creating a supposed hereditary elite which can be used as a public policy argument against cloning whole individuals. However, the nobility

provisions would not serve as a bar to cloning cells, tissue or organs in vitro unless, of course, only individuals of a particular genetic background were allowed to clone a spare organ for themselves.

WHO IS THE PARENT IN CLONING?*

Traditionally, "family" referred to the nuclear family—a household consisting of a husband, a wife, and their children. That traditional view of family, though, is continually being challenged. Divorce, homosexuality, and single parenthood create family structures far different from the traditional concept of family. Additionally, the use of assisted reproductive technologies, including the use of gamete or embryo donors as well as surrogates has lead to familial configurations not contemplated just a few decades ago.

Are these recent family structures and methods of family building any less valuable than the traditional nuclear family created through coital reproduction? The question has not been fully answered—in part, because the answer requires society to consider what values "family" represents and what it means to be a parent. Using the nuclear family as a model, the law has very clearly defined rights and obligations based on one's status as a parent.

> Parents have the right to custody of their child, to discipline the child, and to make decisions about education, medical treatment, and religious upbringing. Parents assign a child a name. They have a right to the child's earnings and services. They decide where the child will live. Parents have a right to information gathered by others about the child and may exclude others from that information. They may speak for the child and may assert or waive the child's rights. Parents have the right to determine who may visit the child and to place the child in another's care.
>
> . . . Parents must care for their child, support him financially, see to his education, and provide him proper medical care.[437]

These rights and obligations, though, become less clear when the roles of mother and father are not as obvious as when a couple produces a child through coital reproduction. Methods of collaborative reproduction necessitate reconsidering what it means to be a parent. Is parenthood defined by biology, genetics, intention, or rearing? These types of questions will need to be answered when sorting out the rights and responsibilities of the potential parents if an individual is cloned.

Current state laws addressing parentage, including paternity acts, surrogacy statutes, and egg donation statutes, are not broad enough to address the multitude of parentage issues raised by the process of cloning through nuclear transfer. The process of cloning will result in a child's having genetic material from as many as four individuals: the person from whom the cell nucleus

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*This section was prepared by Nanette R. Elster, J.D., M.P.H.

was derived, that individual's biological parents, and the woman contributing the enucleated egg cell which contains a small fraction of DNA in the mitochondria. In addition, if the egg with the transferred nucleic material is implanted in a surrogate gestational mother, the child will have two other potential parents—the gestator and, if she is married, her husband. The latter will have rights—even though he has no biological connection to the child—based on the common law presumption that if a woman gives birth within marriage, her husband is the child's legal father, or in some states, specific statutes that provide the surrogate and her husband are the legal parents of a child she has gestated regardless of their genetic contribution.[438] There may also be intended rearing parents unrelated to the individual who is cloned, such as when the cloned individual is deceased, a celebrity, or a favorite relative.

With so many contributors—biologic, genetic, and social—determining who shall assume the parental rights and obligations of the resulting child is very difficult not only from a legal standpoint but also from scientific, psychological, and sociological perspectives. In the cloning scenario, it is unclear which of the contributors is responsible for raising and supporting the resulting child. If parenthood is not clarified, there may be situations in which either the state will bear the responsibility or the child will be caught in a legally complicated, protracted custody battle.[439]

In attempting to determine the parentage of a clone it is going to be necessary to not only consider states' paternity laws, but also any state laws that address parentage in the context of egg donation and surrogacy. There are two types of surrogacy—traditional and gestational. Traditional surrogacy involves a woman agreeing to be inseminated with sperm from the intended father (or a donor), carrying the resulting child to term, and relinquishing all parental rights to the child to the intended father and his wife if he is married. In that situation, the surrogate is providing the egg (which includes mitochondrial DNA and nucleic DNA) and is gestating the fetus. Gestational surrogacy typically involves a woman agreeing to carry an embryo created through in vitro fertilization of the egg and sperm of the intended parents or a donated egg and/or sperm and relinquishing the child to the intended parents. The distinction between the two forms of surrogacy is that with gestational surrogacy, the woman who carries the child to term contributes no genetic material. Currently, at least 34 states have laws addressing artificial insemination by donor,[440] but only 5 states have laws dealing specifically with parentage in egg donation.[441] While 22 states have laws addressing surrogacy,[442] only 8 of those address parentage.[443]

Whether and how these laws might apply to cloning is a complex matter. Under the artificial insemination laws, if a man provides sperm for artificial insemination of a consenting woman and her consenting husband, that couple and not the sperm donor are the legal parents.[444] Because statutes specifically use the term "sperm" or "semen," they arguably do not influence the situation in which a man provides DNA rather than sperm.

The egg donation laws are more likely to be applicable, even though the egg being used in cloning has only mitochondrial DNA, not nucleic DNA. In the five states having egg donation

legislation, the donor is *not* considered to be the mother of the resulting child. Four of the states' statutes specifically assert that the donor has no parental rights or obligations with respect to the resulting child.[445] The Texas statute likely results in the same outcome, but it addresses the issue of legal parentage only from the perspective of the intended parents. It reads, in part:

> If a husband consents to provide sperm to fertilize a donor oocyte by in vitro fertilization or other assisted reproductive techniques and the wife consents to have a donor oocyte that has been fertilized with her husband's sperm, pursuant to his consent, placed in her uterus, a resulting child is the child of both of them.[446]

The language of this statute is significant in the cloning context, because unlike the other four states' laws on egg donation, the Texas statute does not state that the donor relinquishes all parental rights. This law stresses that the intended parents would only be the legal parents if the donated egg is fertilized with the husband's sperm. So, this would not be broad enough to rule out the donor of the enucleated egg as a potential parent in the cloning scenario. The law leaves unanswered the question of the donor's rights and obligations if the egg is not fertilized with the recipient's husband's sperm as would be the case with cloning. One might argue that if a donated egg is enucleated and a nucleus transferred to it, the egg donor may have not only parental rights to a resulting child but also parental obligations such as support.

The surrogate mother laws also figure into the analysis. Although eight states do have statutory presumptions regarding parentage determinations in surrogacy, the states differ over whether the surrogate and her husband are presumed to be the parents or whether the biological father and his wife are presumed to be the parents. Laws in Arizona, North Dakota, and Utah presume that the surrogate and her husband are the legal parents of the child, whereas laws in Arkansas, Florida, Nevada, New Hampshire, and Virginia presume that the genetic father and his wife are the legal parents of the child. Of the eight states, only Arkansas' and Nevada's statutes do not apply to both traditional and gestational surrogacy. The Arkansas statute only covers traditional surrogacy. Because the presumption under the Arkansas statute is that the intended father and his wife are the child's parents, it is likely that the same presumption would apply to gestational surrogacy where both of the intended parents would have a genetic link to the child, but the issue of parentage when donor gametes are used is not certain. The Nevada statute, though, only applies to gestational surrogacy, leaving the determination of parentage in a contested, traditional surrogacy arrangement unresolved.

Florida and New Hampshire impose specific age requirements concerning who can participate in surrogacy arrangements. In Florida, all participants must be 18 or older,[447] and in New Hampshire, all participants must be 21 or older.[448] North Dakota defines both a gestational carrier and a surrogate as "adult woman,"[449] which presumably imposes an age requirement at least for the surrogate.

Another restriction found in the surrogacy statutes which may be even more limiting to cloning than an age requirement is a requirement that the intended parents be married. If marriage

is a requirement and the statute does apply to cloning situations, single individuals interested in cloning themselves would not be able to use the mechanisms of the statute to assert parental rights as an intended parent. Florida, Nevada, New Hampshire, and Virginia specifically define intended parents as being married. In addition, North Dakota[450] uses the terms *husband* and *wife* rather than *intended mother* and *intended father*, which implies that participants need to be married in order for the statute to apply. Other requirements which may limit applicability to cloning include the requirements of the Virginia statute that all participants must undergo a home study and must all meet applicable standards of fitness for adoptive parents.[451]

Three states have additional restrictions regarding recognition and approval of surrogacy contracts which may further limit their applicability to instances of cloning especially by a single male. In Florida, it must be determined by a licensed physician that "[t]he commissioning mother cannot physically gestate a pregnancy to term; . . . gestation will cause a risk of harm to the physical health of the commissioning mother; or . . . will cause a risk of harm to the health to the fetus."[452] Both New Hampshire's and Virginia's statutes have similar requirements that the intended mother be unable to carry the child without risk to herself or the fetus.[453] Virginia's statute differs slightly from New Hampshire's and Florida's in that it also takes into account risks to the psychological health of the mother or fetus. For a surrogacy contract to be approved in Virginia, the intended mother must be "infertile . . . unable to bear a child or . . . unable to do so without unreasonable risk to the unborn child or to the physical *or mental health* of the intended mother or child."[454]

In states that do not have laws addressing a specific reproductive technology, it is necessary to turn to a state's parentage act which may not clearly resolve the question of who is the child's legal mother. In California, for example, the parentage act would find that both the woman who gestates a child and the woman who contributes her genetic material are the child's legal mothers. One section of the act provides that "(a) Between a child and the natural mother, [the parent and child relationship] may be established by proof of her having given birth to the child, . . ."[455] suggesting that the gestator is the mother. Another section, though, allows for the use of a blood test to establish maternity,[456] based on a genetic relationship suggesting that the woman who provided her genetic material is the mother.

The California Supreme Court was confronted with resolving this conundrum in *Johnson v. Calvert*,[457] a gestational surrogacy case in which the surrogate asserted her parental rights to the child. The court resolved the case by looking to the parties' intent, which had been memorialized in a contract. The agreement clearly indicated that the intent of all the parties was for the man and woman whose sperm and egg formed the embryo to be the legal parents of the child. Based on this clearly expressed intent, the court found that the mother of the child was the woman who had contributed her genetic material. If a written contract had not expressed the parties' intent, the outcome of this case may have been different, as California does not have a statutory presumption of parentage in the context of surrogacy. The result may also have differed if donor eggs had been used rather than the eggs of the intended mother. The court would have

had to decide whether gestation, genetic contribution, or intent is determinative of the legal status of motherhood. This is precisely the type of decision that may be necessary if cloning does occur.

The court in *Johnson* gave significant weight to intent, which may indicate a willingness to consider preconception intent in other settings. One legal scholar, Marjorie Schultz, argues that "because parenting involves long-term and multi-faceted commitment, personal intention seems a desirable basis for selecting between two biological claimants who are arguably equally situated."[458] Shultz points out, "[a]s in other arenas of policy, private ordering need not be absolute; particular regulatory constraints on private ordering might be adopted."[459]

Some states have essentially codified the recognition of intent in collaborative reproduction. The surrogacy law in Virginia, for example, provides an elaborate scheme for ultimately recognizing parental intent. The law provides for judicial approval of surrogacy contracts. The law specifies that in order to be judicially approved, specific issues must be addressed in the contracts. Additional requirements for approval include that all parties must have counseling, the surrogate must be married and have had at least one pregnancy and live birth, and at least one of the intended parents is expected to be the child's genetic parent.[460] The statute clearly lays out what is necessary for a court to approve a surrogacy arrangement and legally recognize the intent of the parties.

The state parentage acts, which were cited in *Johnson v. Calvert*, create additional issues with respect to cloning. Every state has a specific statute setting forth presumptions about paternity. Under these legitimacy statutes, a husband of a woman who bears a child during marriage or within a certain number of days after termination, separation, or dissolution of the marriage is presumed to be the father and has legal responsibilities for the child.

The statutes, however, present problems with respect to cloning. First, some states allow exceptions to the presumption of paternity if the husband is sterile. In those states, an infertile husband who wants to be considered the legal father of a clone born to his wife (either using his or her DNA) may not be able to assert paternity under the statute.

Moreover, the statutes create a problem for people wanting to establish parenthood to a clone gestated by a surrogate. Even when the statutory presumption of the surrogate's husband's paternity is rebuttable, the statutes governing paternity do not always provide a mechanism for the biological father to assert his paternity. The genesis of the paternity statutes was to allow a woman to assert that a particular man was the father of her child and to allow her to bring a legal proceeding to compel that man provide child support. To that end, all the statutes allow a mother, expectant mother, or representative of the mother to initiate a paternity action. Some additionally allow the child or a guardian, conservator, or child's best friend or representative to initiate such an action.[461] Some statutes also allow certain public officials, such as state public welfare officials or housing officials, to bring a paternity action (for example, in cases where the state will have to make welfare payments on the child's behalf if a father is not identified to support the child).

Far fewer states have a specific provision for a man wanting to be recognized as the legal father to establish his paternity. While over 19 states specifically provide such a mechanism, in some states a man asserting fatherhood can do so only if there is no presumed father. In those states, the man providing the DNA for the clone may be able to bring a paternity action when an unmarried surrogate bears his child, but not when a married surrogate does so. However, the man providing the sperm may also be able to initiate a paternity action under a provision providing simply for actions by the "father," which is common in at least nine states.[462]

In at least 13 states, there is also a provision for "interested parties" to bring a paternity action, and three states have a provision to allow a relative to bring a paternity action.[463] Arguably, the father could bring a paternity action as an interested party or relative.

However, if there is a provision allowing the "presumed" or "alleged" father to bring a paternity action, the man providing the DNA probably will not be able to use that provision to bring a paternity action if the surrogate changes her mind. He is not the presumed father (if the statute provides that a woman's husband is the presumed father). He is not the "alleged" father either (since the surrogate is not alleging he is the father).

In establishing paternity, states differ in the type of proof they statutorily specify as admissible. In at least 45 states, blood tests can be used.[464] In the District of Columbia, for example, "[a] conclusive presumption of paternity shall be created upon a genetic test result and an affidavit from a laboratory . . . that indicates a 99% probability that the putative father is the father of the child and the Division shall enter a judgment finding the parentage of the child."[465] Similarly, a Tennessee statute provides that "[a]n individual is conclusively presumed to be the father of a child if blood, genetic, or DNA tests show that the statistical probability of paternity is 99% or greater."[466] In contrast, some states find there is a *rebuttable* presumption of paternity even if a 99% probability has been shown under certain circumstances. In Michigan, for example, "[i]f 2 or more persons are determined to have a probability of paternity of 99% or higher, paternity shall be presumed for the person with the higher probability."[467] In Mississippi, there is a rebuttable presumption "affecting the burden of proof, of paternity, if the court finds that a probability of paternity, as calculated by the experts qualified as examiners of genetic tests, is ninety-eight percent (98%) or greater. This presumption may only be rebutted by a preponderance of the evidence."[468]

Some tests used to establish paternity are so general (for example, those tests based on blood type), that a man contributing his nucleic material to create a clone may be found to have a 98 or 99% probability of being the child's father. Other types of tests are so specific, however, that they would identify a nucleic donor as a twin rather than as a father of the child. Thus, it is unclear whether an individual seeking to be considered the parent of a child created with his DNA would be able to use current legal mechanisms to do so.

There is no uniformity among the states concerning the laws governing sperm donation, egg donation, or surrogacy; and there continues to be some uncertainty in assigning parentage in

disputed arrangements. The applicability of these laws to cloning will present even more confusion. Cloning through nuclear transfer presents at least 13 possible parental configurations ranging from as few as 3 possible legal parents to as many as 10.

Surrogacy, egg donation, and sperm donation statutes attempt to address the question of parentage when reproduction occurs with the assistance of individuals other than or in addition to the man and woman seeking to have a child. Cloning, though, unlike collaborative, non-coital reproduction, or even traditional sexual reproduction, may be accomplished with as few as one participant. One woman could transfer nucleic material from one of her cells to her own enucleated egg cell and have the resulting "embryo" transferred to her uterus for gestation. Yet, even in this scenario, parentage issues are raised with which existing laws are ill equipped to deal. For example, if this woman sought child support, her own father and mother may have a legal obligation to support the child because existing paternity testing would find them to be the child's genetic parents. Yet, the woman, too, would be presumed to be the child's mother based on the common law presumption that the woman who gives birth is the legal mother.[469] It is unlikely that in this scenario her maternity would be challenged; however, if it were, the parentage determination would be complicated. In addition to the legal confusion raised by even this most simplistic cloning scenario raises, there are equally baffling psychological and sociological issues raised by the issue of a woman giving birth to her identical twin.[470]

In another possible cloning scenario, cloning may more closely approximate family building in the traditional sense, where a man and woman contribute genetic material to form an embryo which the woman carries to term, than currently accepted and practiced forms of collaborative reproduction. For example, consider a husband and a wife who have chosen to have a child, but the wife has a genetic disease she does not want to pass on to her offspring. To avoid the possibility of passing on this disease, the couple decides to transfer nucleic material from one of the husband's cells to the wife's enucleated egg cell and then transfer the resulting embryo to the wife's uterus. Unlike egg donation or traditional surrogacy, which would accomplish the couple's goal of not passing on the wife's genetic disease to their offspring, cloning allows the couple to reproduce using its own genetic material without the contribution of a third party. In terms of genetics, the husband's parents will also be the resulting child's parents and, in fact, the husband will be the child's twin. If a highly specific paternity test were to be performed, the husband could have a nearly 100% genetic match with the child. This may be indicative that he is not the child's father, "since no two people, aside from identical twins, have the same genetic composition."[471] He may have the intent to be the child's father, and if the child is born during the marriage, he will be presumed to be the child's legal father; but if his status is challenged, a paternity test could reveal that he is the child's identical twin and this may rebut the presumption.

In some states, "[e]ven if the presumption of paternity has been successfully overcome, a party may be stopped from questioning paternity under certain circumstances . . . includ[ing] situations where the parties involved have, by their conduct, accepted the man as the father of the child in question."[472] This is yet another way in which the law currently recognizes intent in the parenting context. This illustrates that in this cloning situation closely akin to traditional family

building, it is possible that the husband and wife choosing to create a child through cloning will be recognized as the child's legal parents, so long as neither of them challenges the other's status.

If a couple creates a child who is the clone of a loved one or an unrelated individual chosen for his or her valued traits, parenting rights would also be dispersed across individuals. If the wife carried the clone to term, the couple would be protected by legal presumptions assigning parenthood to the birth mother and her husband.[473] If paternity testing were done, however, the parents of the cloned individual (and maybe the cloned individual himself or herself) would be able to assert rights to the child.

Even a cloning arrangement which closely resembles traditional reproduction, as between a husband and wife, presents confounding questions not resolvable under existing law. The examples discussed are the simplest potential parental configurations possible in human cloning, yet they raise very profound issues. Existing laws may not effectuate the desired outcome of cloning arrangements and could leave unanswered many questions, including who can make childrearing decisions, who must support the child, who has a right to the child's earnings, and from whom can the child inherit. This confusion about family roles and relationships and the uncertainty of current law to address these issues may present serious psychological, sociological and legal risks for all parties involved in a cloning arrangement.

The matters become even more complicated when a man decides to clone himself by having his DNA fused with a donor egg and gestated by a surrogate. His parents might be viewed as the legal parents of the resulting child. In most states, the egg donor could assert a parental right. In addition, the surrogate generally would have a claim to the child. This would occur either under existing paternity statutes that indicate that the woman who gives birth to the child is the legal mother or, as in Arizona and Utah, where a gestational surrogate and her husband are considered to be the legal parents. Only in Florida, New Hampshire, North Dakota, and Virginia would an "intended" parent (in this case the man cloning himself) possibly have a superior claim to that of the surrogate. But these statutes would not help the man if he were not married.

There are two other likely scenarios in which a surrogate would participate in the cloning situation.[474] One scenario would involve an infertile couple who wants to have a genetically related child. The wife, having had a hysterectomy, cannot carry a child but can still produce eggs. Her husband is sterile, so they decide to fuse her egg cells with his nucleic material and have the resulting embryo gestated by a surrogate. In the second scenario, the wife has had a hysterectomy and oophorectomy, and so the gestator also contributes the egg cell, which is fused with the husband's nucleus.

The first situation resembles gestational surrogacy since the surrogate is contributing no genetic material. As such, the laws in Florida, New Hampshire, North Dakota, and Virginia would likely recognize the intended parents as the child's legal parents.[475] However, the law of North Dakota relies on the parentage act to determine paternity and maternity in gestational surrogacy, and under such analysis the probability of parentage must be 95% or higher.[476] Although, using a

DNA test, there would be greater than a 95% "match" with the intended father, courts might view the test results as indicating twinning, not parenthood. And because the intended mother is only contributing mitochondrial DNA, she would not be a greater than 95% match. The statutes in Arizona and Utah would provide that the surrogate and her husband are the child's legal parents.

Based on a 1994 Arizona Court of Appeals decision, though, this presumption of maternity under the Arizona law is rebuttable. In *Soos v. Superior Court of the State of Arizona*,[477] a married couple entered into a gestational surrogacy contract. During the pregnancy the wife filed for dissolution of the marriage and requested shared custody of the unborn children. The husband asserted that he was the biological father under the existing statute and the surrogate was the legal mother; as such, he asserted that the wife had no standing to request custody. When the triplets were born, the husband was named as the father and took custody. The wife subsequently challenged the constitutionality of the applicable statute. The court found the statute unconstitutional and held that "[b]y affording the Father a procedure for proving paternity, but not affording the Mother any means by which to prove maternity, the State has denied her equal protection of the laws."[478] Therefore, in Arizona, although there is a presumption of maternity in favor of the surrogate, this presumption is rebuttable.

In the second scenario, which resembles traditional surrogacy because the egg of the gestator is utilized, Arizona, North Dakota, and Utah have statutes that would recognize the surrogate and her husband, if she is married, as the child's legal parents. Arkansas statute would be inapplicable because it specifically refers to the surrogate as having been artificially inseminated. It would seem unlikely that the term "inseminated" would include the process of nuclear transfer. Similarly, the law of New Hampshire, which requires one of the intended parents to be a gamete provider, gamete being defined as ovum or spermatozoa,[479] would also be inapplicable. The laws of Florida and Virginia would both find that the intended parents are the child's legal parents.

The examples discussed reflect the difficulty of applying existing law to this new and unprecedented technology. Other assisted reproductive technologies were also not amenable to existing law; therefore, over time, statutes addressing the unique issues raised by such practices have been and continue to be enacted. However, as is seen by the dearth of surrogacy and egg donation statutes, the law does not keep pace with the technological developments. And given the widespread opposition to cloning complete individuals, it will be unlikely that legislators will rush to develop paternity, maternity, or "clonerity" statutes for this new realm which may be considered to be a tacit acceptance of the procedure.

HUMAN RESEARCH IMPLICATIONS

If cloning of an entire individual does occur, there will be extensive scientific and public curiosity about the resulting individual. Consequently, the procedure may be performed as part of a research protocol that would involve observational, psychological, and medical testing on the resulting individual to assess whether physical and psychological development are affected by the

process of cloning. If the resulting individual is a competent adult, he or she would have a clear right to refuse to participate in any follow-up research and would be protected by the federal regulations governing human research, if the research is federally funded, as well as various state laws governing human research, no matter what the source of funding.[480] When the resulting individual is a minor child, however, questions arise regarding what types of research are permissible and who may consent to the child's participation in research.[481]

The previous section discussed the necessity of determining legal parentage of a child born through cloning in order to assess the rights and obligations of all contributors with respect to the child. One reason that parentage must be determined at the outset of a cloning arrangement is to determine who has the responsibility for consenting to medical treatment for the embryo, fetus, and child. Included within that responsibility is the right to consent to medical research involving the child.

The medical and psychological effects of cloning on embryos, fetuses, and resulting children are unknown; therefore, observation and medical testing on the embryo, fetus, and child would likely be necessary to make an assessment of these effects. There will likewise be interest in the psychological implications of taking nucleic material from one child in order to create another child or children. This situation may be similar to the situation in which parents consent to transplantation of an organ from one child to the child's sick sibling, which has been found to be legally permissible.[482]

In general, "competent individuals should not be used in research without their informed and voluntary consent."[483] In fact, the first principle of the Nuremberg Code states that "The voluntary consent of the human subject is absolutely necessary." Similarly, the Federal Regulations provide that "[n]o investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or *the subject's legally authorized representative*."[484] In addition, the section which pertains specifically to research on children requires that the parents or guardians and the child "assent."[485]

The requirement of parental consent will be difficult to satisfy if the child is a clone. Who is responsible and authorized to consent for the child? Which contributor(s) has the child's best interests in mind? Are there ever situations in which research on children should not be done despite parents' authorization? "As a general rule parents, as the natural guardians of their children, have the authority, and even the duty, to consent to medical care on behalf of their children," according to Leonard Glantz.[486] One reason that parents have this authority is that "parents are best able to determine what is in their child's best interest. . . ."[487]

In addition, parents are liable for the support of their children, and this could increase greatly in the event of a physician's error.[488] However, this may not always be appropriate.[489] The parents themselves may not comprehend the purpose or nature of an experiment. Or they may be unduly coerced to participate in research by the researchers and clinicians who helped create the

child, especially in the context of cloning, where this is the only way for the couple to have a genetically related child. Parents' feelings of responsibility to a first child may influence their decision to allow experimentation on a clone, particularly in order to have a "reserve" of organs or bone marrow available if the child should become ill.[490] In some cases, parents may be induced to consent to their children's participation by undue incentives.[491] In a California case,[492] a member of a university Institutional Review Board (IRB) disapproved of a research protocol which permitted parents to consent to their children's participation in nontherapeutic research. He resigned from the IRB and brought a legal action to bar the use of normal, healthy infants as controls in an asthma research project. Apparently, the children were to be injected with drugs and the parents were to receive $300 per year for their children's participation. The case alleged that it would be child abuse for parents to consent to nontherapeutic research on their infants. A trial judge denied the motion for a preliminary injunction, and the case was not pursued any further.[493] It is not inconceivable that incentives such as this may be used to convince parents to consent to their children born through cloning to be the subjects of research. Additionally, parents may be provided with various incentives to consent to cloning of an existing child.

There are limits to what parents can volunteer their children for. The Supreme Court stated in *Prince v. Massachusetts*,[494] that "[p]arents may be free to become martyrs themselves, but it does not follow that they are free in identical circumstances to make martyrs of their children before they reach the age of full and legal discretion when they can make that choice for themselves."[495]

Past a certain age, a mature child should be allowed to decide whether or not he or she wants to assume the risks of an unknown therapy.[496] For example, a child of 12 with a potentially terminal illness such as leukemia may be more capable than the parents of deciding whether or not to participate in an experimental research program.[497] Additionally, a child of 12 may be able to decide whether or not he or she wishes to be cloned in order to have an available bone marrow donor. It is the child's identity which could be compromised. Moreover, there is a question of whether the child whose DNA is used would have parental obligations toward the clone at some time in the future.

Some commentators suggest that where children are capable of assessing information and comprehending the nature and consequences of acting as a research subject, they should be allowed to consent or withhold consent independent of their parents.[498] However, the states which provide statutorily for the participation of minors in research require the co-consent or sole consent of the parent or guardian.[499] Additionally, the federal regulations also outline requirements for permission by parents and assent by the child, where appropriate.[500]

Some commentators argue that children should never be used as research subjects in nontherapeutic experiments[501] because of the problems involved in obtaining informed consent and the possibility that the child's parents or the researcher could be subject to criminal liability for child abuse.[502] Others argue that experiments with children are absolutely essential as results cannot be obtained by other methods or means of study.[503] They would permit such research

where there is an institutional review board review and approval, parental authorization, and the informed consent of the minor when he or she is capable.[504]

The research that may be performed on children born through cloning may be considered to be nontherapeutic research as there is no direct benefit to the child who is the clone. The child would be a research subject in order to observe how the cloning process may affect physical, mental, and psychological development. Some of these analyses could be done without any physically invasive procedures, while others would require intervention.

Under the federal research regulations, research on children involving only minimal risk is allowed so long as the IRB finds that adequate provisions are in place for soliciting the child's assent and permission of the child's parents or guardian.[505] Assent is defined as the child's affirmative agreement to participate and does not include failure to object.[506] Both the child's assent and the parent's or guardian's permission are required under all circumstances. If the research involves greater than minimal risk, but may potentially benefit the child, the IRB must additionally determine that the risk is justified by the anticipated benefit to the child and that the anticipated benefit is at least as favorable to the child as available alternatives.[507] Research that involves greater than minimal risk, and no direct benefit, but is likely to provide knowledge about the subject's disorder is permitted if the IRB determines that the risk is only slightly more than minimal and the procedure is reasonably similar to the established treatment.[508] Where the research is directed toward the alleviation or prevention of a serious children's illness, but is not otherwise approvable, it nevertheless may be conducted if the Secretary of Health and Human Services (after consultation with a panel of experts[509] and the opportunity for public review and comment) determines that the research will be conducted in accordance with sound ethical principles.[510]

The statutes of at least two states contain provisions regarding the use of children as experimental subjects.[511] Virginia requires the informed consent of the child's guardian in addition to the child's consent where the child is capable of giving such consent.[512] New York requires consent of the child's parents or guardians with the approval of an IRB.[513]

Cloning research presents a unique type of research on children because presumably healthy children will be observed and experimented upon to determine how the cloning procedure affected them. It is likely that the testing of such children will be extensive. Even those aspects of the research that do not require physical interventions (such as observation and questionnaires) might be harmful to the child by emphasizing his or her dissimilarity to other children. Forcing a clone child to become a research subject, even with his or her parents' consent, might be stigmatizing and emotionally disturbing to the child.

POTENTIAL TORT CLAIMS BASED ON CLONING

If an entire individual is created by cloning, that individual might be able to bring wrongful life actions against the individual who caused him or her to be brought into being or the scientists

and/or physicians who served as facilitators. Wrongful life cases have succeeded in a few jurisdictions.[514] The claim in such cases is that a child would rather not have been born than have been born with a particular disability. Cases to date have found breaches of duties to the child's parents. For example, in *Curlender v. Bio-Sciences,* the parents were erroneously told by a genetic testing laboratory that the father did not carry the gene for Tay-Sachs when he did, leading to the creation of a child with Tay-Sachs, who successfully sued the laboratory for wrongful life.[515] The court in that case said *in dicta* that the child would also have had a cause of action against her parents for not aborting her. Under that logic, parents are seen as having a duty to future offspring not to give birth to a child with serious disabilities. Some commentators argue similarly that choosing to give birth to a child with a serious disability should be analogized to the parent maiming a child through child abuse.[516]

Some commentators argue that clones would have actions in tort against their creators for "wrongful life" because of their lack of "uniqueness" and invasion of their privacy.[517] Recently, John Robertson argued that because nuclear transplantation cloning denies clones their right to personal privacy and alleged constitutional right to unique genes, it is likely that many would be so psychologically harmed that they would prefer to not have been born at all.[518] Another commentator responded to this concern by arguing that if the legal system allowed clones to bring wrongful life suits, these suits would further undermine notions of human autonomy by reinforcing the idea that humans are machines which are controlled merely by their genes.[519] Replicants whose claimed harm is that their autonomy has been limited—by having a predetermined genotype, by having the value of their talents devalued, by the overcreation of clones of their genotype—would be unlikely to show that they have been so seriously limited so as to be considered to be a wrongful life.

The analysis is more complex when a sterile individual clones himself or herself to have a genetically related child. The child created with the limitation of sterility might be able to claim that that disability is significant enough to be considered to be a wrongful life. Similarly, it might be argued that replicants have been wronged by being denied their uniqueness and by having their future options limited by genetic predetermination. However, it is unlikely that such a claim would give rise to an action for wrongful life, since courts that do recognize such claims limit them to situations in which the child is seriously disabled. A boy who was born "illegitimate" was not allowed to sue his father for wrongful life.[520] And a court speculated that, with respect to deafness, "it seems quite unlikely that a jury would ever conclude that life with such a condition is worse than not being born at all."[521]

The replicant of a cloned individual might also have a cause of action based on tort or property grounds for the creation of too many genetically identical versions which diminish his or her right to distinctiveness. Pizzulli explains the issue in the following way:

> While a given genotype may have been proved to be eminently successful, his duplicate may be relatively unfit *because he is a duplicate*. That is, there is little place for a duplicate genotype in a society which places a premium on uniqueness

and individuality. A duplicate genotype is therefore relatively lacking in fitness, with respect to the posited social/moral environment and is therefore relatively lacking in social worth.[522]

POLICY OPTIONS

This paper was prepared to aid the National Bioethics Advisory Commission in assessing the range of legal options that are possible in the regulation of human cloning. An analysis of existing laws found that there are few statutes that would apply to human cloning. A few states' restrictions on embryo research may apply to cloning,[523] and a federal law would require that clinics offering human cloning as a form of assisted reproductive technology would have to identify themselves and report success rates to the Secretary of Health and Human Services.[524] There is clearly a need for policies addressing human cloning.

In May 1971, Dr. James Watson, the Nobel Prize winner for co-discovering the structure of DNA, authored a seminal article for *Atlantic Monthly* called "Moving Toward the Clonal Man." He explained how cloning could be done and he tried to alert ethicists and scientists that the realization of human cloning was "a matter far too important to be left solely in the hands of the scientific and medical communities.[525] President Clinton has assigned the task of making recommendations about cloning to the National Bioethics Advisory Commission, with the admonition that "any discovery that touches upon human creation is not simply a matter of scientific inquiry, it is a matter of morality and spirituality as well."[526]

This paper has addressed the potential barriers that may have blocked federal attempts to regulate human cloning, such as constitutional challenges based on the commerce clause, scientists' First Amendment right of inquiry, or individuals' or couples' privacy or liberty rights to make reproductive decisions. In each case, it has been shown that human cloning could permissibly be restricted.

Thus, the National Bioethics Advisory Commission does not face undue restrictions in the range of recommendations it could consider. It would be constitutionally permissible to enact a federal ban on creating individuals through human cloning. There is widespread public support for such a ban. Already such prohibitions have been proposed in Congress and 11 states. No legislator has proposed a bill to permit the process.

It would also be permissible to enact restrictions on scientific research on cloned tissue, cells, or organs. Such research is not constitutionally protected as part of reproductive decision making, so governmental regulation or ban of such research would not have to have stringent justifications. Regulation of human cloning research would be constitutional so long as it was rationally related to an important governmental purpose. Under such an analysis, a court could uphold restrictions that require that sufficient animal research is done in advance. Moreover, it would be permissible to require the scientists proposing the research to have "the burden of

proving that the research is vital, cannot be conducted any other way, and is unlikely to produce harm to society."[527]

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APPENDIX A: POTENTIAL PARENTAL CONFIGURATIONS IN HUMAN CLONING

By Nanette R. Elster, J.D., M.P.H.

	CONTRIBUTORS	POTENTIAL PARENTS
I	Intended Mother's Egg Intended Mother's Nucleus Intended Mother as Carrier	1. Intended Mother 2. Intended Mother's Mother 3. Intended Mother's Father [4. Intended Mother's Husband]
II	Donor's Egg Intended Mother's Nucleus Intended Mother as Carrier	1. Egg Donor 2. Intended Mother 3. Intended Mother's Mother 4. Intended Mother's Father [5. Intended Mother's Husband]
III	Donor's Egg Intended Father's Nucleus Intended Mother as Carrier	1. Egg Donor 2. Intended Father 3. Intended Father's Mother 4. Intended Father's Father 5. Intended Mother
IV	Intended Mother's Egg Intended Father's Nucleus Gestational Carrier	1. Intended Mother 2. Intended Father 3. Intended Father's Mother 4. Intended Father's Father 5. Gestational Carrier [6. Gestational Carrier's Husband]
V	Donor's Egg Intended Mother's or Intended Father's Nucleus Gestational Carrier	1. Egg Donor 2. Intended Mother or Intended Father 3. Intended Mother's or Intended Father's Mother 4. Intended Mother's or Intended Father's Father 5. Intended Mother's or Intended Father's Spouse 6. Gestational Carrier [7. Gestational Carrier's Husband]
VI	Intended Mother's Egg Intended Father's Nucleus Intended Mother as Carrier	1. Intended Mother 2. Intended Father 3. Intended Father's Mother 4. Intended Father's Father
VII	Donor's Egg Intended Mother's or Intended Father's Nucleus Donor as Carrier	1. Egg Donor/Carrier [2. Carrier's Husband] 3. Intended Mother or Intended Father 4. Intended Mother's or Intended Father's Mother 5. Intended Mother's or Intended Father's Father [6. Intended Mother's or Intended Father's Spouse]

APPENDIX A: POTENTIAL PARENTAL CONFIGURATIONS IN HUMAN CLONING (continued)

VIII	Donor A's Egg Donor B's Nucleus Intendend Mother as Carrier	1. Egg Donor 2. Nucleus Donor 3. Nucleus Donor's Mother 4. Nucleus Donor's Father 5. Intended Mother [6. Intended Father]
IX	Donor A's Egg Donor B's Nucleus Gestational Carrier	1. Egg Donor 2. Nucleus Donor 3. Nucleus Donor's Mother 4. Nucleus Donor's Father 5. Gestational Carrier [6. Gestational Carrier's Husband] 7. Intendend Mother [8. Intended Father]
X	Donor A's Egg Donor A's Nucleus Gestational Carrier	1. Donor A 2. Donor A's Mother 3. Donor A's FAther 4. Gestational Carrier [5. Gestational Carrier's Husband] [6. Intended Mother] [7. Intended Father]
XI	Donor A's Egg Donor B's Nucleus (Donor born thru egg and sperm donation) Gestational Carrier	1. Donor A 2. Donor B 3. Donor B's egg donor 4. Donor B's sperm donor 5. Donor B's Legal Mother 6. Donor B's Legal Father 7. Gestational Carrier [8. Gestational Carrier's Husband] [9. Intended Mother] [10. Intended Father]
XII	Intended Mother's Egg Dodnor Nucleus (from the child of the Intended Mother and the Intended Father) Intended Mother as Carrier	1. Intended Mother 2. Nucleus Donor 3. Intended Father
XIII	Intended Mother's Egg Donor's Nucleus Donor as Carrier	1. Intended Mother 2. Nucleus Donor 3. Nucleus Donor's Mother 4. Nucleus Donor's Father [5. Nucleus Donor's Spouse]

Endnotes

1. *All Things Considered*, Cloning roundtable, R. Seigel, L. Wertheimer (hosts), D. Rosenberg, R. Portilo, T. Peters, L. Kass (guests), February 24, 1997 (transcript on file with author).

2. M. Specter, A new creation: The path to cloning—A special report, *The New York Times*, March 3, 1997, p. A1.

3. In 1993, embryologists at George Washington University split human embryos, making twins and triplets. See K. Sawyer, Researchers clone human embryo cells; Work is small step in aiding infertile, *The Washington Post*, October 25, 1993, A4. These embryos were not implanted into a woman for gestation. This procedure is distinguishable from cloning by nuclear transfer.

4. S. Begley, Little lamb, who made thee?, *Newsweek*, March 10, 1997, 53-57. See also I. Wilmut, A.E. Schnieke, J. McWhir, A.J. Kind, and K.H.S. Campbell, Viable offspring derived from fetal and adult mammalian cells, *Nature*, 385:810-813, 1997.

5. Transcript of Clinton's remarks on cloning, *U.S. Newswire*, March 4, 1997.

6. Begley, supra note 4.

7. National brief—Washington D.C.: NIH director plays down cloning effect, *Los Angeles Times*, February 27, 1997, A9.

8. Begley, supra note 4.

9. Although these are the most pressing legal issues raised, the rest of this paper goes beyond these issues to address other legal concerns, such as the human subjects' concerns regarding research on a clone, the application of the nobility clause of federal and state laws to cloning, and the liability issues associated with cloning whole individuals.

10. Fla. Stat. Ann. § 390.001(6) (West 1993); La. Rev. Stat. Ann. § 9:121 et seq. (West 1991); Me. Rev. Stat. Ann. tit. 22, § 1593 (West 1992); Mass. Gen. Laws Ann. ch. 112, § 12J (West 1996); Mich. Comp. Laws Ann. § 333.2685 et seq. (West Supp. 1997); Minn. Stat. Ann. § 145.421 (West 1989); N.D. Cent. Code § 14-02.2-01 (1991); N.H. Rev. Stat. Ann. § 168-B:15 (Supp. 1996); Pa. Cons. Stat. § 3216 (West Supp. 1996); R.I. Gen. Laws § 11-54-1 (1994).

11. Three other states' fetal research bans—those of Illinois, Louisiana, and Utah—have already been struck down on those grounds.

12. N.H. Rev. Stat. Ann. § 168-B:15(1) (Supp. 1996).

13. N.H. Rev. Stat. Ann. § 168-B:15(2) (Supp. 1996).

14. La. Rev. Stat. Ann. § 9:121 (West 1991).

15. Id., § 9:122.

16. Id.

17. *U.S. v. Lopez*, 514 U.S. 549, 115 S.Ct. 1624 (1995).

18. Over 40 states have laws outlawing firearms on or near school grounds. *U.S. v. Lopez*, 115 S.Ct. 1624, 1641 (1995) (Kennedy and O'Connor, JJ., concurring).

19. See, e.g., *Daniel v. Paul*, 395 U.S. 298 (1969); *Perez v. U.S.*, 402 U.S. 146 (1971); *U.S. v. 62 Packages*, 48 F.Supp. 878 (W.D. Wisc. 1943); *U.S. v. Undetermined Number of Unlabeled Cases*, 21 F.3d 1026 (10th Cir. 1994).

20. *U.S. v. Dinwiddie*, 76 F.3d 913 (8th Cir. 1996), cert. denied, 117 S.Ct. 613 (1996); *U.S. v. Wilson*, 73 F.3d 675 (7th Cir. 1995); *Heart of Atlanta Motel v. U.S.* 379 U.S. 241 (1964).

21. *Abbott v. Bragdon*, 912 F.Supp. 580 (D. Me. 1995), aff'd, F.3d, 1997 WL 85096 (1st Cir. 1997).

22. *U.S. v. Wilson*, 73 F.3d 675 (7th Cir. 1995).

23. *Abbott v. Bragdon*, supra note 21.

24. Lottery Case, 188 U.S. 321 (1903) (the power to regulate under the interstate commerce clause includes the power to prohibit).

25. *Henley v. Wise*, 303 F.Supp. 62 (N.D. Ind. 1969).

26. *Margaret S. v. Edwards*, 488 F.Supp. 181, 220-221 (E.D. La. 1990). See also *Margaret S. v. Treen*, 597 F.Supp. 636 (E.D. La. 1984), aff'd sub. nom. *Margaret S. v. Edwards*, 794 F.2d 994 (5th Cir. 1986); *Wynn v. Scott*, 449 F.Supp. 1302 (1978), aff'd, sub. nom., *Wynn v. Carey*, 599 F.2d 193 (7th Cir. 1979).

27. See, e.g., *Griswold v. Connecticut*, 381 U.S. 379 (1965); *Eisenstadt v. Baird*, 405 U.S. 438 (1972).

28. *Planned Parenthood v. Casey*, 505 U.S. 833, 112 S.Ct. 2791 (1992).

29. *Planned Parenthood v. Casey*, 505 U.S. 833, 112 S.Ct. 2791, 2810 (1992).

30. 405 U.S. 438 (1972).

31. *Eisenstadt v. Baird*, 405 U.S. 438, 453 (1972).

32. *Lifchez v. Hartigan*, 735 F.Supp. 1361 (N.D. Ill.), aff'd without opinion, sub nom., *Scholberg v. Lifchez*, 914 F.2d 260 (7th Cir. 1990), cert. denied, 498 U.S. 1069 (1991).

33. J. Robertson, Statement to the National Bioethics Advisory Commission, March 14, 1997, 83.

34. G. Annas, Testimony on Scientific Discoveries and Cloning: Challenges for Public Policy, before the Subcommittee on Public Health and Safety, Committee on Labor and Human Resources, United States Senate, March 12, 1997, 4.

35. See the discussion of risks, *infra* in Part II.

36. These standards were suggested by George Annas in Senate testimony. George Annas, testimony on Scientific Discoveries and Cloning: Challenges for Public Policy, before the Subcommittee on Labor and Human Resources, United States Senate, March 12, 1997.

37. Approximately .01 percent of our DNA is encoded outside the nucleus or mitochondrial DNA. S. Tilghman, Statement to the National Bioethics Advisory Commission, March 13, 1997, 170-171. The clone will have mitochondria from the egg. It may also have mitochondria from the cell that was used to provide the nucleic DNA. Id. 171. For more information about mitochondrial DNA, see J.M. Shoffner, Maternal inheritance and the evaluation of oxidative phosphorylation, *Lancet*, 348:1283-1288, 1996.

38. See, e.g., Ariz. Rev. Stat. § 25-218 (1996).

39. L.B. Andrews, Alternative reproduction, in S.B. Schatkin (ed.), *Disputed Paternity Proceedings*, vol. 2, New York: Matthew Bender, 1990, § 30.02, 30-11.

40. M.M. Shultz, Reproductive technology and intent-based parenthood: An opportunity for gender neutrality, 1990 *Wisc. L. Rev.* 297 (1990); *Johnson v. Calvert*, 851 P.2d 776 (Cal. 1993) (en banc), cert. denied, 114 S.Ct. 206 (1993) and cert. dismissed 114 S.Ct. 374 (1993).

41. Begley, supra note 4.

42. Tilghman, supra note 37, 172.

43. T.H. Maugh II, Brave new world, *Los Angeles Times*, February 27, 1997, B2.

44. See id.; see also P.N. Spotts, R. Marquand, A lamb ignites a debate on the ethics of cloning, *The Christian Science Monitor*, February 26, 1997, 3; see also F.C. Pizzulli, Note, Asexual reproduction and genetic engineering: A constitutional assessment of the technology of cloning, 47 *S. Cal. L. Rev.* 476, 483 (1974).

45. Begley, supra note 4, 55.

46. Testimony of Ian Wilmut, Federal Document Clearing House Congressional Testimony, March 12, 1997.

47. Cloning of sheep has remarkable implications, Copley News Service, February 24, 1997.

48. L. Reibstein, G. Beals, A cloned chop, anyone?, *Newsweek*, March 10, 1997, 58.

49. S. Stolberg, Sheep clone researcher calls for caution science, *Los Angeles Times*, March 1, 1997, A18.

50. See G. Kolata, Scientists urge senators not to rush to ban human cloning, *The New York Times*, March 13, 1997, B11 (testimony of Ian Wilmut before the Senate hearings on cloning, March 12, 1997).

51. Begley, supra note 4.

52. Id.

53. J.M. Nash, The age of cloning, *Time*, March 10, 1997, 62-65.

54. Id.

55. P. Kendall, W. Neikirk, Cloning breakthrough a large step on much larger road, *Chicago Tribune*, February 25, 1997, 1. See also, Maugh, supra note 43.

56. J. Gross, Thinking twice about cloning, *The New York Times*, February 27, 1997, B1.

57. Begley, supra note 4.

58. Kolata, supra note 50; see also Don't rush anti-cloning laws, *Los Angeles Times*, March 13, 1997 (Governor Pete Wilson commenting that he would not consider a bill banning cloning human research if it would hinder "important" biotechnology research designed to fight cancer, AIDS, and other diseases).

59. Kolata, supra note 50; see also Pizzulli, supra note 44.

60. Kolata, supra note 50.

61. Begley, supra note 4.

62. Kolata, supra note 50.

63. Maugh, supra note 43; see also Stolberg, supra note 49.

64. C. Krauthammer, A special report on cloning, *Time*, March 10, 1997, 60; see also Stolberg, supra note 49.

65. Id.

66. Tilghman, supra note 37, 169.

67. Kendall, supra note 55.

68. H. Wray, J.L. Sheler, T. Watson, The World after cloning, *U.S. News and World Report*, March 10, 1997, 59.

69. J. Katz, *Experimentation with Human Beings*, New York: Russell Sage Foundation, 1972, 977.

70. Maugh, supra note 43; see also, J. Laurence, Regulations are relatively liberal, *The Times*, February 26, 1997.

71. Stolberg, supra note 49.

72. Id.

73. W. Gaylin, We have the awful knowledge to make exact copies of human beings, *New York Times Magazine*, 56(March 5):48, 1972.

74. Kolata, Medicine's troubling bonus: Surplus of human embryos, *New York Times*, March 16, 1997, 1; Fox on Trends (Fox Television), March 19, 1997.

75. J.B.S. Haldane, Biological possibilities for the human species in the next thousand years, in *Man and His Future*, G. Wolstenholme (ed.), 1963, 337, cited in Pizzulli, supra note 44, 490 n. 66.

76. Fletcher, Ethical aspects of genetic controls, *N Eng J Med*, 285:776, 779, 1971.

77. Haldane, supra note 75, 354-355, cited in Pizzulli, supra note 44, 520.

78. J. Kluger, Will we follow the sheep?, *Time*, March 10, 1997, 67.

79. Gross, supra note 56 (comments by Father Richard McCormick).

80. *All Things Considered*, supra note 1 (comments of Leon Kass).

81. Id. (equating the decision of who to immortalize as not dissimilar to the activities in Nazi Germany and the historical legal racism that inflicted our country); see also S. Schmickle, Cloning debate full of mystery and wonder, *Star Tribune*, March 2, 1997, 14.

82. See NIH director plays down cloning effect, *Los Angeles Times*, February 27, 1997, A9.

83. Id.

84. Kluger, supra note 78.

85. Id.

86. Robertson Statement, supra note 33, 86.

87. Krauthammer, supra note 64.

88. Kluger, supra note 78.

89. Nash, supra note 53.

90. C.P. Gilman, *Herland*, New York: Pantheon Books, 1979.

91. Nash, supra note 53.

92. A. Manning, Pressing a 'right' to clone humans, some gays foresee reproduction option, *USA Today*, March 6, 1997, D1.

93. L. Schilinger, Postcard from New York, *The Independent* (London), March 16, 1997, 2 (discussion of the Clone Rights United Front demonstrations in New York to dissuade New York legislators from passing a bill that would make human cloning research a felony).

94. Manning, supra note 92.

95. Id.; see also Schilinger, supra note 93.

96. Schilinger, supra note 93.

97. Tilghman, supra note 37, 173.

98. See Nash, supra note 53; see also Spotts and Marquand, supra note 44.

99. See Stolberg, supra note 49 (Ian Wilmut warning against prematurely banning all cloning research; from testimony before the Senate hearings on cloning research, March 12, 1997).

100. The law and medicine, *The Economist*, March 1, 1997, U.S. ed., 59; see also Pizzulli, supra note 44, 484 (citing Briggs and King, Transplantation of living nuclei from blastula cells into eucleated frogs' eggs, *Proc Nat Aca Sci, U S A*, 38:455, 1952).

101. Pizzulli, supra note 44, 484, 487.

102. Id., 487.

103. P. Recer, Sheep cloner says cloning people would be inhumane, Associated Press, March 12, 1997 (reported testimony of Dr. Ian Wilmut and of Dr. Harold Varmus before the Senate, March 12, 1997, regarding the banning of human cloning research).

104. Id. (comments of Dr. Ian Wilmut, testifying that as of yet he does not know of "any reason why we would want to copy a person. I personally have still not heard of a potential use of this technique to produce a new person that I would find ethical or acceptable.").

105. Tilghman statement, supra note 37, 146.

106. Id., 147.

107. Recer, supra note 103.

108. Nash, supra note 53.

109. Recer, supra note 103.

110. Id.; see also Nash, supra note 53.

111. See Recer, supra note 103; see also J. Laurence, and M. Hornsby, Warning on human clones, *The Times*, February 23, 1997; see also, Whatever next?, *The Economist*, March 1, 1997, 79 (discussing the problems associated of having mitochondria of egg interact with donor cell).

112. Hello Dolly, *The Economist*, March 1, 1997, 17 (discussion of the pros and cons of aging research which could result from nuclear transplantation cloning); cf. T. Monmaney, Prospect of human cloning gives birth to volatile issues, *Los Angeles Times*, March 2, 1997, A2 (comments of Dr. Elias).

113. Monmaney, supra note 112.

114. Nash, supra note 53.

115. Id. See also Tilghman, supra note 37, 145 (discussing the problem of mutations).

116. Gross, supra note 56; see also K.L. Woodward, Today the sheep. . ., *Newsweek*, March 10, 1997, 60.

117. *All Things Considered*, supra note 1; see also J. Coleman, Playing God or playing scientist: A constitutional analysis of laws banning embryological procedures, 27 *Pac. L.J.* 1331, 1351 (total ban on embryological procedures violates the Constitution); see also Pizzulli, supra note 44, 489 (cloning "subhumans" solely for organs would lead society to view clones as "manufactured arrangements of cells" whose civil liberties would be infringed).

118. Krauthammer, supra note 64, 61.

119. R. Wright, Can souls be xeroxed?, *Time*, March 10, 1997, 73; see also Krauthammer, supra note 64.

120. Pizzulli, supra note 44, 510 (citation omitted).

121. *Talk of the Nation*, February 24, 1997 (transcript on file with author).

122. Pizzulli, supra note 44, 497.

123. Id., 492.

124. Id., 509.

125. Id., 509 (citation omitted).

126. Id., 509 (citation omitted).

127. Id., 499 (citation omitted).

128. Id., 503 n.140.

129. Id., 512.

130. Id., 514. Pizzulli points out that a person's self-image may be at odds with an "objective" description of himself or herself (id.), and that overestimation of abilities might spur one to achieve goals otherwise thought unattainable (id., 515).

131. For a review of the studies, see L.B. Andrews, Prenatal screening and the culture of motherhood, 47 *Hastings L.J.* 967 (1996).

132. L. Tribe, Technology assessment and the fourth discontinuity: The limits of instrumental rationality, 46 *S. Cal. L. Rev.* 617, 648 (1973).

133. There is much evidence of the widespread belief in genetic determinism. See, e.g., D. Nelkin, S. Lindee, *The DNA Mystique: The Gene as Cultural Icon,* New York: W.H. Freeman & Company, 1995.

134. Pizzulli, supra note 44, 499 (citation omitted). Such an argument, however, ignores the role of having a culture of thinking; reflective individuals who can react to and are influenced by such a change.

135. Fletcher, Ethical aspects of genetic controls, *New Eng J Med,* 285:776, 781, 1971.

136. G.B. Johnson, What rights should a cloned human have? *St. Louis Post-Dispatch*, March 20, 1997, B7.

137. Id.

138. Genesis the sequel, *Newsday*, March 9, 1997, G1.

139. Id.

140. Bader, M., Threats from cloning shouldn't be overstated, *Portland Oregonian*, March 9, 1997, A8 (arguing that as long "[a]s the human gene pool is intact, humans will be able to adapt to the extent that is within their overall makeup to do so.").

141. Who agrees cloning has research benefits, *The Times-Picayune*, March 12, 1997, A8 (the World Health Organization has condemned human cloning as "ethically unacceptable," but warns that other cloning research could be medically beneficial and therefore should continue.).

142. Id.

143. Id.

144. Pizzulli, supra note 44, 529.

145. Gross, supra note 56.

146. Id.

147. Vatican calls for a global ban on cloning, Reuters North American Wire, February 26, 1997.

148. Kolata, supra note 50.

149. Kluger, supra note 78.

150. Amer, M.S., Comment: Breaking the mold: Human embryo cloning and its implications for a right to individuality, 4 *UCLA L. Rev.* 1659, 1666 (1996) (citing Elmer-Dewitt, P., Cloning: Where do we draw the line?, *Time,* November 8, 1993, 65).

151. Id.

152. Pizzulli, supra note 44, 498.

153. Pizzulli, supra note 44, 524-25.

154. Vatican calls for a global ban on cloning, Reuters North American Wire, February 26, 1997.

155. Id.

156. There are currently bills introduced in Alabama, California, Florida, Illinois, Maryland Missouri, New Jersey, New York, Oregon, South Carolina, West Virginia and in the U.S. Congress. See S.B. 511 (Ala. 1997); S.B. 1344 (Cal. 1997); H.B. 1237 (Fla. 1997); H.B. 1829 (Ill. 1997); H.B. 2235 (Ill. 1997); H.J.R. 28 (Md. 1997); H.B. 824 (Mo. 1997); A.B. 2849 (N.J. 1997); A.B. 5383 (N.Y. 1997); S.B. 2877 (N.Y. 1997); S.B. 1017 (Ore. 1997); H.B. 3617 (S.C. 1997); S.B. 410 (W. Va. 1997); S. 368, 105th Cong., 1st Session (1997); H.R. 922, 105th Cong., 1st Session (1997); H.R. 923, 105th Cong., 1st Session (1997).

157. For a discussion of these precedents, see Andrews, L.B., The legal status of the embryo, 32 *Loy. L. Rev.* 357 (1986).

158. See Parts VII and VIII, infra.

159. Fla. Stat. Ann. ’390.001(6) (West 1993); La. Rev. Stat. Ann. ’9:121 et seq. (West 1991); Me. Rev. Stat. Ann. tit. 22, ’1593 (West 1992); Mass. Gen. Laws Ann. ch. 112, ’12J (West 1996); Mich. Comp. Laws. Ann. ’333.2685 et seq. (West Supp. 1997); Minn. Stat.

Ann. ’145.421 (West 1989); N.D. Cent. Code ’14-02.2-01 (1991); N.H. Rev. Stat. Ann. 168-B:15 (Supp. 1996); 18 Pa. Cons. Stat. ’3216 (West Supp. 1996); R.I. Gen. Laws § 11-54-1 (1994).

160. Minn. Stat. Ann. § 145.421 (West 1989).

161. Mich. Comp. Laws Ann. § 333.2685 (West Supp. 1997).

162. Fla. Stat. Ann. § 390.001(6) (West 1993); Me. Rev. Stat. Ann. tit. 22, § 1593 (West 1992); Mass. Gen. Laws Ann. ch. 112, § 12J (West 1996); Mich. Comp. Laws Ann. § 333.2685 et seq. (West Supp. 1997); N.D. Cent. Code § 14-02.2-01 (1991); R.I. Gen. Laws
§ 11-54-1 (1994).

163. 18 Pa. Cons. Stat. § 3216 (West Supp. 1996).

164. Also note that few of the states which have research/experiment statutes are among the group (small but growing fast) of states which have introduced legislation to ban cloning. This situation lends itself to argument from both sides as well. On one hand, these states may assume that their current statute would cover cloning and a new statute would be duplicative. On the other hand, the lack of legislative action may indicate satisfaction with unregulated cloning.

165. Minn. Stat. Ann. § 145.421 (West 1989).

166. *Webster’s Third New International Dictionary, Unabridged,* Springfield, MA: Merriam Webster, Inc., 1986.

167. 18 Pa. Cons. Stat. § 3216 (West Supp. 1996).

168. 18 Pa. Cons. Stat. § 3203 (West Supp. 1996).

169. Fla. Stat. Ann. § 390.001(6) (West 1993); Me. Rev. Stat. Ann. tit. 22, § 1593 (West 1992); Mass. Gen. Laws Ann. ch. 112, § 12J (West 1996); Mich. Comp. Laws. Ann. § 333.2685 et seq. (West Supp. 1997); N.D. Cent. Code § 14-02.2-01 (1991); R.I. Gen. Laws
§ 11-54-1 (1994).

170. Fla. Stat. Ann. § 390.001 (West 1993).

171. Me. Rev. Stat. Ann. tit. 22, § 1593 (West 1992).

172. Mass. Gen. Laws Ann. ch. 112, § 12J(a)(I) (West 1996); Mich. Comp. Laws. Ann. § 333.2687 (West Supp. 1997) (the Michigan statute protects "embryo, fetus, or neonate," but the definition of the group is the same: "best medical judgment of a physician."); N.D. Cent. Code § 14-02.2-01(4) (1991); R.I. Gen. Laws § 11-54-1(c) (1994).

173. Mass. Gen. Laws Ann. ch. 112, § 12J(a)(I) (West 1996); N.D. Cent. Code § 14-02.2-01(1), (3) (1991); R.I. Gen. Laws § 11-54-1(c) (1994).

174. Mich. Comp. Laws Ann. § 333.2685 et seq. (West Supp. 1997).

175. See Mass. Gen. Laws Ann. ch. 112 § 12J(a)(I) (West 1996) (creating exception to preserve the life or health of the fetus or mother); Mich. Comp. Laws Ann. § 333.2685(1) (West Supp. 1997) (creating exception for therapeutic procedures); Minn. Stat. Ann. § 145.422 (West 1989) (creating exception to preserve the life or health of the fetus or mother and for "experimentation which verifiable scientific evidence has shown to be harmless to conceptus"); 18 Pa. Const. Stat. § 3216 (West Supp. 1996) (allowing therapeutic procedures); R.I. Gen. Laws § 11-54-1 (1994) (creating exception to preserve the life or health of the fetus or mother).

176. Robertson Statement, supra note 33, 94.

177. N.H. Rev. Stat. Ann. 168-B:15 (Supp. 1996).

178. Zorn, E., 'Brave new world' awaits debaters of abortion rights, *Chicago Tribune*, March 9, 1997, B1.

179. La. Rev. Stat. Ann. § 9:121 (West 1991).

180. La. Rev. Stat. Ann. § 9:122 (West 1991).

181. Id.

182. La. Rev. Stat. Ann. § 9:123 (West 1991).

183. La. Rev. Stat. Ann. § 9:124 (West 1991).

184. Id.

185. Id.

186. La. Rev. Stat. Ann. § 9:126 (West 1991).

187. La. Rev. Stat. Ann. § 9:129 (West 1991).

188. La. Rev. Stat. Ann. § 9:130 (West 1991).

189. La. Rev. Stat. Ann. § 9:131 (West 1991).

190. La. Rev. Stat. Ann. § 9:126 (West 1991).

191. Id.

192. La. Rev. Stat. Ann. § 9:130 (West 1991).

193. Id.

194. Id.

195. La. Rev. Stat. Ann. § 9:131 (West 1991).

196. La. Rev. Stat. Ann. § 9:127 (West 1991).

197. La. Rev. Stat. Ann. § 9:132 (West 1991).

198. La. Rev. Stat. Ann. § 9:122 (West 1991).

199. See, e.g., Cal. Bus. & Prof. Code § 2254 (West Supp. 1997).

200. See, e.g., N.M. Stat. Ann. § 24-9A-6 (1994) (providing for imprisonment for up to one year or the payment of a fine up to $1,000 or both).

201. Mass. Gen. Laws Ann. ch. 112, § 12J(a)(VI) (West 1996). An Institutional Review Board's reasonable, well-documented written approval provides a complete defense to criminal prosecution of the researcher. Id.

202. Mass. Gen. Laws. Ann. ch. 112 § 12J(b)(I).

203. Mass. Gen. Laws. Ann. ch. 112 § 12J(b)(III).

204. Mass. Gen. Laws. Ann. ch. 112 § 12J(b)(VI).

205. Mass. Gen. Laws. Ann. ch. 112 § 12J(b)(VII).

206. Mass. Gen. Laws. Ann. ch. 112 § 12J(b)(VIII).

207. 735 F.Supp. 1361, 1364 (N.D. Ill. 1990), aff'd without opinion, sub nom., *Scholberg v. Lifchez*, 914 F.2d 260 (7th Cir.), cert. denied, 498 U.S. 1068 (1991).

208. Id., 1364-65.

209. Id., 1364.

210. 794 F.2d 994 (5th Cir. 1986).

211. Id., 999.

212. Id.

213. Id. A concurring judge found this analysis to be contrived and opined that the provision was not unconstitutionally vague. Id., 1000 (Williams, J., concurring). Instead, he suggested that the prohibition was unconstitutional because "under the guise of police regulation the state has actually undertaken to discourage constitutionally privileged induced abortions." (Id., 1002, citing *Thornburgh v. American College of Obstetricians and Gynecologists*, 106 S.Ct. 2169, 2178 (1986)). The concurring judge pointed out that the state had "failed to establish that tissue derived from an induced abortion presents a greater threat to public health or other public concerns than the tissue of human corpses [upon which experimentation is allowed]." Id. Moreover, the state had not shown a rational justification for prohibiting experimentation on fetal tissue from an induced abortion, rather than a spontaneous one. Id.

214. *Margaret S. v. Edwards*, 794 F.2d 994, 999 (5th Cir. 1986).

215. Id.

216. Utah Code Ann. § 76-7.3-310.

217. *Jane L. v. Bangerter*, 61 F.3d 1493 (10th Cir. 1995).

218. S. 368, 105th Congress, 1st session, § 1(B) (1997).

219. 42 U.S.C.A. § 263a-1 et seq. (Supp. 1996).

220. 42 U.S.C.A. § 263a-7(1) (Supp. 1996).

221. 42 U.S.C.A. § 263a-1(b) (Supp. 1996).

222. Id.

223. 42 U.S.C.A. § 263a-5 (Supp. 1996).

224. 42 U.S.C.A. § 263a-1(a)(2) (Supp. 1996).

225. 42 U.S.C.A. § 263a-5 (Supp. 1996).

226. 42 U.S.C.A. § 263a-2 (Supp. 1996).

227. N.H. Rev. Stat. Ann. § 168-B:13 (Supp. 1993)

228. 18 Pa. Cons. Stat. Ann. § 3213(e) (1983).

229. La. Rev. Stat. Ann. § 9:128 (West 1991).

230. See, e.g., Ark. Code Ann. § 23-86-118(d) (1992); Hawaii Rev. Stat. § 432:1-604(6) (1994); 215 ILCS 5/356m(b)(1)(c) (1993); Md. Ann. Code art. 48a §§ 477EE(6) and 470W (1994).

231. 1997 Mo. H.B. 824 (introduced March 6, 1997); Md. H.J.R. 28 (introduced March 20, 1997).

232. Fla. H.B. 1237 (introduced March 7, 1997).

233. South Carolina H.B. 3617 § 16-17-745(B) (introduced March 11, 1997). A similar provision exists in New York Assembly Bill 5383 (introduced March 4, 1997).

234. 1997 N.Y.S.B. 2877 (introduced February 26, 1977); 1997 N.Y.A.B. 5383 (introduced March 4, 1997); 1997 Ill. H.B. 2235 § 5 (introduced March 10, 1997).

235. S. 368, 105th Congress, 1st session, § 1 (B) (1997).

236. The bill was introduced on March 4, 1997.

237. S.B. 511 § 1. Anyone who "intentionally, knowingly, or recklessly" clones a human being is guilty of a Class B felony. Id., § 2.

238. Cal. S.B. 1344 (introduced March 11, 1997).

239. This was introduced on March 4, 1997.

240. Fla. H.B. 1237 (introduced March 7, 1997).

241. 1997 Ill. H.B. 2235 § 5 (introduced March 10, 1997).

242. Id., § 10.

243. Id., § 5.

244. Md. H.J.R. 28 (introduced March 20, 1997).

245. Mo. H.B. 824 (introduced March 6, 1997).

246. N.J.A.B. 2849 § 1 (introduced March 24, 1997).

247. Id., § 2(b).

248. Id., § 2(c).

249. S.B. 2877 (introduced on February 26, 1997).

250. Id., § 4825.

251. Id., § 4826. Such actions are a Class D felony. Id., penal law § 125.70.

252. Id., Penal Law § 105.18. This is a Class B felony. Id.

253. Id., § 4827.

254. 1997 N.Y.A.B. 5383 (introduced March 4, 1997).

255. Ore. S.B. 1017 § 1 (introduced March 19, 1997).

256. Id., § 2.

257. S.C.H.B. 3617 § 16-17-45(A).

258. W.Va. S.B. 410 (introduced March 21, 1997).

259. U.S. Const. art. I, § 8, cl. 1.

260. U.S. Const. art. I, § 8, cl. 3.

261. See, e.g., 42 U.S.C.A. § 1395nn(b)(2)(B) (1995).

262. 45 C.F.R. § 46.201 et seq. (1996).

263. Transcript of Clinton remarks on cloning, U.S. Newswire, March 4, 1997.

264. U.S. Const., art. I, § 8 cl. 3.

265. *U.S. v. Lopez*, 115 S.Ct. 1624, 1630 (1995).

266. 42 U.S.C.A. § 274e (1991).

267. Human Research Subject Protections Act of 1997, S. 193 § 3(9) (1997).

268. *Carter v. Carter Coal Co.*, 298 U.S. 238 (1936) (holding provisions of the Bituminous Coal Act of 1935 regarding minimum wages, wage agreements, and collective bargaining unconstitutional on the basis that mining constituted "production," which is an "antecedent" of, not a part of, "commerce").

269. *U.S. v. Lopez*, 115 S.Ct. 1624 (1995).

270. 18 U.S.C. § 922 (q)(1)(A). The term "school zone" is defined as "in, or on the grounds of, a public, parochial or private school" or "within a distance of 1,000 feet from the grounds of a public, parochial or private school." 18 U.S.C. § 921(a)(25).

271. *Lopez*, 115 S.Ct., 1626.

272. U.S. Const., Art. I, § 8.

273. *Lopez*, 115 S.Ct., 1626 (citing The Federalist No. 45, pp. 292-293 [C. Rossiter ed. 1961)].

274. *Gregory v. Ashcroft*, 501 U.S. 452, 458 (1991).

275. 9 Wheat. 1, 189-90 (1924).

276. Id., 196.

277. *Lopez*, 115 S.Ct., 1628.

278. 301 U.S. 1 (1937).

279. Id., 37.

280. *Maryland v. Wirtz*, 392 U.S. 183, 197 n. 27 (1968).

281. 312 U.S. 100 (1941).

282. *U.S. v. Darby*, 312 U.S. 100, 118 (1941).

283. 452 U.S. 264 (1981).

284. 402 U.S. 146 (1971).

285. 379 U.S. 294 (1965).

286. 379 U.S. 241 (1964).

287. For example, in *Daniel v. Paul*, 395 U.S. 302 (1969), the U.S. Supreme Court held that an Arkansas amusement facility isolated on a country road nonetheless affects interstate commerce because a substantial portion of the food served at the snack bar (Id., 1701) moved in interstate commerce as well as the "sources of amusement" which included paddle boats leased from an Oklahoma company and a juke box which was manufactured out of state and played records manufactured out of state (Id., 1702).

288. 42 U.S.C.A. § 2000a (1994).

289. *Heart of Atlanta Motel, Inc. v. U.S.*, 379 U.S. 261 (1964).

290. Id., 358.

291. Id.

292. Id., 355-358.

293. *Lopez* 115 S.Ct., 1629-1630. In affirming regulation of activities that "substantially affect" interstate commerce, the Lopez court established that consistency with prior case law required a test that analyzed whether the regulated activity "substantially affects" interstate commerce as opposed to whether it "affects" interstate commerce.

294. *Lopez* 115 S.Ct., 1634.

295. Id., 1625, 1630-1641.

296. Id., 1640 (Kennedy, J., concurring).

297. Id., 1630-1631.

298. Id., 1631.

299. Merritt, D.J., Commerce!, *94 Mich. L. Rev.* 674, 696 (1995).

300. Id., 696.

301. Id.

302. *Lopez*, 115 S.Ct., 1631.

303. Id., 1632.

304. Merritt, supra note 299, 689 n. 65.

305. *Lopez,* 115 S.Ct., 640-641 (Kennedy, J., concurring).

306. Id., 1632.

307. Merritt, supra note 299, 701.

308. Id., 693 n. 74 (citing *U.S. v. Lopez,* 2 F.3d 1342, 1366 (5th Cir. 1993), aff'd., 115 S.Ct. 1624 (1995)).

309. Merritt, supra note 299, 703.

310. See for example, *NLRB v. Jones & Laughlin Steel Corp.,* 301 U.S. 1 (1937) (responding to severe worker dissatisfaction and a series of violent strikes) and *Perez v. U.S.,* 402 U.S. 146 (1971) (responding to the perception that organized crime was too far flung for state law to handle).

311. *Lopez,* 115 S.Ct., 1632.

312. Id.

313. Id.

314. Id.

315. Id.

316. This changed in 1957 in the landmark case, *Bing v. Thunig,* 163 N.Y.S. 2d 3, 143 N.E. 2d 3 (N.Y. 1957).

317. Wing, K.R., A.M. Silton, Constitutional authority for extending federal control over the delivery of health care, 57 *N.C. L. Rev.* 1423, 1470 (1979).

318. 29 U.S.C.A. § 203(S)(1)(B) (Supp. 1997) (establishing minimum wage and working condition requirements for certain defined employers engaged in interstate commerce).

319. 29 U.S.C.A. § 152(14) (Supp. 1997) (imposing collective bargaining requirements on employers engaged in interstate commerce).

320. 15 U.S.C.A. § 1 et seq. (1973).

321. 29 U.S.C.A. § 203(b) (1978) (FLSA); 29 U.S.C.A. § 152(b) (1973) (NLRA); 15 U.S.C.A. § 12 (Supp. 1996) (Sherman Act).

322. *Hospital Building Co. v. Trustees of Rex Hospital*, 425 U.S. 738 (1976) (holding that hospital had sufficient nexus with interstate commerce to invoke federal jurisdiction of Sherman Act). See also *Summit Health, Ltd. v. Pinhas*, 111 S.Ct. 366 (1991) (holding that jurisdictional elements of the Sherman Act were satisfied because ophthalmological services affect interstate commerce; because physicians and hospitals serve nonresident patients, they receive Medicare payments, and peer review proceedings routinely distributed across state lines affect doctors' employment opportunities throughout the Nation).

323. *National Organization of Women, Inc. v. Scheidler*, 510 U.S. 249, 114 S.Ct. 798, 803-806, 127 L.Ed.2d 99 (1994); *Wilson v. U.S.*, 73 F.3d 675 (7th Cir. 1995), cert. denied, 117 S.Ct. 47 (1996).

324. *Abbott v. Bragdon*, 912 F.Supp. 580 (D. Me. 1995), aff'd., 107 F.3d 934, 1997 WL 85096 (1st Cir. 1997); *U.S. v. Morvant*, 898 F.Supp. 1157 (E.D. La. 1995).

325. 42 U.S.C.A. § 12182(a) (1995).

326. 42 U.S.C.A. § 12181(7) (1995).

327. 912 F.Supp. 580 (D. Me. 1995), aff'd., ——F.3d ——, 1997 WL 85096 (1st Cir. 1997).

328. *Abbott v. Bragdon*, 912 F. Supp. 580, 593 (D. Me. 1995), aff'd., —— F.3d ——, 1997 WL 85096 (1st Cir. 1997).

329. Id.

330. Id., 594.

331. Wing and Silton, supra note 317, 1471.

332. 21 U.S.C.A. § 321 et seq. (1972).

333. 21 U.S.C.A. § 331 (1972).

334. *U.S. v. 62 Packages*, 48 F.Supp. 878 (W.D. Wisc. 1943).

335. See, e.g., M-D-D-I Reports, "The Gray Sheet" (March 17, 1997) (referring to lawsuit challenging FDA's policy on PET radiopharmaceuticals).

336. 192 F.Supp. 51 (E.D. Mich. 1961). See also *U.S. v. Undetermined Number of Unlabeled Cases*, 21 F.3d 1026 (10th Cir. 1994) (holding that urine and saliva specimen containers used in HIV-testing are subject to FDA regulation).

337. 39 Cases, 192 F.Supp., 52.

338. Id.

339. 42 U.S.C.A. § 262(a) (Supp. 1997).

340. The proposed Human Tissues Safety Act of 1996, S. 2195, would bring within FDA regulation "human tissue," which is defined as "a collection of similar human cells which is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a disease or condition in a human or for reproduction." If the Food, Drug, and Cosmetic Act were amended to include the regulation of human tissue, it is likely that embryos that result from cloning would fall within the proposed definition of "human tissue."

341. Cal. Health & Safety Code § 121200 (1996).

342. Id.

343. Rivas, M.S., The California AIDS initiative and the Food and Drug Administration: Working at odds with each other?, 46 *Food Drug Cosm. Law J.* 107, 125 (1991).

344. Id.

345. 18 U.S.C.A. § 248 (1994).

346. 18 U.S.C.A. § 248(a)(1)(1994).

347. 18 U.S.C.A. § 248(a)(2)(1994).

348. 18 U.S.C.A. § 248(a)(3)(1994).

349. *U.S. v. Wilson*, 73 F.3d 675, 680 (7th Cir. 1995).

350. *Cheffer v. Reno*, 55 F.3d 1517, 1520 (11th Cir. 1995).

351. Id., 1520; Wilson 73 F.3d, 681.

352. Cheffer, 55 F.3d, 1520; Wilson, 73 F.3d, 681 (holding unique scarcity of certain reproductive health services necessitates substantial interstate travel).

353. Cheffer, 55 F.3d, 1520; Wilson, 73 F.3d, 682.

354. Cheffer, 55 F.3d, 1520; Wilson, 73 F.3d, 680-682.

355. 42 U.S.C.A. § 263a (Supp. 1996).

356. 138 Cong. Rec. H5349-01 (1992).

357. Id.

358. 42 U.S.C.A. § 263a-2(b) (Supp. 1996).

359. Cheffer, 55 F.3d, 1520.

360. Lopez, 115 S.Ct. 1629 (1995).

361. *U.S. v. Dinwiddie*, 76 F.3d 913, 919 (8th Cir. 1996), cert. denied, 117 S.Ct. 613 (1996). The court noted that "[s]ubstantial numbers of women travel across state lines to obtain reproductive-health services." Id. (citation omitted).

362. This estimate is from Dr. W. Bruce Currie, biologist at Cornell University. Begley, supra note 4.

363. *U.S. v. Robertson*, 514 U.S. 669 (1995).

364. A legislative assistant in Senator Glenn's office suggested that the national exchange of research results justifies Congress' authority under the commerce clause to regulate the use of human subjects in all research, including those projects that do not receive federal funding. See proposed Human Research Subject Protections Act of 1997, S. 193.

365. See Andrews, L., *Medical Genetics: A Legal Frontier*, Chicago: American Bar Foundation, 1987, chapter 3.

366. *Lopez*, 115 S.Ct., 1641 (Kennedy, J., concurring).

367. Some states have proposed laws, however. See, e.g., N.Y. S.B. 2877 (February 26, 1997); Al. S.B. 511 (March 4, 1997).

368. California S.J.R. (March 4, 1997).

369. Francione, G.L., Experimentation and the marketplace theory of the First Amendment, 136 *U. Pa. L. Rev.* 428-429 (1987).

370. One of the powers of the legislative branch under the patents and copyrights clause of the U.S. Constitution is [t]o promote the Progress of Science and useful Arts, by securing for limited times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries. U.S. Const. Art. I, § 8, cl. 8.

371. Coleman, supra note 117, 1386-1387.

372. Stolberg, supra note 49.

373. Sen. Tom Harkin, D-Iowa, today said that he is investigating President Clinton's authority to ban federal spending for human cloning research, *Congress Daily*, March 12, 1997.

374. Recer, supra note 103 (testimony of Senator Tom Harkin before the Senate hearings on cloning research on March 12, 1997).

375. Robertson, J., The scientist's right to research: A constitutional analysis, 51 *S. Cal. L. Rev.* 1203-1279, 1213 (1977). Robertson argues that the right to participate as a research subject is protected by the Fourteenth Amendment's right to privacy as recognized in *Roe v. Wade*, 410 U.S. 113 (1973). This right arises from an individual's privacy interest in autonomous decision-making concerning the use of his or her body in an experiment designed to further medical knowledge or to be of personal benefit. Id.

376. Id., 1212. Coleman argues that "[v]arious Supreme Court decisions, read together, seem to acknowledge a freedom to conduct research which is anchored in the freedom of speech." Coleman, supra note 117 (citations omitted). See also *Roth v. United States*, 354 U.S. 476, 484 (1957) (noting that the Continental Congress cited scientific advancement as a reason for protecting freedom of the press); see also *Sweezy v. New Hampshire*, 354 U.S. 234, 250 (1957) (noting that "[t]eachers and students must always remain free to inquire, to study and to evaluate, to gain new maturity and understanding; otherwise our civilization will stagnate and die.").

377. Robertson, supra note 375, 1204.

378. *Branzburg v. Hayes*, 408 U.S. 665, 705 (1972).

379. Coleman, supra note 117, 1338.

380. *Buckley v. Valeo*, 435 U.S. 765 (1978).

381. Branzburg, 408 U.S., 681-682.

382. 262 U.S. 390 (1923).

383. Id., 399.

384. *Henley v. Wise*, 303 F.Supp. 62 (N.D. Ind. 1969).

385. Id., 67.

386. Margaret S. I, 488 F.Supp. 181, 220-221 (E.D. La. 1980). See also *Margaret S. v. Treen*, 597 F.Supp. 636 (E.D. La. 1984), aff'd sub. nom *Margaret S. v. Edwards*, 794 F.2d 994 (5th Cir. 1986); *Wynn v. Scott*, 449 F.Supp. 1302, 1322 (N.D. Ill. 1978), aff'd sub nom., *Wynn v. Carey*, 599 F.2d 193 (7th Cir. 1979).

387. Robertson, supra note 375, 1212.

388. Id., 1253.

389. Id., 1254.

390. Id., 1256.

391. *U.S. v. O'Brien*, 391 U.S. 367, 376-377 (1968).

392. Id.

393. See, e.g., *Griswold v. Connecticut*, 381 U.S. 379 (1965); *Eisenstadt v. Baird*, 405 U.S. 438 (1972).

394. *Planned Parenthood v. Casey*, 505 U.S. 833, 112 S.Ct. 2791 (1992).

395. *Planned Parenthood v. Casey*, 505 U.S. 833, 112 S.Ct. 2791, 2810 (1992).

396. 405 U.S. 438 (1972).

397. *Eisenstadt v. Baird*, 405 U.S. 438, 453 (1972).

398. *Lifchez v. Hartigan*, 735 F.Supp. 1361 (N.D. Ill.), aff'd without opinion, sub nom., *Scholberg v. Lifchez*, 914 F.2d 260 (7th Cir. 1990), cert. denied, 111 S.Ct. 787 (1991).

399. 735 F. Supp. 1361 (N.D. Ill. 1990), aff'd without opinion, sub nom., *Scholberg v. Lifchez*, 914 F.2d 260 (7th Cir. 1990), cert. denied, 498 U.S. 1068 (1991).

400. Id., 1377 (citations omitted). The court also held that the statute was impermissibly vague because of its failure to define "experiment" or "therapeutic." Id., 1376.

401. Pizzulli, supra note 44, 550.

402. Robertson statement, supra note 33, 83. This seems to be a reversal of Robertson's earlier position that cloning "may deviate too far from prevailing conception of what is valuable about reproduction to count as a protected reproductive experience. At some point attempts to control the entire genome of a new person pass beyond the central experiences of identity and meaning that make reproduction a valued experience." Robertson, J., *Children of Choice: Freedom and the New Reproductive Technologies*, Princeton, NJ: Princeton University Press, 1994, 169.

403. Id.

404. Coleman, supra note 117.

405. Annas, G.J., Human cloning, *ABA Journal*, May 1997.

406. Annas, G., Scientific Discoveries and Cloning: Challenges for Public Policy, testimony before the Subcommittee on Public Health and Safety, Committee on Labor and Human Resources, United States Senate, March 12, 1977, 4.

407. See, e.g., *Griswold v. Connecticut*, 381 U.S. 479 (1965); *Eisenstadt v. Baird*, 405 U.S. 438 (1972); *Roe v. Wade*, 410 U.S. 113 (1973); *Planned Parenthood of Southern Pennsylvania v. Casey*, 505 U.S. 833 (1992).

408. See *Lifchez v. Hartigan*, 735 F.Supp. 1361 (N.D. Ill.), aff'd without opinion, sub nom. *Scholberg v. Lifchez*, 914 F.2d 260 (7th Cir. 1990), cert. denied, 498 U.S. 1068 (1991).

409. See the discussion of risks, supra in Part II.

410. Mauro, T., Sheep clone prompts U.S. panel review, *USA Today*, February 25, 1997, A1.

411. Pizzulli, supra note 44, 502

412. Id., 512.

413. Id.; see also, Amer, supra note 150.

414. Valerio Barrad, C.M., Comment, Genetic information and property theory, 87 *Nw. U. L. Rev.* 1037, 1050 (1993).

415. Id.

416. Id.

417. See Amer, supra note 150, 1669 n. 50; see also A wolf in sheep's cloning? Fantasies abound about what cloning animals means to the human race, *The Edmonton Journal*, March 2, 1997.

418. See Amer, supra note 150.

419. Pizzulli, supra note 44, 557. "[L]arge-scale cloning of a limited number of genotypes would decrease the adaptive potential of man." Id., 560.

420. Id., 559.

421. This useful term was introduced by Francis Pizzulli, supra note 44, 481.

422. Under the Thirteenth Amendment of the U.S. Constitution, "[n]either slavery nor involuntary servitude, except as punishment for crime whereof the party shall have been duly convicted, shall exist within the United States, or any place subject to their jurisdiction." U.S. Const. Amend. 13, § 1.

423. Pizzulli, supra note 44, 515.

424. Id., 517-522.

425. Id.

426. Tribe, supra note 132, 649.

427. Pizzulli, supra note 44, 583.

428. Id., 493.

429. Kluger, supra note 78, 70 (Varmus commenting that human cloning is repugnant to the American public).

430. Pizzulli, supra note 44, 525-527.

431. Id.

432. *Horst, Mayor, & Co., et al. v. Moses*, 48 Ala. 129, writ dismissed, 82 U.S. 389 (1872).

433. Pizzulli, supra note 44, 581.

434. Pizzulli poses a counter argument—"That granting a talented person the right to clone on the basis of his genetic constitution is based on a claim of personal merit, and that it does

not necessarily follow that he is being accorded preferential treatment on the basis of his ancestry." Id., 580 n. 503.

435. Id. If legislatures were to enact laws regarding who could be cloned, this would also likely run afoul of state constitutional provisions prohibiting special legislation.

436. Lest it be thought that an argument based the nobility clause is far-fetched, it should be noted that the nobility clause has been revitalized by recent scholarship applying it to issues of affirmative action and political activity. See, e.g., Lobsenz, J.E., Bakke, Lochner, and law school: The nobility clause versus a republican form of medicine, 32 *Me. L. Rev.* 1 (1980) and Eisgruber, C.L., Political limits and the powers of government, 44 *UCLA L. Rev.* 1297 (1994).

437. King, A.E., Solomon revisited: Assigning parenthood in the context of collaborative reproduction, 5 *UCLA Women's L.J.* 329 (1995).

438. See, e.g., Utah Code Ann. § 76-7-204 (1995).

439. See, e.g., In re Baby M., 537 A.2d 1227 (N.J. 1988).

440. See, Andrews, L.B., N.R. Elster, Legal issues in fertility management, in *Infertility in the Male*, 3rd ed., L.I. Lipshultz, S.S. Howards (eds.), St. Louis: Mosby Year Book, 1997, 476-484, 477.

441. Fla. Stat. Ann. § 742.14 (West Supp. 1997); N.D. Cent. Code § 14-18-04 (Michie 1991); Okla. Stat. Ann. tit. 10 § 555 (West Supp. 1997); Texas Family Code § 151.102 (1996); Va. Code Ann. § 20-158 (Michie 1995).

442. Ariz. Rev. Stat. Ann. § 25-218 (1991); Ark. Code Ann. § 9-10-201 (Michie 1993); D.C. Code Ann. § 16-401 et seq. (Supp. 1996); Fla. Stat. Ann. §§ 63.212, 742.15 (West 1985 and Supp. 1997); Ind. Code Ann. § 31-8-2-1 (West Supp. 1996); Iowa Code Ann. § 710.11 (West 1993); Ky. Rev. Stat. Ann. § 199.590 (Michie 1995); La. Rev. Stat. Ann. § 9:2713 (West 1991); Mich. Comp. Laws Ann. § 722.851 et seq. (West 1993); Neb. Rev. Stat. § 25-21-200 (1989); Nev. Rev. Stat. § 126.045 (Michie Supp. 1995); N.H. Rev. Stat. Ann. § 168-B:16 (1994); N.Y. Dom. Rel. Law § 121 et seq. (McKinney Supp. 1997); N.D. Cent. Code § 14-18-05 (1991); Tenn. Code Ann. § 36-1-102146 (1996); Utah Code Ann. § 76-7-204 (1995); Va. Code Ann. § 20-160 (Michie 1995); Wash. Rev. Code Ann. § 26.26.210 et seq. (West Supp. 19976); W. Va. Code § 48-4-16 (1996); Wisc. Stat. Ann. § 69.14(h) (West 1990); Wyo. Stat. Ann. § 35-1-410(d) (1997).

443. Ariz. Rev. Stat. Ann. § 25-218 (1991); Ark. Code Ann. § 9-10-201 (Michie 1993); Fla. Stat. Ann. § 742.16 (West Supp. 1997); Nev. Rev. Stat. Ann. § 126.045 (Michie 1995);

N.H. Rev. Stat. Ann. § 168-B:16 (1994); N.D. Cent. Code § 14-18-05 (1991); Utah Code Ann. § 76-7-204 (1995); Va. Code Ann. § 20-158(D) (Michie 1995).

444. See, e.g., Conn. Gen. Stat. § 45a-774 (1994); 750 ILCS 40/3 (1996) and Wash. Rev. Code § 26.26.050 (1996).

445. Fla. Stat. Ann. § 742.14 (West Supp. 1997); N.D. Cent. Code § 14-18-04(1) (1991); Okla. Stat. Ann. tit. 10 § 555 (West Supp. 1997); Va. Code Ann. § 20-156 (Michie 1995).

446. Texas Fam. Code Ann. § 151.102(a) (West 1996).

447. Fla. Stat. § 742.15 (West Supp. 1997).

448. N.H. Rev. Stat. Ann. § 168-B:17(I) (1994).

449. N.D. Cent. Code § 14-18-01 (1991).

450. N.D. Cent. Code § 14-18-03 (1991).

451. Va. Code Ann. § 20-169 (Michie 1995).

452. Fla. Stat. § 742.15(2) (West Supp. 1997).

453. N.H. Rev. Stat. Ann. § 168-B:17 (1995); Va. Code Ann. § 20-160 (Michie 1995).

454. Va. Code Ann. § 20-160 (Michie 1995) (emphasis added).

455. Cal. Fam. Code § 7610 (1994).

456. See, Cal. Fam. Code §§ 7550, 7650 (1994).

457. 19 Cal. Rptr. 2d 494 (1993).

458. Shultz, supra note 40, 332. Another legal commentator, also espousing an intent-based allocation of parenthood, articulates the value of such a private ordering approach to assigning roles in collaborative reproduction. She explains that:

> The benefits of private ordering in general, and in the context of collaborative reproduction in particular are many. Privatization of familial relationships advantages all members of the family; it protects the best interests of the child and furthers the adults' autonomy. Allocation of parental status by prebirth agreement clarifies adult-child relationships from the beginning of the child's life. It enables intending parents to

> exercise parental authority and receive legal recognition of their functional status throughout the course of the child's life. It provides certainty to the child and structure to the family. Moreover, it ensures that relationships within families of consent have been thought out and planned, through negotiation and compromise.

King, supra note 437.

459. Shultz, supra note 40, 370.

460. Va. Code Ann. § 20-160 (1996).

461. See discussion of specific states' approaches in Andrews, L.B., Alternative reproduction, in *Disputed Paternity Proceedings*, vol. 2, S.B. Schatkin (ed.), New York: Matthew Bender, 1990, § 30.02, 30-11.

462. Id., 30-11.

463. Id.

464. Id., 30-12.

465. D.C. Code § 16-2343.1(e) (1996).

466. Tenn. Code Ann. § 24-7-112 (1996).

467. Mich. Stat. Ann. § 25.496 (1996).

468. Miss. Code Ann. § 93-9-27 (1996).

469. See, e.g., Schiff, A.R., Solomonic decisions in egg donation: Unscrambling the legal conundrum of legal maternity, 80 *Iowa L. Rev.* 265, 267 (1995) (opining that the presumption would establish legal parenthood for a woman who gave birth using a donated egg in the context or currently used forms of collaborative reproduction).

470. These issues are discussed supra in Section IIIB.

471. Schatkin, S.B. (ed.), *Disputed Paternity Proceedings*, 4th ed., vol. 1, New York: Matthew Bender, 1990.

472. Faust, H., Challenging the paternity of children born during wedlock: An analysis of Pennsylvania law regarding the effects of the doctrines of presumption of legitimacy and

paternity by estoppel on the admissibility of blood tests to determine paternity, 100 *Dick. L. Rev.* 963, 964 (1996).

473. See, e.g., Cal. Fam. Code § 7610.

474. A third but unlikely scenario is possible which would occur when the egg cell of the intended mother is fused with the nucleic material of the gestator.

475. The law in Nevada is not applicable, though, because it specifically states that the egg and sperm must be from the intended parents, but in this scenario, there is no sperm contributed by the intended father.

476. A blood test could reveal that the intended father is the twin brother of the child. "In the analysis of a typical paternity case, exhibiting approximately 40 bands in the two DNA fingerprints of the child, there will be approximately 17 maternal specific bands, 17 paternal specific bands, and 6 to 8 bands shared between the mother and alleged father and/or the mother, child and alleged father." Schatkin, supra note 473, 118-131 (footnote omitted).

477. 897 P.2d 1356 (1994).

478. Id., 1361.

479. N.H. Rev. Stat. Ann. § 168-B:1 (1996).

480. See Andrews, L.B., *Medical Genetics: A Legal Frontier,* 1987, chapter 3.

481. For a discussion of the use of children as research subjects, see Glantz, L., The law of human experimentation with children, in *Children as Research Subjects: Science, Ethics, and Law,* M.A. Grodin, L.H. Glantz (eds.), New York: Oxford University Press, 1994, 122; Grodin, M.A., J.J. Alpert, Children as participants in research, *Pediatric Clinics of North America*, vol. 35, Philadelphia: W.B. Saunders Co., 1980, 1389-1401, 1390; Levine, R., Children as research subjects, in *Children and Health Care,* Kopelman, Moskop (eds.), Norwell, MA: Kluwer Academic Publishers, 1989; Levine, R., *Ethics and Regulation of Clinical Research,* Baltimore: Urban and Schwartzenberg, 1981, 156.

482. See, e.g., *Hart v. Brown*, 289 A.2d 386 (1972).

483. Brock, D.W., Ethical issues in exposing children to risks in research, in *Children as Research Subjects: Science, Ethics and Law,* M.A. Grodin, L.H. Glantz (eds.), New York: Oxford University Press, 1994, 81.

484. 45 C.F.R. § 46.116 (1996) (emphasis added).

485. 45 C.F.R. § 46.408 (1996).

486. Glantz, supra note 483, 104.

487. Id.

488. Andrews, L., *Medical Genetics: A Legal Frontier*, Chicago: American Bar Foundation, 1987, 44-45.

489. Rozovsky, F.A., *Consent to Treatment: A Practical Guide*, Boston: Little, Brown & Co., 1984, 540.

490. The difficulties with this, including its possible violation of the Thirteenth Amendment, are discussed in this paper supra, Part IX.

491. Andrews, supra note 490, 45.

492. *Nielsen v. Board of Regents*, Civ. No. 665-049 (Super. Ct. San Francisco, Cal. filed August 23, 1973).

493. Andrews, supra note 490, 45.

494. 321 U.S. 158 (1944).

495. Id., 170.

496. Rozovsky, supra note 491, 540.

497. Id.

498. Id., 541.

499. N.Y. Pub. Laws. Ann. § 2442 (McKinney's 1996); Va. Code Ann. § 32.1-162.18 (1996 Supp.).

500. 45 C.F.R. § 46.408 (1996).

501. Levine, supra note 483, 157.

502. Woody, Legal and ethical concepts involved in informed consent to human research, 18 *Cal. W. L. Rev.* 50, 63-64, 72 (1981).

503. Christoffel, T., *Health and the Law: A Handbook for Health Professionals,* New York: Free Press, 1982, 293.

504. Id.

505. 45 C.F.R. § 46.404; § 46.408 (1986).

506. 45 C.F.R. § 46.402(b) (1986).

507. 45 C.F.R. § 46.405 (1986).

508. 45 C.F.R. § 46.406 (1986).

509. 45 C.F.R. § 46.407(b) (experts from disciplines such as science, medicine, education, law, or ethics).

510. 45 C.F.R. § 46.407(b)(2)(ii) (1986).

511. Supra note 501 (N.Y. and Virginia).

512. Va. Code Ann. § 32.1-162.18 (1996 Supp.).

513. N.Y. Public Health Law § 2442 (McKinney 1985).

514. For a general discussion of such claims, see Andrews, L.B., Torts and the double helix: Legal and ethical issues raised by the Human Genome Project, 29 *Houston L. Rev.* 149, 155-157 (1992). It should also be noted that at least seven states (Indiana, Minnesota, Missouri, North Dakota, Pennsylvania, South Dakota, and Utah) have adopted statutes to prohibit an individual from bringing a wrongful life suit. Id., 160 n. 54.

515. *Curlender v. Bio-Science Lab.*, 165 Cal. Rptr. 477 (Ct. App. 1980).

516. Shaw, M., Conditional prospective rights of the fetus, 5 J. L. Med. 63, 99 (1984).

517. Id., 537l; see also Brodie, I., Clinton acts swiftly to avert abuse of breakthrough, *The Times,* February 26, 1997 (citing that the clone would have an action for wrongful life based on its denial of uniqueness).

518. Robertson, J., Genetic selection of offspring characteristics, 76 *B.U. L. Rev.* 421, 437 (1996).

519. Pizzulli, supra note 44, 541.

520. *Zepeda v. Zepeda*, 190 N.E.2d 849, 859 (Ill. App. Ct. 1963), cert. denied, 379 U.S. 945 (1964).

521. *Turpin v. Sortini*, 643 P.2d 954, 962-963 (Cal. 1982).

522. Pizzulli, supra note 44, 543 n. 320.

523. See in particular the discussion of the Louisiana and New Hampshire laws in Part IV, supra.

524. 42 U.S.C.A. § 263a-1 et seq. (Supp. 1996).

525. Safire, W., Clonalities, *The New York Times*, February 27, 1997, A23.

526. Transcript of President Clinton's remarks on cloning, U.S. Newswire, March 4, 1997.

527. These standards were suggested by George Annas in Senate testimony. Annas, G., Scientific Discoveries and Cloning: Challenges for Public Policy Testimony, before the Subcommittee on Labor and Human Resources, United States Senate, March 12, 1997, 8.

CLONING HUMAN BEINGS

Cloning: An International Comparative Overview

Commissioned Paper
by Bartha Maria Knoppers, J.D.
University of Montreal

CONTENTS

INTRODUCTION

The cloning of the sheep called Dolly involved a different technique than that used in embryo twinning or splitting. In "Dolly," a quiescent *adult* mammary cell was placed in the *unfertilized* ovum of a sheep whose nucleus had been removed. This was followed by the transfer of the *subsequent embryo* into a surrogate mother sheep, its normal division as an embryo, and then by the birth of a sheep genetically identical to the donor (except for the mitochondrial DNA which came from the ovum donor). (*Nature*, 1997, vol. 385, February 27, 810-1)

Two months earlier (December 15-18, 1996) in Strasbourg, France, at the Third Symposium on Bioethics of the Council of Europe on Medically-Assisted Procreation and the Protection of the Human Embryo, the renowned biologist Dr. Anne McLaren of the United Kingdom had stated in her report on "Research on Embryos in Vitro: The Various Types of Research" that "[a]reas of research that are widely regarded as ethically unacceptable and often prohibited by law include the following: . . . 3) cloning by nuclear substitution" (CDBI/SPK(96) (22), p. 6). At the same meeting, J. Egozcue, the Spanish expert, in his report on "Research in Human Conceptuses" reiterated that "[o]ther lines of research are forbidden or even penalized, although in some cases they may correspond to extremely useful models for the study of some special situations, that do not carry with them any danger, menace or unethical load. Among them are cloning, parthenogenesis, the production of chimeras, interspecies fertilization (with the exemption of the human-hamster system), any modification of the genome (or of the non-pathological genome, as in the Spanish law) and germ-cell therapy" (CIBD/SPK (96) (5), p. 7).

The scope of this international, comparative study on "human" cloning covers the last decade (1986–96) of laws, bills, and official policy statements on the legal and ethical issues with regard to research in human genetics and new reproductive technologies. While it includes international,[1–5] regional (Europe),[6–12] and national coverage[13–37] of these issues, it excludes the United States and animal cloning and does not cover legislation on human tissues generally. International and regional positions will be treated in a first part (I) followed by the division of the different national positions covering 13 countries into five categories in the second part (II): (1) legal prohibitions on research on gametes and/or embryos; (2) legal prohibitions on embryo twinning; (3) legal prohibitions specific to the cloning technique used in the creation of "Dolly"; (4) recommendations on cloning as found in bills, policy statements, or ethical guidelines; and finally, (5) recent government actions in relation to "Dolly."

INTERNATIONAL POSITIONS

Recently, two international ethics committees, one governmental (UNESCO)[1] and the other nongovernmental (HUGO),[2] were deliberately created for the study of the ethical, legal, and social issues surrounding human genetics. Neither has an explicit statement on cloning. The UNESCO International Bioethics Committee has as its mandate "the preparation of an international instrument on the protection of the human genome" (1993).

The preamble of UNESCO's proposed *Universal Declaration on the Human Genome and the Protection of Human Rights* recalls the universal principles of human rights as found in the international instruments and recognizes that: "research on the human genome and the resulting applications open up vast prospects for progress in improving the health of individuals and of humankind as a whole, but emphasiz[es] that such research should fully respect human dignity and individual rights, as well as the prohibition of all forms of discrimination based on genetic characteristics." In particular, article 4 foresees the need for scientific research, but such research should have therapeutic aims. It provides that: "[r]esearch, which is necessary to the progress of knowledge, is part of the freedom of thought. Its applications, especially in biology and genetics, should relieve suffering and improve the health of individuals and the well being of humankind as a whole" and that "[b]enefits from advances in biology and genetics should be made available to all, with due regard to the dignity and rights of each individual." Moreover, article 5 maintains that: "[n]o research applications should be allowed to prevail over the respect for human dignity and human rights, in particular in the fields of biology and genetics." These provisions taken together would disallow any form of genetic research such as cloning when interpreted by a signatory country to run afoul of their purpose and scope.

A universal declaration, when adopted, is an international statement of principles that eventually may become part of customary law and so have force of law, but *ab initio* serves a hortatory function and is meant to guide nations in their domestic legislation. Absence of specific provisions on cloning, however, does not mean that the positions taken (which must by reason of their origin and vocation be general in nature) are without normative value and impact. They apply therefore to the legitimacy of cloning as a research endeavor.

The International Ethics Committee of HUGO in its *Statement on the Principled Conduct of Genetic Research* was also concerned with research under the Human Genome Project and Human Genome Diversity Project generally, and not with any particular form of research. However, the *Statement* in its background principles refers to the "acceptance and upholding of human dignity and freedom." The deliberate creation of a clone could well fall within the purview of concerns enumerated therein, including the possible "reduction of human beings to their DNA sequences and attribution of social and other human problems to genetic causes" referred to in its preamble.

While easily dismissed as too broad and vague, these international approaches which are necessarily the result of compromise may, as we shall see, prove to be more inclusive than the narrow, scientific definitions often found under national legislation.

Turning to the Council of Europe and then to the European Union, November 26, 1996 saw the adoption by the Council of Europe (40 countries) of the *Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*.[6] Upon signature, this *Convention* is binding upon member states. Again, even though there is a chapter on the "Human genome" (Chapter 4), no mention is made of cloning. Article 2 of the *Convention*, however, states:

> "Parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine." Moreover, like the proposed UNESCO *Declaration*, "[s]cientific research in the field of biology and medicine shall be carried out freely, subject to the provisions of this *Convention* and the other legal provisions ensuring the protection of the human being" (article 15).

It is also important to note that earlier recommendations of the Council of Europe either covered medical research and reproductive technologies in general or were "subject specific," that is, covered cloning. Beginning with the latter, that is medical research with human beings, in 1990, the Council stated in its preamble to *Medical Research on Human Beings*[8] that "medical research should never be carried out contrary to human dignity." It also maintained that such research "should take into account ethical principles" and that "[a]ny medical research which is unplanned, or contrary to any of the preceding principles, or in any other way contrary to the ethics or law, or not in accordance with scientific methods in its design and cannot answer the questions posed should be prohibited or, if it has already begun, stopped or revised, even if it poses no risk to the person(s) undergoing the research" (article 16).

Prior to the adoption of the 1996 Council of Europe *Convention*, a 1989 *Recommendation on the Use of Human Embryos and Fetuses in Scientific Research*[10] provided that "[t]he removal of *cells* (author's emphasis), tissues, or embryonic or fetal organs, or of the placenta or the membranes, if live, for investigations other than of a diagnostic character and for preventive or therapeutic purposes shall be prohibited" (Appendix D.9). The general tenor of this text, covering the fetus and the embryo however, would lead one to conclude that it was "embryonic cells" that were envisaged (see explanatory paragraphs 3 to 7). This may be because an earlier "cloning-specific" recommendation of 1986, *Use of Human Embryos and Fetuses for Diagnostic, Therapeutic, Scientific, Industrial and Commercial Purposes*,[12] which defined cloning as "the creation of identical human beings by cloning or any other method, whether for race selection purposes or not" (section 14(A)(iv)), without further explanation, had already recommended to governments of its member states that such a technique be forbidden.

Another "cloning-specific" recommendation by the Council of Europe can be found in an 1989 information document entitled *Principles in the Field of Human Artificial Procreation*.[11] This information document was originally to be a recommendation but was not adopted by the Council of Ministers, since two member states disapproved of assisted conception techniques. It would have prohibited "[t]he use of techniques of artificial procreation to create identical human beings by cloning or by any other method . . ." (principle 20). Then in 1994, the Parliamentary Assembly of the Council of Europe in its recommendation on the protection of patentability of material of human origin asked that "techniques for cloning" be prohibited (article 13iii(b)).[7]

Turning now to the resolutions of the European Parliament of the European Union, the first *Resolution on the Ethical and Legal Problems of Genetic Engineering*[9] was adopted in

1989. It maintained that "[t]he European Parliament as regards clones, considers that the only possible response to the possibility of producing human by cloning and to experiments with a view to the cloning of humans must be to make them a criminal offence" (article 41).

Finally, three statements of international non-governmental organizations bear mention here. The first is that of the International Law Association in its 1988 *Resolution on Reproductive Technologies and the Protection of the Human Person*.[5] The position of the association was that "[c]onsidering the dignity inherent in all human beings, . . . any research or manipulation of human genetic material shall be for *therapeutic* purposes and shall be subject to the approval and control of an ethics committee" (article 1) (author's emphasis). Penal sanctions were asked for. Similarly, the 93rd Inter-Parliamentary Conference of 1995, in its wish to promote "universal principles and rights," mentioned "the inviolability of the human body and the intangibility of the genetic heritage of the human species."[4] Finally, the 1996 *Charter on Sexual and Reproductive Rights* of the International Planned Parenthood Federation[3] also mentions the right to human dignity and access to "safe" and "acceptable" reproduction technologies (article 103) without further definition.

At the international level, then, there is no doubt that respect for human dignity and respect for the intangibility of the human body, its constituent parts, reproductive tissues, and even down to the cell(s) are irreparably linked. While the need for, and value of, research involving humans are reaffirmed, both the proposed UNESCO *Declaration* and the European *Convention* would limit such research in the "genetic arena" to *therapeutic* interventions. These two overarching instruments implicitly refute human cloning. This is underscored not only by the more specific prohibitions on cloning, as found in the recommendations and resolutions just examined, but by national positions.

NATIONAL POSITIONS

Before turning to the specific positions found in the thirteen countries under study, it is important to emphasize that like the international instruments just examined, the objectives of these national positions are largely similar. Indeed, the stated object of the majority is to protect the dignity of all persons in relation to uses of human genetic materials.[17,20,28,33,34,35] Cloning is seen as "diminish[ing] the value of human individuality"[18,34] and as "violat[ing] basic norms of respect for human life"[19] and the "integrity of the human species."[24]

(1) Research on Embryos

Some countries with legislation on new reproductive technologies restrict such techniques to the use of "viable cells" in order to achieve pregnancy" (Austria, France)[16,23] and "to avoid the transmission to a child of a particularly serious disease" (France, Spain).[23,31] Four countries prohibit experimentation with fertilized eggs (Norway)[28] or with human embryos (France),[23] or experiments which have as their purpose "developing methods for achieving potentially hereditary genetic effects" (Sweden),[32] that is, to "develop certain characteristics" (Switzerland).[33] It is interesting to note, however, that while research with fertilized ova and with embryos are

explicitly mentioned, no country has prohibited by specific mention in law research on unfertilized gametes, and so, at first glance, the "Dolly" technique might not be prohibited. Yet, as just mentioned, if research on fertilized ova or embryos generally, or the legitimate applications of the techniques of medically assisted procreation which involve the prior obtaining of ova and sperm are themselves severely constrained to the therapeutic purposes mentioned above, cloning could well be understood to be excluded from the ambit of licit practice.

(2) Embryo Twinning

Often countries with an explicit prohibition on human cloning cover embryo splitting or twinning, but not the "Dolly" technique. An example of this is the 1995 *Infertility Treatment Act* of the state of Victoria in Australia.[14] It bans cloning as well as the attempt to clone with penal sanctions, but defines cloning as "to form, outside the human body, a human embryo that is genetically identical to another embryo or person" (article 3). Similarly, the 1990 *German Embryo Protection Law*[25] also prohibits "artificially caus[ing] a human embryo to develop with the same genetic information as another embryo, fetus, living person or deceased person" (article 6(1) (again with penal sanctions). Depending on how the phrase "causes a human embryo to develop" is interpreted, this definition may or may not cover "Dolly." Paradoxically, the 1990 *Human Fertilization and Embryology Act*[37] of the United Kingdom, which proscribes "replacing a nucleus of a cell of an *embryo* with a nucleus taken from a cell of any embryo, person or subsequent development of an embryo" (article 3(3)(d)) (emphasis added) may also not be inclusive. The 1995 Code of Practice of the Human Fertilization and Embryo Authority repeats this definition in its list of activities that are prohibited by law. It adds that it "will not license research projects involving embryo splitting with the intention of increasing the number of embryos for transfer" (article 10.5).

Irrespective of whether such precise scientific definitions include the Dolly technique, it is clear that in these countries the intent was to prohibit human cloning. The potential limits of the precise legal provisions, however, point to the danger of using scientific definitions in a legislative text.

(3) "Dolly" Technique

Two countries have legislation that simply prohibits research on the creation or production of "genetically identical human beings" (Denmark, Spain)[21,22,30] without further definition. Such legislation is sufficiently broad to be inclusive of both embryo twinning and the "Dolly" technique by concentrating on "the result" rather than the technique itself.

(4) Bills, Policy Positions, and Ethical Guidelines

Of the thirteen countries under study, only Canada[17] and Switzerland[34] currently have bills on reproductive technologies. The Canadian bill would make it a criminal offense to "manipulate an ovum, zygote or embryo for the purpose of producing a zygote or embryo that contains the same genetic information as a living or deceased human being, or, zygote, embryo or fetus" (article

4(1)(a)). This bill, which would *inter alia* cover the "Dolly" technique, has passed first reading and is broader in its scope than the report of the Canadian Royal Commission on New Reproductive Technologies,[14] which had recommended "the prohibition of human zygote/embryo research related to cloning" (rec. #184). In Switzerland, the current federal bill on medically assisted procreation proposes criminal sanctions for "the artificial creation of genetically identical beings"[34] (article 2(n)) (author's translation) and again would be inclusive in scope.

Other countries have either study papers prohibiting the "production of genetically identical individuals,"[29] or describing the creation of genetically identical preembryos (twinning)[27,35] and recommending its prohibition,[36] or codes of ethics in the same vein. Examples of the latter are found in Australia, where the 1996 National Health and Medical Research Council ethical guidelines[13] considered as ethically unacceptable "experimentation with the intent to produce two or more genetically identical individuals" (guideline 11.3). These guidelines apply in the states where there is no relevant legislation (guideline 6.1). This recent statement follows a 1982 position[15] that also considered as ethically unacceptable "[c]loning experiments designed to produce from human tissues viable or potentially viable offspring that are multiple and genetically identical" (no 8). Another example is in Canada, where parallel to the bill before Parliament just described, three research councils are preparing a *Code of Conduct for Research Involving Humans*[20] that would simply state that "cloning of human beings [is] ethically unacceptable" (article 16.10). It is interesting to note that while a 1993 Norwegian report[29] recommended to Parliament the prohibition of the "production of genetically identical individuals" (p. 33), the 1994 Norwegian law on the medical use of biotechnology[28] simply prohibits "research on fertilized eggs" (article 3-1).

Government Actions

On March 4, 1997, the Italian Ministry of Health established a three-month moratorium on cloning research in humans and animals.[26] On June 26, 1996, the President and Chancellor of the Swiss Confederation, in a message[35] on both a new popular initiative on new reproductive technologies and the recently proposed federal bill,[34] reiterated his country's position against the "artificial creation of genetically identical beings."

CONCLUSIONS

Either indirectly or directly, all of the international and national sources have focused their attention on the issue of cloning. Some limited themselves to broader statements of the principles of human rights in the need to preserve human dignity and integrity; others circumscribed the goals, scope, and type of medical research involving human beings and the new reproductive technologies; while other more direct prohibitions on cloning either addressed embryo twinning techniques or simply mentioned the prohibition on the creation of identical human beings and thus, in the latter case directly covered the Dolly technique. The latter approach, which proscribes the goal rather than the technique, avoids the pitfalls and confusion of ambiguous or too precise legislation.

Irrespective of the route chosen, the gambit of approaches symbolizes the difficulties inherent in legislating with regard to scientific advances, especially in a prospective fashion. The criminal law is a vehicle that sanctions behaviors that are considered morally reprehensible in a given society. "Crimes," however, require definition for the sake of certainty, and so techniques that we can only "imagine" may in their very description escape sanction. Human rights legislation seeks to guarantee and promote the well-being of persons and humanity but its actualization in the scientific context is difficult. Ethical guidelines fulfill both a principled and self-regulatory function but are often without sanction. Depending on the technology under scrutiny and jurisdictional issues, different legal tools and approaches are available. The problem lies in our limited understanding of present and future scientific advances. "Dolly" is but another lesson in humility.

References

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International

1. Third Session of UNESCO's International Bioethics Committee (IBC) (Paris, September 27-29, 1995), (1996) 47 (1) *IDHL* 107.

2. HUGO statement on the principled conduct of genetics research, May 1996, *Genome Digest* at 2.

3. International Planned Parenthood Federation, *Charter on Sexual and Reproductive Rights*, (1996) 47 (4) *IDHL* 546.

4. *Resolution on Bioethics and Its Implications Worldwide for Human Rights Protection*, adopted by the 93rd Inter-Parliamentary Conference on 1 April 1995, (1995) 46 (3) *IDHL* 401.

5. *Resolution on Reproductive Technologies and the Protection of the Human Person*, adopted at the 63rd Conference of the International Law Association (Warsaw, August 21-27, 1988), (1990) 41 (4) *IDHL* 723.

Europe

6. *Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, Directorate of Legal Affairs, Strasbourg, November 1996, DIR/JUR (96) 14.

7. *Recommendation 1240 (1994) on the Protection of Patentability of Material of Human Origin*, adopted by the Parliamentary Assembly on April 14, 1994, (1994) 45 (4) *IDHL* 565.

8. *Recommendation No. R (90) 3 of the Committee of Ministers to Member States Concerning Medical Research on Human Beings*, adopted by the Committee of Ministers on February 6, 1990, at the 443rd meeting of Ministers' Deputies, (1990) 41 (3) *IDHL* 461.

9. "Resolution on the Ethical and Legal Problems of Genetic Engineering," March 16, 1989, April 1990 *Bull. Med.* 57, 8, a. 41.

10. *Recommendation 1100 (1989) on the Use of the Human Embryos and Foetuses in Scientific Research*, in text adopted, Parliamentary Assembly, 40th Session, Party III, a. D. 9. in Appendix.

11. Principles in the field of Human Artificial Procreation, contained in an information document entitled *Human Artificial Procreation*, published by the Council of Europe in 1989, (1989) 40 (4) *IDHL* 907.

12. *Recommendation 1046 (1986) on the Use of Human Embryos and Foetuses for Diagnosis, Therapeutic, Scientific, Industrial and Commercial Purposes*, in text adopted, Parliamentary Assembly, 38th Session, Party II, a. 14 A. iv.

National

Australia

13. National Health and Medical Research Council, *Ethical Guidelines on Assisted Reproductive Technology*, Commonwealth Department of Health and Family Services, 1996.

14. Victoria: Infertility Treatment Act 1995 (assented to June 27, 1995), No. 63/1995, a. 3 et 47.

15. National Health and Medical Research Council, *Statement on Human Experimentation and Supplementary Notes (Supplementary Note 4: In Vitro Fertilization and Embryo Transfer, October 1982); Supplementary Note 5: The Human Fetus and the Use of Human Fetal Tissue, October 1983, Rec. 2*, No. 8.

Austria

16. Federal law of 1992 (Serial No. 275) Regulating Medically Assisted Procreation (The Reproductive Medicine Law), and Amending the General Civil Code, The Marriage Law, and the Rules of Jurisdiction, (1993) 44 (2) *IDHL* 247.

Canada

17. Bill C-47, An Act respecting Human Reproductive Technologies and Commercial Transactions Relating to Human Reproduction, 2nd Sess., 35th Parliament, 45 Elizabeth II, 1996, a. 4 (1) a) et 8.

18. *Voluntary Moratorium on New Reproductive and Genetic Technologies*, pronounced by the Minister of Health, at the National Press Theatre, Ottawa, ON, July 27, 1995, Government of Canada.

19. Royal Commission on New Reproductive Technologies, *Proceed with Care*, Final Report, Ottawa: Minister of Government Services Canada, 1993, vol. 1 & 2, rec. # 184.

20. Draft, *Code of Conduct for Research Involving Humans*, Prepared by the Tri-Council Working Group: The Medical Research Council of Canada, The Natural Sciences and Engineering Research Council of Canada, The Social Sciences and Humanities Research Council of Canada, Minister of Supply and Services Canada, 1996, a. 16.10.

Denmark

21. Law No. 503 of 24 June 1992 on the Scientific Ethics Committee System and the Examination of Biomedical Research Projects, (1992) 43 (4) *IDHL* 758, a. 15 (1).

22. Law No. 353 of 3 June 1987 on the Establishment of an Ethical Council and the Regulation of certain Forms of Biomedical Research, (1988) 39 (1) *IDHL* 95, a. 11 (1).

France

23. Law No. 94-654 of 29 July 1994 on the Donation and Use of Elements and Products of the Human Body, Medically Assisted Procreation, and Prenatal Diagnosis, (1994) 45 (4) *IDHL* 473, Art. L. 152-2, L. 152-14, 152.8 et 152.18.

24. Law No. 94-653 of 29 July 1994 on Respect for the Human Body, (1994) 45 (4) *IDHL* 498, a. 16-4.

25. Law of 13 December 1990 for the Protection of Embryos (the Embryo Protection Law), (1991) 42 (1) *IDHL* 60, a. 6.

Italy

26. Decree (March 4, 1997) by the Italian Ministry of Health establishing a three-month moratorium for all kinds of cloning experimentation in humans and animals, personal communication with Stefano Rodota, March 7, 1997.

Netherlands

27. Committee of the Health Council of the Netherlands, *Heredity: Science and Society*, (The Hague, 1989, 57-58.

Norway

28. Law No. 56 of 5 August 1994 on the Medical Use of Biotechnology, (1995) 46 (1) *IDHL* 51, a. 3(1).

29. Ministry of Health And Social Affairs, *Biotechnology Related to Human Beings*, Parliamentary Report No. 25 (1992-93) to the Storting on Biotechnology related to Human Beings, Oslo, 1993, Report no. 25, 1992-1993, 33.

Spain

30. Law No. 35/1988 of 22 November 1988 on Assisted Procedures, (1989) 40 (1) *IDHL* 82, a. 20 (2) (B) (k) et (l).

31. Law No. 42/1988 of 28 December 1988 on the Donation and Use of Human Embryos and Fetuses or their Cells, Tissues, or Organs, (1991) 42 (1) *IDHL* 64. (v. a. 2 (e) et 8 (2) a contrario).

Sweden

32. Law No. 115 of 14 March 1991 Concerning Measures for the Purposes of Research or Treatment in Connection with Fertilized Human Oocytes, (1993) 44 (1) *IDHL* 58.

Switzerland

33. Genetics and Assisted Procreation, Amendment of Federal Constitution, Dated 13 of August 1992, (1992) 43 (4) *IDHL* 745.

34. *Projet de loi fédérale sur la procréation médicalement assistée (LPMA)*, 1996, a. 2m and 36.

35. *Message relatif à l'initiative populaire pour la protection de l'être humain contre les techniques de reproduction artificielle (Initiative pour une procréation respectant la dignité humaine, PPD) et à la loi fédérale sur la procréation médicalement assistée (LPMA),* du 26 juin 1996, au nom du Conseil fédéral suisse: Le président de la Confédération, Delamuraz; Le chancelier de la Confédération, Couchepin, 96.058, 45, 82, 87.

36. *Rapport au Département de l'intérieur et au Département fédéral de justice et police, Commission d'experts pour la génétique humaine et la médecine de la reproduction,* Berne, 19 août 1988.

United Kingdom

37. Human Fertilisation and Embryology Act (1990) (U.K.), 1990, c. 37, in Morgan, D., R.G. Lee, *Blackstone's Guide to the Human Fertilisation and Embryology Act 1990 Abortion & Embryo Research, the New Law,* London: Blackstone Press Limited, 1991, a. 3 (3) (d) and 41 (b).

CLONING HUMAN BEINGS

Do Research Moratoria Work?

Commissioned Paper
by Robert Mullan Cook-Deegan, M.D.

CONTENTS

PREFACE

On Constitution Avenue in the nation's capital, just inside from Einstein's statue, the workings of democracy looked a lot like bedlam. Protesters sang, "We shall not be cloned" to the tune of "We Shall Overcome." "A banner quoting Adolph Hitler 'We will create the perfect race,' was unfurled and tauntingly waved in the faces of the scientists until one biologist, in a fit of pique, ripped it apart."[1] It was March 7, 1977, at the National Academy of Sciences (NAS), and the subject at hand was governance of recombinant DNA research. Two bills had been introduced in Congress to regulate such research, and fourteen more would follow in the next few years; legislation was deemed inevitable, and the debate was about what it would say not whether it would pass. The city council of Cambridge, Massachusetts, had just a few weeks earlier rescinded a moratorium on recombinant DNA research after a rancorous debate; several other local governments had passed similar ordinances imposing local moratoria. Cambridge Mayor Alfred Vellucci was in Washington to complain about not having been invited to the NAS symposium and to ask who would control recombinant DNA research.

Unknown to those at the symposium, another ruckus was stirring across the continent. At the University of California, San Francisco (UCSF), Axel Ullrich and his colleagues had learned earlier that week, on March 1, that they had inadvertently violated the National Institute of Health (NIH) guidelines for recombinant DNA research. Ullrich had cloned the rat insulin gene in a vector that had been provisionally "approved" by NIH's Recombinant DNA Advisory Committee (RAC) in mid-January but had not yet been "certified" by the NIH director. Peter Seeburg, another UCSF postdoctoral researcher, had also cloned rat growth hormone using the same uncertified vector. On March 19, Ullrich destroyed the bacteria containing the cloned insulin gene, following the recommendation of his lab chief (and department chair) William Rutter, who had discussed the matter with NIH Deputy Director DeWitt Stetten, Jr. Ullrich then cloned the insulin gene again using another, technically inferior and less safe, vector after it was certified for use on April 18. The cloning of the insulin gene, the first mammalian gene so captured, was announced at a triumphal May 23 press conference by UCSF laboratory directors William Rutter and Howard Goodman. Rutter and Goodman did not mention, and reporters did not yet know to ask, about the inadvertent breach of NIH guidelines.

Genetic technology was racing ahead, and government was struggling to keep up. The chaotic spring of 1977 marked the first cloning of a mammalian gene and the launch of a congressional debate that lasted several years. It was a confusing period of political turbulence, buffeting those who did recombinant DNA research, the Members of Congress and executive branch officials who funded and oversaw such research, and those who feared the consequences of its unfettered pursuit. In the end, the nation stumbled into a process for reviewing recombinant DNA research that enabled scientific progress but also ensured public scrutiny and set technical limits. The policy history of recombinant DNA research, including human gene therapy and congressional efforts to constrain fetal research, illustrate how the United States Government has contended with controversial emerging biomedical technologies. This paper recounts some

historical precedents and draws lessons from those experiences, as background for the National Bioethics Advisory Commission's (NBAC's) deliberations about human cloning.

FRAMEWORK OF THIS PAPER

A brief introductory section focuses on a **definition** of "moratorium" that pertains to the accounts that follow. The historical summaries begin with **fetal research**, because this was the first subject of a federal bioethics commission and because it involves many legislative moratoria through both authorization and appropriations statutes, as well as *de facto* moratoria in the executive branch. Fetal research also highlights the importance of regulations governing human subjects in research. **Recombinant DNA research** never became the subject of statutory constraint, but concern about biohazards from such research did lead to NIH guidelines and a new process to monitor compliance with them, separate from but parallel to human subjects review. As concern about the biohazards diminished in the early 1980s, a new controversy erupted over the deliberate introduction of DNA into humans to treat disease, or **human gene therapy**. General concern about human gene transfer, sharply exacerbated by a highly publicized premature human experiment, led to an extension of RAC review into clinical protocols. More than two hundred gene therapy protocols have been approved worldwide, but these have been confined to introduction of genes into cells that do not produce sperm and eggs, so changes are not inherited. The United States, the United Kingdom, and Germany exemplify three alternative approaches to proscribing introduction of DNA into sperm cells, egg cells, their precursors, or early embryos, leading to inherited changes through **germ line gene therapy.**

The discussion of historical background is followed by a summary of **policy lessons** that emerge from the cases. The main body of the paper is confined to factual accounts and limited interpretations, but does not contain recommendations. I have added a brief final section with my own **observations.** This section can easily be removed without jettisoning the earlier background material.

WHAT IS A MORATORIUM?

The *Oxford English Dictionary* lists only one definition of "moratorium," "a legal authorization to a debtor to postpone payment for a certain time."[2] The word is used much more broadly now to include a pause in the action, but it is not clear it should be stretched so far as some decisions covered later in this paper. In some cases, the meaning is appropriate—a suspension of activity pending further analysis or other action; in others it is clear that "moratorium" refers to "a ban I don't want to call a ban," with a deliberately disingenuous implication of transience. Some of the rhetoric surrounding human cloning falls into each category. Some of the cases below are true moratoria, the classic example being the period during which scientists refrained from doing recombinant DNA experiments while guidelines for safe practices were being devised.

In other cases, "moratorium" is not the word that has been used at all, but the case fits into analysis here because the factual similarity merits treatment. Fetal research has been the

subject of moratoria, and partial bans. Germ line gene therapy is banned in several countries, but it is nonetheless relevant for discussion here because in several ways it is the closest historical parallel. The congressional language about embryo and fetal research has been temporary because of the nature of NIH authorization and appropriation, not by intent, which has clearly been a permanent ban on federal funding of controversial experiments, with full knowledge that the same research would go on under private auspices.

The closest analogy to human cloning may well be germ line gene therapy—deliberate changes in human DNA intended to be inherited. This is because it is quite difficult to imagine an urgent clinical reason to clone a human now, much as scenarios for germ line gene therapy were difficult to concoct a decade ago. The motivation for a ban or moratorium seems to be some combination of preserving social values, fear of loss of social control, or harm to the products of the technology (people born from germ line gene therapy or human cloning). And finally, the technological risks appear to be mainly social and moral rather than technical, in contrast to the concern about biohazard to researchers and the public if recombinant DNA were to create uncontrollable replicating pathogens.

The prospect of inherited genetic intervention predates the Watson-Crick discovery that Mendel's inherited elements—genes—are stretches of DNA. A decade ago, the consensus was that no one could do germ line genetic interventions safely and reliably. Transgenic animals existed, but the methods were inapplicable to humans because there was a constant risk of malformed animals and the probability of effecting a desired genetic change was low (and so it remains, although much improved). Opinion split about the prudence of banning germ line gene therapy. On one hand, there seemed little to be lost by banning it, with some prospect of public assurance as a benefit. On the other hand, some voices pointed out that if the technology evolved sufficiently, one might imagine clinical scenarios, however rare, where it could be useful. Policy on deliberate germ line intervention now varies from barely permissive to explicitly proscriptive. In the United States, "the RAC will not *at present* entertain proposals for germ line alternations" [emphasis added].[3] This felicitous turn of phrase, a relic of NBAC member James Childress from a previous role, says the door is closed but RAC might open it in response to an appropriate knock. This was a deliberate decision, as an outright ban was urged by the Council for Responsible Genetics (CRG) in 1985, and the RAC subcommittee elected to stick with its language. German law, by contrast, says that such intervention is a criminal act, period.[4] In the United Kingdom, a licensing authority oversees embryo research, but it precludes licenses to genetically alter germ line cells.

The proposed germ line intervention discussed below commends RAC's prescience. For ten years, RAC has had a *de facto* ban on germ line gene therapy, but last year a concrete, clinically defensible proposal was proposed, and if it proves technically feasible, a protocol might come forward. In this clinical scenario, the harm of germ line therapy is speculative and vague, and most of the risks and consequences long debated do not pertain, yet the potential benefits are straightforward. RAC could simply choose to review the protocol if need be, after announcing a change in policy. In Germany, the parliament must alter a statute before such a move is possible.

Such a proposal comes forward, and indeed the National Advisory Board on Ethics and Reproduction has reliable information that a pregnancy to avoid maternal mitochondrial disease is underway, although not in a setting that uses federal research dollars. In Germany, a couple wanting to use this technique to have a genetically related healthy child would be blocked in exercising their choice by a German law that does not appear to protect any present or future individual from a particular harm. Whether this state involvement is appropriate turns on one's political philosophy, but it is unlikely to comport well with American values.

This recent offshoot of the germ line gene therapy debate exemplifies how language intended to constrain a technology can have unintended side effects. The language used to impose constraints matters a great deal, and yet it is quite difficult to foresee uses of emerging technology with sufficient precision to craft that language. Constraints on human cloning will face this same dilemma. As an alternative to precise legal definitions of what is proscribed, a review process for a broad spectrum of activities can leave judgments of risk and benefit to case-by-case analysis.

CONGRESSIONAL MORATORIA ON FETAL RESEARCH

Research on the Fetus was the first report of the first federal bioethics commission, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.[5] This report was due four months after the Commission got started. Congress in 1974, much like President Clinton in 1997, wanted careful deliberation, but wanted it now. Section 213 of Public Law 93-348, the same statute that created the National Commission, also imposed the first legislative moratorium on fetal research, barring research "on a living fetus before or after the inducted abortion of such fetus unless such research is done for the purpose of assuring the survival of such fetus" until the National Commission had made its recommendations to the Secretary of Health Education and Welfare (which would today be the Secretary of Health and Human Services). The moratorium stemmed from Scandinavian research involving tissue taken from fetuses after induced abortions, followed by revelations that NIH was supporting some fetal research. Outrage greeted press accounts of the research, leading to street demonstrations in Washington. Among those organizing the protests was Eunice Kennedy Shriver, whose brother, Senator Edward Kennedy, was championing the legislation to establish the National Commission.

The National Commission inventoried ongoing fetal research. As the commission countenanced actual research efforts, hard-edged ideology gave way to a search for common ground and criteria that might be used to mark its boundaries. Michael Yesley, executive director, later noted:

> "Fetal research appeared at the outset to be a topic on which the disputants were so far apart that the National Commission would be unable to make recommendations that were satisfactory to all or most of the concerned parties. . . . Many who had expressed outrage at the reports of research involving severed fetal heads anticipated that the National Commission would produce a whitewash of science, while many scientists feared that the National Commission would

> overreact to the public outcry by unjustifiably terminating some areas of valuable research. Instead, the National Commission made recommendations that enabled most fetal research to continue, yet imposed conditions to assure that such research would be ethically acceptable."[6]

The Commission adopted the principle that fetuses intended for abortion be treated equally to those intended for birth, leading to recommendations that only research intended to benefit the fetus or posing "minimal" risk be permitted. The National Commission issued another seven reports and ceased to exist in 1978. Most of its recommendations, including those governing fetal research, were incorporated into federal regulations, which became Title 45, Part 46 of the Code of Federal Regulations (45 CFR 46). 45 CFR 46 is the section of U.S. administrative law that governs human subjects in research. The fetal research recommendations of the National Commission, for example, were incorporated into subparts 208 and 209 of 45 CFR 46. Under 45 CFR 46, institutions that conduct federally funded research involving human subjects sign an "assurance" document with the Office of Protection from Research Risks (OPRR). OPRR is part of NIH, but serves all parts of the federal government for this purpose.

The National Commission made many recommendations for fetal research and about vulnerable populations. The Commission recognized, however, that any firm and fast rules would prove inadequate, so it also recommended that a review body be established to consider waivers to enable research on in vitro fertilization, research that posed more than "minimal risks" for children and fetuses, or otherwise deviated from the standards laid out in the regulations. The National Commission intended to leave the door open for meritorious research in exceptional cases, in subpart 204 mandating "one or more Ethical Advisory Boards" to review research protocols falling outside the other parts of the regulation. These boards became singular in implementation—as the Ethics Advisory Board (EAB)—which was chartered in 1976 and 1979,[7] and operated from 1977 through 1980. The EAB issued reports recommending exemptions from the Freedom of Information Act for some records retained by the Centers for Disease Control and NIH and on fetoscopy (which entailed more than minimal risk and so required special EAB approval).[8–11] The EAB also made recommendations about *in vitro* fertilization and embryo transfer, finding some research acceptable and recommending a change in the regulations to accommodate it, but these were never accepted by the Secretary of the Department of Health, Education, and Welfare (which became the Department of Health and Human Services with the creation of a Department of Education under President Carter).[9] The EAB's modifications to the regulations were not proposed as formal regulations. Instead, section 205 of the regulations continued to prohibit funding of human *in vitro* fertilization unless reviewed by the EAB, which later that year ceased to exist.

The National Commission also recommended establishment of a successor *deliberative* body, another national bioethics commission but with a broader mandate than human subject protections. Public Law 95-622 established the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (President's Commission). This

large and unwieldy title accurately described the President's Commission's broader mandate. One consequence of creating the President's Commission was the demise of the EAB.

The EAB did issue reports and also review protocols, but the diversion of the EAB's budget to sustain the President's Commission allowed only the deliberative function to continue. Loss of the EAB removed the only avenue for national review for *in vitro* fertilization or review of any protocols requiring waiver of 45 CFR 46 provisions. This, in effect, imposed a moratorium on fetal research posing more than minimal risk, unless expected to enhance the health of the particular fetus.

With the demise of the EAB, the source of the moratorium on any research falling outside 45 CFR 46 was no longer legislative, but caused by the executive branch's failure to establish a review body stipulated in its own regulations. The language of the regulations also introduced a legal lacuna, which was ambiguous but never tested. *In vitro* fertilization (IVF) was prohibited, but other experimentation on human embryos was not, because the fetal research provisions applied to a fetus, defined as "the product of conception from time of implantation" (subpart 203). Conceivably, an embryo created without federal funds could be the subject of research before implantation, and an argument could have been made for use of federal funds in such research.

The regulations applied (and still apply) to institutions that receive federal funds for research involving human subjects. Research on *in vitro* fertilization nonetheless continued, at private research centers funded by clinical fees, donations, and other nonfederal sources. The congressional Office of Technology Assessment (OTA) observed in 1988 that "the effect of this moratorium on federal funding of IVF research has been to eliminate the most direct line of authority by which the Federal Government can influence the development of embryo research and infertility treatment to as to avoid unacceptable practices or inappropriate uses." Failure to fund such research led to inability to control it or even monitor it.

The President's Commission operated from 1980 to 1983. Fetal research was not the theme of any of its 11 reports, although it did point to the problematic nature of a de facto moratorium on certain kinds of research. Even as the President's Commission went out of business in 1983, a debate about replacing it commenced. Representative Albert Gore introduced a bill to create a successor body to review developments in "human genetic engineering." A long and circuitous legislative journey ultimately led to creation of the Biomedical Ethics Advisory Committee in Public Law 99-158. This was a to be a small congressional analytical agency modeled on OTA, governed by a congressional Biomedical Ethics Board. That body operated for eight months, but was never able to get to its mandated tasks, which included a review of the "minimal risk" criterion for fetal research. The same 1985 law imposed a legislative moratorium on research "on a nonviable living human fetus *ex utero* or a living fetus *ex utero*" unless the research was intended to enhance its prospects of survival or posed "no added risk of suffering, injury, or death to the fetus." It stipulated that the standard for evaluating risk be no different for

research on fetuses intended for abortion than for those intended for birth (the National Commission principle, originally proposed by LeRoy Walters).

The legislative moratorium was repeated in the 1988 NIH authorization. A different, but related topic was also the subject of a special NIH review. Preliminary experiments using fetal tissue transplanted into adults to treat Parkinson's disease provoked a controversy in 1988 and 1989. In response to an NIH request to fund such research, Assistant Secretary of Health Robert Windom imposed a funding moratorium until NIH received the report of an ad hoc panel to address 10 questions that he posed. The most contentious of the questions dealt with connections between fetal tissue research and elective abortion. The panel issued a short report containing recommendations that were then accepted by the Advisory Committee to the Director of NIH. The Secretary of DHHS, however, rejected the use of tissue from elective abortions, in a tale recounted by James Childress.[12] Since he is an NBAC member, NBAC has direct access to much more intimate knowledge of the proceedings, and there is little virtue in recounting it here.

The fetal tissue transplantation controversy and a House hearing convened by Representative Weiss, drawing on OTA's 1988 infertility report, almost led DHHS Secretary Otis Bowen to charter a new EAB. He intended to do so but left office just before signing the charter. (As an aside, this EAB was chartered to combine the deliberative and protocol review functions, which may have doomed it even if it had come into being.) The 1985 legislative moratorium on fetal research remained until early in the Clinton Administration.

Newly elected President Bill Clinton urged Congress to lift the legislative ban on fetal research in January 1993 (*Federal Register*, vol. 58, p. 7468), and the relevant provisions were indeed removed from that year's NIH reauthorization, Public Law 103-43. NIH's first moves were cautious, however, in part because of a breaking controversy. Plans to assemble a panel for advice took shape in September 1993. In October, press accounts of research involving the "cloning" of a human embryo at George Washington University caused a public stir. NIH contemplated reentry onto this treacherous turf with understandable trepidation. In early 1994, NIH established a Human Embryo Research Panel to advise it about how to use its restored funding authority.

That panel's experience was reminiscent of the fetal tissue transplantation panel five years before. Recommendations were forwarded to the Advisory Committee to the Director of NIH, which recommended their adoption to NIH Director Harold Varmus. Within hours, however, President Clinton stepped forth to reject one recommendation of the NIH panel, saying, "I do not believe that federal funds should be used to support the creation of human embryos for research purposes, and I have directed that NIH not allocate any resources for such research," in the same statement that first announced his intention to create NBAC (Presidential statement, December 2, 1994). The President was silent on the panel's many other recommendations. The panel recommended that a group inside NIH review compliance with the guidelines. The Human Embryo Research Panel's deliberations are chronicled by R. Alta Charo as "The Hunting of the Snark."[13] She is an NBAC member, and so further review here is unnecessary.

The President's venture into the ethics of fetal research does not end the story. The Republican landslide in the 1994 congressional elections brought with it renewed interest in legislative constraints on fetal research. NIH was up for reauthorization in 1996, but the bills proved controversial, and fetal research provisions were among the sources of controversy. The NIH authorization was not a sufficiently high legislative priority, and NIH can operate for most purposes under a standing authorization, so no reauthorization bill was passed. A legislative moratorium on fetal research was restored, however, via language in the NIH appropriation for both fiscal years 1996 and 1997. These appropriation provisions were extremely controversial, involving floor debate that invoked allusions to Nazi atrocities (by proponents of the ban) and the Flat Earth Society (by opponents). The fetal research funding bans were in and out of House and Senate appropriation bills at different stages, but the final version included the Dickey-Wicker amendment proscribing embryo and fetal research, which survived a July 1996 attempt to excise it, and was passed in the final funding resolution in September. That language precludes use of NIH funds for "the creation of a human embryo or embryos for research purposes; or research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses" [in 45 CFR 46].[14]

In sum, a legislative moratorium imposed to allow the National Commission to report on fetal research gave way to criteria for fetal research in human subjects regulations, with a "safety valve" CEAB review of protocols that posed greater risks or involved *in vitro* fertilization. The EAB operated for three years, but its recommendations were never approved by the Secretary. The EAB was allowed to die in 1980, creating an executive branch ban on *in vitro* fertilization and fetal research outside the criteria specified in 45 CFR 46. (This was often called a *de facto* moratorium, but it was a ban). In 1985, a legislative moratorium was reimposed, pending comment from a congressional bioethics committee, via NIH reauthorization. The congressional committee was defunded in 1989 without having issued a report, and the moratorium became a ban until 1993, when Congress lifted the ban. During 1994, NIH accepted funding proposals for review while its Embryo Research Panel met. In 1995, a legislative ban was reimposed, this time not in the NIH authorization statute, but through the appropriations process. Whether the appropriations language will be included with 1998 appropriations is not yet clear, and NIH reauthorization may also be considered this year in Congress, although controversial features such as fetal research could preclude passage or even serious committee action.

MORATORIA ON RECOMBINANT DNA RESEARCH

When biomedical researchers think of research moratoria, they are apt to think first of the recombinant DNA story of the mid-1970s. It began with an experiment that Stanford molecular biologist Paul Berg proposed in 1970 to Janet Mertz as a graduate student research project. It would have entailed splicing together a monkey virus, SV40, and a bacterial virus (phage) and inserting the new construct into bacteria. Mertz discussed the experiment at a course she took in June 1971 at Cold Spring Harbor Laboratory on Long Island, one of the birthplaces of molecular biology. Her classmates and instructors, especially Robert Pollack, were worried that this might enable the bacteria to copy and transmit potentially harmful genes. Pollack called Berg to dissuade

him from the experiment. Worry about the hazards of working on tumor viruses were the subject of a January 1973 meeting chaired by Berg at Asilomar, but recombinant DNA was not the focus there. Berg and Mertz's gene-splicing experiment was dropped, but concern was rekindled with the advent of gene-splicing experiments in bacteria a few years later—as the recombinant DNA era dawned in 1973 with the work of Herbert Boyer of UCSF and Stanley Cohen of Stanford (they first conceived their collaboration in a cafe on Waikiki in November 1972). (This paragraph and the following account derived from several sources.[15–20])

A Gordon Conference in June 1973 was the first nationally conspicuous event in the recombinant DNA debate, initiating a public discussion through a letter to the President of the National Academy of Sciences, Philip Handler, and David Hogness, President of the Institute of Medicine. The letter was drafted by the conference co-chairs, Maxine Singer of the National Cancer Institute and Dieter Soll of Yale, and circulated to the conferees in July before being sent to Washington. It urged formation of a committee to formulate guidelines for the safe conduct of recombinant DNA experiments. Handler referred the Singer-Soll letter to the newly formed Assembly of Life Sciences of the National Research Council (the operating arm of the Academy). The Singer-Soll letter was subsequently published in *Science* that September,[21] greatly expanding the audience for the debate about recombinant DNA. The notion of potential biohazard from gene splicing was new to many in that audience, but not to Singer, as she was a friend of Paul Berg's. They had worried together over his proposed SV40-phage splicing idea in 1970. When the Academy asked her advice, she suggested that Berg chair the proposed committee, and he was contacted.

The resulting committee met in April 1974 at MIT, and included four past or future Nobelists in addition to Berg (a Nobelist six years later) and three other scientists. The committee reported in July. They recommended a moratorium on certain experiments until their hazards could be better assessed, that NIH establish a committee to craft guidelines and review proposals, and that an international meeting be convened to discuss potential biohazards.[22, 23] This set the stage for the famous Asilomar conference of February 1975.

Whereas the first Asilomar conference dealt with biohazards of viral research but did not address recombinant DNA, the second and far more famous Asilomar conference focused on biohazards of recombinant DNA specifically. The conference was again organized by a committee chaired by Paul Berg. The second Asilomar conference brought together biologists, mainly molecular biologists, with a smattering of lawyers and reporters. The Berg committee invited 150 participants, 60 from outside the United States; 16 were reporters who agreed not to file reports until after the meeting was over.[18] When the conference ended on February 27, 1975, it was immediately followed by a press conference, and the reporters who had attended were free to start filing their stories. A final report from the Asilomar conference was submitted in late April, was formally reviewed by independent sources, approved on May 20, and rushed into print in the June 5 issue of *Science* and that month's *Proceedings of the National Academy of Sciences*.[24, 25] The day the Asilomar conference ended, the NIH's Recombinant DNA Advisory Committee (RAC) met in Bethesda, Maryland, adopting the draft statement of the Asilomar conference as its interim

rules for federally funded research. The RAC had been born and began to walk, if only on shaky legs.

The voluntary moratorium, largely conceived and imposed by the molecular biology community on itself, thus was supplanted by a federally sanctioned set of guidelines and a prospective group review process. No violations of the voluntary phase of the recombinant DNA moratorium are known to have occurred. There were two known violations of the RAC guidelines for federally funded research, plus one alleged infraction at Harvard that was widely publicized but turned out to be a bureaucratic snarl rather than a real infraction. These cases shed light on different aspects of research moratoria.

The first two cases were about laboratory experiments that either actually took place outside the guidelines (University of California, San Francisco) or without proper NIH authorization documents on file (Harvard). The third case, involving University of California, Los Angeles (UCLA) physician Martin J. Cline, entailed introduction of recombinant DNA into two thalassemic patients, one in Israel and one in Italy. Of these, only Cline's actions were found to be deliberate violations of recombinant DNA guidelines, and even here, the violations of human subject protections were much more significant than infraction of the recombinant DNA guidelines. The Cline debacle set the stage for RAC's prospective review of human gene therapy protocols.

Cloning Rat Insulin and Growth Hormone in pBR322 at UCSF

Two genes, for rat insulin and rat growth hormone, were cloned using the plasmid pBR322 before it was certified by the NIH director. These experiments took place in January through March 1977, following a January RAC meeting at which pBR322 was provisionally "approved" pending further data. This was an action of the RAC, but the guidelines called for "certification" by the NIH director before a cloning vector could actually be used. Alex Ullrich cloned insulin and Peter Seeburg's growth hormone. Most of the attention, both scientifically and in the investigations of infractions in late 1977, focused on the insulin gene.

Axel Ullrich, a German postdoctoral researcher who had been in the United States only six months, apparently did not understand that approval was not the same as certification when he started his experiments. The information was relayed by phone, first from Miami (after the RAC meeting) to a postdoc in the Boyer laboratory, and then again from that laboratory to Ullrich. Even formal certification decisions were often communicated by phone, not only at UCSF but at most universities, because of the intense scientific competition (necessitating very fast communication) and also because the NIH Office of Recombinant DNA Activities was, by its own admission, "desperately understaffed."[26] The fact that two different people at UCSF took the same action suggests both that the competitive urge to use state-of-the-art methods was shared, and that neither Ullrich nor Seeburg was alone in his misunderstanding of the rules. The infractions took place at UCSF mainly because that is where the pBR322 vector was created and one of the places where gene cloning methods were most advanced.

By the time Ullrich confirmed that he had succeeded in cloning insulin, on March 2, 1977, he had known since a laboratory meeting on February 4 that pBR322 was not certified for use. At a March 1 meeting in Utah, William Garland of NIH confirmed to laboratory director Howard Goodman that pBR322 was not certified for use. After a conversation between William Rutter and NIH Deputy Director DeWit Stetten, Ullrich destroyed bacteria containing the pBR322 vectors that included the insulin gene inserts–the first mammalian gene ever cloned.[1, 27, 28] In the end, the experiments that broke the guidelines were technically safer than the ones that experiments using other cloning vectors. The vector designers turned out to be right about its safety, although that was not confirmed by empirical data until May 1977. The vector pBR322 was certified for use in cloning experiments on July 7, 1977.

The violations came to light on September 30, 1977, when *Science* reporter Nicholas Wade ran a story.[29] This led to wide media coverage for several months, and Senate hearings that November. Investigations at UCSF and NIH resulted in "no further action" being taken.[30] Further information about the infractions came to light in a federal patent case decided against the University of California last December.[31] New facts and documents were uncovered through legal discovery proceedings, court testimony, and expert analysis of data in the June 1977 *Science* paper and the related U.S. Patent 4,652,525. That case remains under appeal in the Court of Appeals, Federal Circuit. It was argued orally on January 6, 1997 (docket number 96-1175), and a decision is pending. Several relevant facts and interpretations remain in dispute.

Most of the disputed facts have little bearing on NBAC's interest about whether infractions of research moratoria take place. None of the parties to this litigation dispute that the infraction took place and was initially inadvertent; the disputes center on what took place when knowledge of the infraction became known. The final outcome of this case may, however, influence judgments of what happens when infractions do occur. The continuing dispute is not about whether an infraction occurred (it did), whether it was initially inadvertent (it was), or whether it posed a real risk to safety (it did not). Instead, this case shows how new regulatory or legal constraints imposed on research can complicate scientific discovery, influence scientific competition, and may even bear on patent rights—in this case, whether the patent on the first cloned mammalian gene is judged valid. The December 1995 decision of the judge explicitly calls into question findings from the UCSF and NIH investigations of late 1977, statements in the November 1977 Senate hearing, and completeness of the patent disclosure (see appendix C). The federal judge's decision hinges on facts that the NIH and UCSF investigations failed to bring to light, and thus implicitly raises doubts about the adequacy of previous investigations. Relevant sections of the judge's decision are reprinted as Appendix A.

Recombinant DNA Experiments without a Memorandum of Agreement between Harvard and NIH

Another guidelines infraction was alleged soon after the UCSF case was reported in *Science.* Charles Thomas at Harvard Medical School was one of the early users of recombinant DNA methods. He sat on the NIH committee that developed the guidelines. He believed the dangers of

recombinant DNA were "imaginary" or "totally conjectural,"[32, 33] and made no secret of this. A Freedom of Information Act inquiry from the Environmental Defense Fund discovered that no formal "memorandum of agreement" covering his experiments was on file at NIH.[34] His outspokenness no doubt made him a juicy target. The revelations were covered in the scientific press, then spilled over into the mainstream media and became the subject of a Senate hearing.

Investigations at both Harvard and NIH ultimately concluded that "at no time were Dr. Thomas' [sic] laboratory practices out of compliance with the applicable guidelines or conducted in a manner that would constitute a hazard." Dr. Thomas admitted that he "misspoke" to the Harvard biosafety committee. He claimed that NIH grants were being held up pending approval of his laboratory at the next-to-highest physical containment specifications (ventilation was insufficient, and it was never so certified, but in the meantime, Dr. Thomas departed Harvard for the Scripps Clinic and Research Foundation). Dr. Thomas' strategy was a transparent attempt to pressure the Harvard biosafety committee to approve his laboratory by leading it to believe their approval process was holding his research grant hostage. This manipulation, while unethical, did not bear directly on the allegations of violating the recombinant DNA guidelines, and says little about respect for the moratorium. Researchers in his laboratory were interviewed, and none asserted that he ever failed to abide by the NIH guidelines, whatever he thought about their merit. He publicly chafed at the rules, but all agreed that he played by them.

Dr. Thomas had many documents on file at both Harvard and NIH, including an agreement that was not forwarded to NIH a month before the case came to light. In the end, this was not an infraction of the guidelines but a bureaucratic tangle, and responsibility was shared among NIH, Harvard, and Dr. Thomas. Dr. Thomas's grants to do recombinant DNA research (not all work) were put on hold for five months while the investigations were underway. When those investigations were complete, the recommendation was to allow Dr. Thomas to resume recombinant DNA research using NIH funds.[35] In the end, Dr. Thomas was vindicated. From the documentary record, it appears he endured research constraints while under investigation and suffered bad publicity for being obstreperous and Machiavellian, but he neither violated the guidelines nor broke the earlier voluntary moratorium.

Introduction of Recombinant DNA into Thalassemic Patients in Israel and Italy

In July of 1980, UCLA physician Martin J. Cline inserted recombinant DNA into two patients with the blood disease thalassemia, one in Israel and one in Italy. In doing so, he violated the U.S. recombinant DNA guidelines (which covered any experiments using molecules created with federal research dollars) and human subjects regulations (which cover research by investigators at institutions with a signed human subjects agreement, regardless of whether the work is federally funded or not and whether or not it takes place in the United States). As a consequence, Dr. Cline resigned as chair of his department, had several grants terminated early, and for three years had to submit the report of the investigation to those reviewing any proposals he made to do recombinant DNA, to do research involving human subjects, or to request NIH funding.[36, 37]

REVIEW OF SOMATIC CELL GENE THERAPY PROTOCOLS

The most significant aspect of the Cline case was its violation of human subjects regulations, but its main impact was on how gene therapy entered the world, under the framework of the recombinant DNA guidelines. A month before Dr. Cline did his experiments abroad, the general secretaries of the three major U.S. religious denominations (Protestant, Roman Catholic, and Jewish) wrote to President Jimmy Carter.[38] Their letter opened, "We are rapidly moving into a new era of fundamental danger triggered by the rapid growth of genetic engineering" and went on to note, "Those who would play God will be tempted as never before." From a group of august theologians, that statement carried some weight. The clerics then turned to public policy and process, "We believe, after careful investigation, that no government agency or committee is currently exercising adequate oversight or control, nor addressing the fundamental ethical questions in a major way." Among other things, they were concerned about the 1980 Supreme Court decision allowing patenting of a bacterium, the famous *Diamond v. Chakrabarty* case.

As the President's Commission was beginning to operate, Alexander Capron, Executive Director, got wind of the letter. The President's Science Advisor, Frank Press, turned the letter over to the Commission. The letter became one origin of its report *Splicing Life.*[39] The Commission addressed public fears and pointed to the distinction between somatic cell therapy (which would affect only the person treated) and germ line treatment (which could be inherited). It discussed reconfiguring or augmenting RAC, with appointment of a Genetic Engineering Commission to "deal solely with this field" and also the possibility of a successor bioethics commission (the President's Commission was slated to go out of existence several months hence).[39] The report was released, became the subject of a House hearing before Representative Gore (at which Dr. Cline presented a defense of his work),[40] and led ultimately to the creation of the Biomedical Ethics Advisory Committee, and thence NBAC, through a long and complicated lineage.

The President's Commission report was commended to the RAC, which in 1984 set up a Working Group on Human Gene Therapy chaired by LeRoy Walters of Georgetown University's Kennedy Institute of Ethics. That Working Group was reconstituted as a RAC subcommittee, which went on to produce the first document laying down guidelines for RAC's review of gene therapy protocols, the "points to consider" document that raised over one hundred questions in seven main areas.[41] This document survives as Appendix M to the recombinant DNA guidelines, having been modified several times, but not fundamentally changed.[3] With diminishing duties other than gene therapy, the subcommittee was merged into the full RAC in 1991.[41] As of December 1996, RAC had considered 149 protocols.[42] Last year, NIH Director Harold Varmus proposed to dismantle the RAC, leaving review of gene therapy protocols to the Food and Drug Administration (FDA).

FDA does review gene therapy and somatic cell alterations,[43] and Varmus observed that protocol review by NIH was redundant and that public purposes could be served by hosting national conferences to promote dialog. Dr. Varmus's proposal met opposition, and RAC will be

retained in smaller form, reducing membership from 25 to 15. RAC will be responsible for "(1) Identifying novel human gene transfer experiments deserving of public discussion... (2) Identifying novel ethical issues relevant to specific human applications of gene transfer and recommending appropriate modifications to the *Points to Consider*... (3) Identifying novel scientific and safety issues... (4) Publicly reviewing human gene transfer clinical trial data... [and] (5) Identifying broad scientific and ethical/social issues... for Gene Therapy Policy Conference topics" (Office of Recombinant DNA Activities, 1997 #15; Office of Recombinant DNA Activities, 1997 #94).

MORATORIA ON GERM LINE GENE THERAPY

The President's Commission set the tone for much of the subsequent debate about gene therapy. Its distinction between germ line and somatic cell therapy guided the policy discussion, most notably in the form of Council of Europe Recommendation 934, citing a right to inherit a genome that "has not been tampered with," but also open to therapeutic interventions (with the suggestion that a list might be drawn up of conditions possibly warranting gene therapy).[44] Second thoughts about the moral and clinical significance of the somatic-germ line distinction began to appear with the 1990 Declaration of Inuyama, the statement resulting from an international meeting. It noted that germ line alteration would be "technically much more difficult than that of somatic cells and is not at present in prospect. However, such therapy might be the only means to treat certain conditions, and therefore continued discussion of both its technical and its ethical aspects is essential. Before germ-cell therapy is undertaken, its safety must be very well established, for changes would affect the descendants of patients."[45, 46]

The final clause about safety was added not only to note multigenerational impact, but following discussion of a serious problem faced by germ line therapy but not somatic therapies—the fact that any inserted genes would have to go through all of embryonic and fetal development without triggering a developmental mishap. This was a high hurdle indeed, since no animal models of human development can fully simulate the timing of intricate gene regulation, and controlled expression of many genes not expressed in adults. The thinking at Inuyama was that debate about germ line gene therapy would become serious with progress toward technology for extremely specific replacement of mutated genes with their exact non-mutated counterparts, leaving the genes in the same chromosomal site and subject to the same local regulatory effects. If such a technique were developed—and it would surely be developed first in other organisms—then it would quite likely be safe throughout development (and virtually no other technique would be). At that point, some clinical scenarios would become sufficiently safe to make possible application in some rare situations.

Walters and Palmer devote a chapter to possible scenarios for germ line intervention. Their book also includes a survey of targeted genetic alterations in other organisms, by molecular biologist Mario Capecchi of the University of Utah, because it is the key enabling technology necessary before human germ line changes make sense.[47] One such scenario discussed in Inuyama involved two parents with recessive disorders wishing to have a child without the disorder.

Another was to address diseases requiring genetic change in many different organs whose cells do not divide in adults (such as muscle, heart, and nerve cells), requiring modification before organs differentiate during embryonic development (Wivel 1993, 95).

All nations that have explicitly addressed germ line gene therapy have opted to constrain it. In the United States, the "will not entertain proposals" language of RAC prevails. As noted before, Germany, Denmark and some other nations have made germ line alterations in humans a criminal act. In the United Kingdom, the experiments are subject to a licensing authority that was created by law. The licensing authority has discretion, but only within statutory parameters. The legislative language has caused some problems in the case of a mother who desired fertilization using the sperm of her husband, whose sperm was obtained and frozen after he was comatose and could not give written consent for its use. The artful solution in this case has been to export the sperm to another European Union country, where the fertilization and insemination can take place.

The proscriptions on germ line intervention were largely academic but edged toward more concrete form in 1995, when Donald Rubinstein and colleagues proposed "a nine step protocol at the germ-line level for the curative treatment of a genetic disorder."[48] The protocol was unexpected because it focused on mitochondrial disease, thus framing germ line intervention in a new way.

Mitochondria are small membrane-enclosed organelles inside most cells in the body. They contain several dozen genes, some of which cause diseases when mutated. Mitochondria are not inherited with the other chromosomes, but reside in the mother's egg at time of fertilization, and so inheritance is exclusively maternal. All children of an affected woman are at high risk, although expression can be variable, depending on the severity of the mutation, on whether all mitochondria are mutated or there is a mix of mitochondrial gene types, and on modulation by other genes.

The proposed protocol would fertilize the egg of an affected woman with her husband's sperm, thus making the nuclear genes the usual 50-50 mix of mother's and father's genes. The nucleus of the mother's egg would be removed, however, and placed into the enucleated egg of another woman before fertilization. This would replace the mother's cytoplasm, containing the mutated mitochondria, with the donor woman's just before fertilization. Like other children, the resulting child would retain the nuclear genome of the mother and father but all mitochondria would derive from eggs of the donor woman.

The child's cells would be genetically altered, but not in the way most writers addressing germ line intervention have assumed. This protocol entails manipulation of an egg and not an embryo, but depending on details of language, the technique might or might not be covered by proscriptions intended to thwart embryo research and *in vitro* fertilization. The technique certainly causes inherited changes in subsequent generations, and in that sense is a germ line manipulation. It does not entail recombinant DNA, however, and so would not be subject to RAC review unless

voluntarily submitted to it. It would be subject to Institutional Review Board (IRB) review if conducted at an institution that receives federal funding for research under an agreement with the OPRR, and is thus governed by the U.S. human subject protection regulations. (The reported pregnancy under way using this technique, or a similar one, was apparently undertaken by a private institution. I have no direct information about it, even about whether it is taking place in the United States, nor is the case publicly known). This technique is very likely a criminal act under the German law, which addresses genetic alterations, and also perhaps a Danish law, which addresses manipulations of all or part of an embryo (although since the nuclear transplant takes place before fertilization, it might be exempt). Because it would alter the genetics of an embryo, it appears to be outside the range of experiments that can be licensed in the United Kingdom.

The couple's intent might not be a cure for future generations, but only to rid their genetically related child of consequences from the mother's mitochondrial mutation. If male, the child would not pass his mitochondria on. But any female child would pass the mitochondria inherited from the donor woman's enucleated egg. The technique deliberately induces maternally inherited changes intended to avoid mitochondrial genetic defects, and would be transmitted via germ line (egg) cells. It is, in this sense, germ line gene therapy and would be proscribed by most formulations of bans on germ line manipulation. It is not, however, gene splicing of the kind that was debated and intended to be stopped by those bans. It is hard to argue that the mitochondrial genetic changes carry the moral risk that lies beneath the germ line gene therapy debate, and the case for state intervention seems weak. Yet it is easy to construct reasonable scenarios in which a woman might well want to avoid mitochondrial disease while retaining the benefits of having genetically related children.

If the technique were proven safe in animal experiments (and the developmental safety considerations about mitochondrial inheritance are considerably less worrisome than nuclear genes, so considerations raised earlier do not pertain), then this scenario could present a case lesson in the dangers of premature bans. The desire of a woman (and man) to have a healthy genetically related child could be pitted against existing germ line legal constraints. It is not entirely clear what harm the constraints would be preventing in this scenario, and hard to construct much public benefit, but the damage to the couple's reproductive liberty is quite clear.

In the United States, RAC could simply remove the "will not entertain at present" language in its guidelines by administrative fiat after announcing publicly its intention to do so, or it might choose to construe the protocol as a gene therapy protocol to cure a specific child that has the inadvertent effect of causing changes that female offspring would transmit to their progeny. Most scenarios for use of the technique, however, would not even require RAC review at all, unless the mitochondrial or nuclear genes were altered using recombinant methods. RAC might nonetheless accept such a protocol for review, and judge its safety and technical prospects for success. In the United Kingdom, the licensing authority could also possibly consider the case, subject to interpretation of its statute. In Germany, respecting the couple's reproductive choice would entail a criminal act. Changing the law would require a public process and considerable delay. It would also put a private family decision on public display, and potentially threaten the

personal privacy of the couple if names and other details came to light. Altering national statutes to accommodate reasonable clinical investigations, in any event, seems an awkward route to sensible public policy.

LESSONS FROM OVERSIGHT OF FETAL RESEARCH, RECOMBINANT DNA RESEARCH, AND HUMAN GENE THERAPY

The legislative and bureaucratic history of fetal research is all well and good, but what has it meant to research? Has it led to a real moratorium?

The various legislative bans on federal funding were never expected to block all scientific research on *in vitro* fertilization. If the intention were to ban all human cloning, then this moratorium on federal funding is not the appropriate model. Private sector activity was anticipated and understood by lawmakers to be going on. In many respects, the situation now is much as OTA reported it a decade ago. The federal moratorium has shifted *in vitro* fertilization and related research to private centers that do not receive federal funds for research on human subjects, and so can conduct work outside 45 CFR 46. Thus most of the work takes place outside the research mainstream. With the possible exception of some research undertaken by Mark Hughes that overlapped with activities funded by the National Center for Human Genome Research last year, however, the federal moratorium appears to have held. (The Hughes case may or may constitute an infraction. Federal funding for Dr. Hughes was cut off when this came to light, but the nature, extent, or even existence of work that was federally funded and fell afoul of federal guidelines has not been publicly disclosed. A congressional inquiry has been initiated).

For most of the past 23 years, a ban has remained in place for federally funded *in vitro* fertilization and fetal research of more than minimal risk. This ban has been punctuated by two periods when proposals were considered for federal funding—1978–1980, when the EAB existed to review proposals (including some fetoscopy studies that were approved), and 1994-1995, when NIH assembled a panel to consider what criteria should guide funding for fetal research. The boundaries of the moratorium have shifted slightly with the shift from NIH authorization statute to executive branch back to NIH authorization to ban removal to new bans imposed by annual appropriations. Fetal research has proven irresolvable within Congress, and has provoked repeated fights. With a shift to the appropriations committees, such fights can now be expected to take place every year, meaning more or less continually.

The various moratoria on fetal research were initially imposed by Congress, and subsequent moratoria were either due to actions of Congress or decisions not to act by Secretaries of Health and Human Services (in several cases over the years, usually to spare the President from precipitating controversies that policy change would entail). The various bans were imposed because of ethical concerns, not biohazard danger to patients, or lack of informed consent. The dangers were not palpable to the investigators whose freedom of inquiry was constrained. The risks were to unborn fetuses, and for early embryonic research in particular, the moral standing of the "research subject" was a matter of moral belief, often grounded in theology.

Yet biomedical researchers are by occupation empirical sorts, intellectually contentious and skeptical of assertion not grounded in experiment. Fetal research moratoria have been fought over by factions in Congress and among political appointees in DHHS, and recently joined by the President himself. The terms of the debate have not been framed as risks that might be empirically assessed, as was possible with recombinant DNA. The debate on fetal research has been largely derived from the savage and divisive policy debates over abortion.

Congress has not been able to resolve the controversy, but instead has been itself poisoned by it. With the shift of the moratorium to appropriations language in 1995, the rancorous debate can now affect funding for all of DHHS and the Departments of Labor and Education, bundled with NIH in the same appropriations bill. The shift to appropriations was made because disagreement blocked NIH authorization. NIH has a standing permanent authorization that lessens the need for reauthorization. The funding bills must pass each year, however, one way or another. With authorization blocked, the fetal research battle shifted to the appropriations process. In the past two years, the fetal research provision has been one major reason that a Labor-HHS-Education Appropriations Act has not been passed as a separate law, but instead has been lumped with other incomplete funding bills as the new fiscal year threatens to dawn. With linkage to the appropriations process that must go forward every year, and always faces a daunting schedule, fetal research funding could escalate from a nasty intermittent sting to a hardy perennial controversy.

Fetal research bans and the recombinant DNA moratorium followed by guidelines were research constraints that originated from different sources for different reasons. Both sets of constraints, however, were respected for the most part. In the case of recombinant DNA, this was at first because of genuine concern about biohazard, soon followed by an understanding that a breach of the guidelines could undermine public faith and threaten the research effort. The guidelines were followed not only for federally funded work but on a voluntary basis by those doing research with private funds. While this paper summarized a few infractions and alleged infractions of the recombinant DNA guidelines, the main story here is the remarkable success in creating guidelines that adapted to new knowledge and were for the most part respected throughout the scientific community.

In the case of fetal research, the federal ban has not extended to the privately funded research sector. Many in the research community do not regard the federal ban on *in vitro* fertilization research and fetal research as prudent, but the ban has held out of respect for the legal line-drawing by Congress and surely also some fear of the impact that violating the ban might have on other research. Because of contending moral values, however, this ban is a constant source of conflict.

Respect for constraints on research involving human subjects, in contrast, runs strong and deep. Respect for persons involved in research is fundamentally different from the speculative risks of biohazard attending a new technology or the moral values embedded in a fetal research ban. The human subject regulations derive from principles well understood even before the

Nuremberg Code.[49] The human subject regulations are an accepted fact of modern research. The relevant U.S. regulations, 45 CFR 46, are just two decades old, but two generations of investigators now regard them as a matter of course that ultimately strengthen research. Many conceivable experiments that could produce interesting data simply are not done. Moral boundaries are respected; they may be porous, but they are constantly patrolled by Institutional Review Boards. The Advisory Committee on Human Radiation Experiments discovered that the IRB system is far from perfect and some unethical experiments still proceed (Advisory Committee on Human Radiation Experiments 1995, 97)—and this is one reason for NBAC's existence, to continue an unfinished agenda of human subject protections. There can be little doubt, however, that norms of clinical research have changed over the past few decades.

LeRoy Walters, in responding to a previous draft of this paper, noted that the RAC process could take on even the world's best known experts in an emerging and highly conspicuous field, in part because of its process and stature. Success may have depended on several features of the RAC process (Walters 1997, 98):

open public meetings,

involvement of nationally recognized experts,

expertise spanning biology, medicine, law, ethics, public policy, and consumer advocacy,

appointment of experts familiar with the field but not direct competitors,

use of expert *ad hoc* consultants when needed,

rotation of membership,

regular and accurate coverage by the public media, and

frequent revision of the "points to consider" document.

One lesson from the Cline case is that when the potential rewards are exceedingly large, human subject protections are all the more important, because scientific priority and fame are powerfully seductive. The Cline case tested the IRB and recombinant DNA review processes. The punishment meted out was swift and fair. Cline remained a scientist, but was stripped of his chairmanship, lost several grants, and found getting grants much harder than before his infraction. The main damage was to his reputation and ability to do science. Few molecular biologists would fail to recognize Martin Cline's name even after more than a decade and a half. His censure was meaningful to the scientific community. If indeed Dr. Cline's actions were driven by a desire to enhance his reputation, then the penalty that mainly damaged that reputation was appropriate and proportionate.

SOME PERSONAL OBSERVATIONS

A proposed moratorium on human cloning would share with fetal research a grounding in public outrage over what is much more a moral than a technical or public health concern. The purpose of a human cloning moratorium would be to prevent a moral wrong rather than to save lives or forestall biohazard. Arguments for a human cloning moratorium also hinge on theological and moral beliefs, as abortion and thus fetal research positions often do. The moral standing of the resulting human beings, however, is not in question, and so, unlike the debate about fetal and embryonic research, disagreement about personhood should not be as central, and theological tenets may be less likely to confront deep social divisions. This might diminish the passions, and it may also reduce pressure to impose a moratorium in the first place. Unlike fetal research, however, the object of a moratorium might well be to block *any* human cloning, not just the use of taxpayers' money in its pursuit.

If the object of the effort is to stop all cloning, not just experiments funded by the federal government, then *in vitro* fertilization and fetal research are poor models. Since it is currently difficult to foresee any compelling reasons to go ahead with human cloning, then the main intent of a moratorium might be to thwart an egocentric billionaire. If in some currently unimagined scenario, some benefit could be postulated, then the IRB system, if supplemented by a mechanism for review and debate at the national level, might well be up to the task, addressing the policy concern with only the need to strengthen national review of the existing human subject protections. If that is the problem being solved, then a moratorium on federal funding similar to the one on fetal research would be useless.

The UCSF story paradoxically suggests that a moratorium can matter a great deal, not just because it changed scientists' behavior, but also because it distorted the rules of scientific competition in surprising ways, and planted a seed of discord that is now a factor in patent rights still being decided by federal courts two decades later.

There are limits to the respect scientists will accord a research constraint if they believe strongly in the potential knowledge to be gained. If the recombinant DNA guidelines had been more burdensome, less flexible, or (worse) scientifically suspect, the walls would likely have been breached more than the two times we know about (once deliberately, once inadvertently). Although biohazard was initially perceived to be real, with time the risks appeared more and more speculative while the power of the technology became more apparent. And the rewards were sweet. The races to clone mammalian genes were high stakes. It was one thing to hold position for a few laps under the caution flag, quite another to put a permanent governor on the engine.

If Martin Cline had only violated the recombinant DNA guidelines, his violations would have seemed far less significant. In fact, his case is telling in three regards. First, the recombinant DNA portion of the infraction said more about truth-telling—how Dr. Cline dealt with his collaborators and the people he was "treating"—than it did about the validity of the recombinant DNA guidelines. They were intended to prevent biohazard, but in this case they may have mainly

contributed to weakening an already questionable experiment. When the initial guidelines were extended into the clinical realm, before the Human Gene Therapy Working Group began to grapple with the specific issues in gene therapy 1983, the guidelines were poorly suited for clinical experiments. Second, the bureaucratic decision to exempt the experiment from review was perverse because it removed scrutiny while weakening the likelihood of clinical benefit, which was already extremely low. Third, and most on point when contemplating rules governing human cloning, the Cline case revealed the pathologies of multiple parallel reviews.

Dr. Cline's experiments were either safe and likely to work or not, and the most important considerations were those that an IRB should review, not whether recombinant DNA was involved or not. Yet the local UCLA IRB encountered serious difficulty in reviewing the protocol, in part because it was an experiment with national, even worldwide implications, but review was local. When RAC shifted to reviewing human gene therapy, it in effect became a national IRB for such experiments. This was highly beneficial for the science and for the protection of the human subjects involved, for several reasons. Human gene therapy has always been "hot," and those who do it are local stars because they attract money, prestige, and publicity. It can be difficult for local IRBs to contend with the local star, but when review moves to the national level, NIH can bring in the nation's best minds without worrying as much about local impact. The procedures generally get more thorough technical review at a higher level of expertise. The RAC process is open and visible because unlike FDA review it is public. And it is credible and accountable because the deliberations are covered by the media, especially when major decisions are made or when controversies come to light. It is good for the science because the right information is gathered to comply with the "points to consider" document, which was itself drafted and revised following an open process.

These positive aspects of gene therapy review highlight the consequences of not having an EAB to perform the same functions for other kinds of research. Gene therapy demonstrates that a national IRB can function, despite the fact that RAC was technically operating under recombinant DNA guidelines rather than human subject regulations. Yet this came to be only because the trivial and marginally relevant fact that recombinant DNA was involved in gene therapy. That fact enabled a national committee to construct a document that addresses the same points IRBs should be concerned about.

If NIH had clicked its heels twice, it could have had a review process for difficult research issues all along. The successful national review model grew out of recombinant DNA, but if history were logical, it should have grown out of the human subjects' protections. In the past decade, NIH has careened from crisis to crisis about embryo and fetal research, research involving the cognitively and emotionally impaired, and fetal tissue research. FDA has been excoriated over its handling of RU486, use of placebos in drug trials for schizophrenia, and insufficient regard for AIDS patients and cancer patients to get access to clinical trials. Yet the nation has in its handling of gene therapy a credible model for a transparent and accountable system of national review. The lesson for NIH is the need for the ability to convene national-level IRBs to review particularly vexing research areas. The lesson for FDA is to make its rulemaking and deliberations more open.

The lesson for human cloning may be that it is just one of many possible issues to arise in doing research that involves people or people-to-be. Creating another *ad hoc* committee or new process may well create the kinds of bureaucratic difficulties, with ambiguously overlapping jurisdictions that appeared in the Cline case.

All three efforts to impose research moratoria must confront an uncomfortable fact: they work well in general but may be violated by isolated individuals.

As a final personal opinion, the temptation to blend functions of national deliberation and analysis with review of complex research protocols that raise difficult issues should be resisted. The gene therapy review process under RAC served well by first posing the right questions about clinical protocols and then reviewing protocols. On a few occasions, RAC has also attempted to mediate a national debate, but with no success comparable to the National or President's Commissions. The Ethics Advisory Board also issued some reports, as well as serving to review protocols, but these reports did not have nearly the impact of the National and President's Commissions. The National and President's Commissions, the radiation experiments committee, and now NBAC are spared the review of specific protocols, so they can commission papers, discuss options, and concentrate staff effort on gathering information, writing reports, and the business of policy analysis.

The Ethics Advisory Board did a bit of both deliberating and protocol review. It was arguably closer to success in protocol review than effecting change through its reports. The Ethical, Legal and Social Implications Working Group of the NIH and DOE was successful in helping launch a research program, but had minimal success in its policy forays—with scant publication and no systematic information gathering, report writing, document review, or other features associated with credible policy analysis. The Ethics Advisory Board, as laid out in the 1988 proposed charter, would have mixed analysis with the traffic cop role. So would the EAB functions laid out by the 1993 NIH reauthorization. We have examples of successful public policy deliberation about topics in bioethics, and relatively successful review processes for protocol review for human subjects protections and for gene therapy; but models for doing both are not promising.

NBAC's engagement with the human cloning question demonstrates the virtues of having a deliberative commission in place. NBAC was there to catch the ball. The key missing element seems to be national protocol review. The local infrastructure for human subjects review already exists in the form of IRBs, but the national superstructure of an EAB does not. If concerns about human cloning justify further action, the most pressing need may be to formulate guidelines or terms of a moratorium or ban, and then to review protocols if benefits are plausibly in prospect. This is just what the gene therapy working group did fourteen years ago. In that case, the fear was that without such guidelines, the technology would rush ahead. In the case of human cloning, there seems no pressing clinical or other practical need for the technology but rather a need for reassurance that whatever progress occurs in genetics and cloning technology, there is a credible process for assessing its technical merit and social impact before experiments are tried.

APPENDICES
APPENDIX A: THE UCSF CASE

The UCSF infractions of recombinant DNA guidelines were caused by confusion over regulatory permission to insert mammalian genes into the recombinant plasmid pBR322, named for Francisco "Paco" Bolivar of Mexico and native Californian Raymond Rodriguez. Bolivar and Rodriguez were postdoctoral researchers working in Herbert Boyer's laboratory who designed a circular DNA molecule (plasmid) that dramatically simplified gene cloning. It contained genes to enable selection of bacteria containing it, with a gene conferring penicillin resistance and another gene for tetracycline resistance whose disruption by insertion of a foreign DNA would cause bacteria to stop growing but not to die. It also had splice sites for a variety of DNA-cutting enzymes.

Many of the cloning vectors still used today are direct descendants of this cleverly craf-ted plasmid. It was easier to use than other vectors available at the time, and Bolivar and Rodriguez also reasoned that it would be less liable to pass from bacterium to bacterium, reducing the risk of proliferating outside deliberate control. But it was also new, and the RAC review process meant formal certification, with review by the committee and formal certification by the NIH director. Confirmation of the plasmid's safety awaited data produced by Stanley Falkow and Jorge Gros at the University of Washington. The data showed pBR322 plasmids in weakened bacterial strains to be "the safest plasmid-host systems currently available."[50] Those data were not available until May 1977, and the vector was not certified until July 7.[30]

The competition to clone mammalian genes was intense. Gene jockeys were not so named just because of alliteration. Molecular genetics was characterized by long hours, and as a marathon neared the finish line—the cloning or sequencing of a gene, for example—work went on around the clock. The insulin race was particularly competitive, with a UCSF group contending with Walter Gilbert's Harvard crew, another group at the City of Hope Hospital, and who knew who else? The urge to use the technique most likely to work best and fastest was strong. This day-by-day, hour-by-hour competition was a stark contrast with the quarterly RAC meetings.

Boyer attended a Miami Winter Symposium in January 1977, and the RAC was scheduled to meet afterward. Boyer had sent a letter requesting approval of pBR322 in December 1976. The RAC met January 15-17. It provisionally approved pBR322, but RAC wanted more data before certification by the NIH director. Boyer phoned from Miami to Rodriguez in the UCSF lab with the news. Rodriguez phoned Ullrich. Ullrich proceeded to begin the multi-step cloning procedure, starting from some isolated DNA thought to contain rat insulin genes. By the end of February, he thought he had the gene. Howard Goodman then attended a conference in Park City, Utah, where RAC's executive secretary, William Gartland, unambiguously stated that pBR322 was not certified for use. Goodman then knew for sure the experiments had violated the recombinant DNA guidelines.

Just days before the Washington NAS meeting that began this paper, Ullrich confirmed he had cloned the insulin gene by examining DNA sequence data from one pBR322 clone. After an

internal debate among UCSF collaborators, Ullrich destroyed bacteria containing the pBR322 vector with its insulin-gene inserts on March 19.[1, 27] He cloned insulin in another vector, pMB9, after that vector was certified in April. That cloning effort was announced in May 1977 and published in *Science* that June.[51]

These parts of the story are not contested. Appendix C, the federal district court's decision, includes information about what happened after it became apparent an infraction had occurred. The contested findings cover a few points relevant to this paper—what was done with any DNA *derived from* the insulin-containing pBR322 constructs (as opposed to the destroyed bacterial clones), the chronology of events, the accuracy and completeness of various statements about these events, and the disposition of patent rights.

Had the violations come to light in the spring of 1977, the legislative outcome might have been different. Congress was considering bills to impose more stringent and permanent constraints on recombinant DNA research. NIH director Fredrickson was doing all he could to keep review flexible and locate it at research institutions to the degree possible. The Washington clamor was at a perilous juncture. From Fredrickson's perspective, if the scientists didn't like RAC, they should try what Congress had in mind. News of the UCSF violation at this critical juncture might have scuttled the strategy and led to legislation with more central and less flexible review.

Analysts offer several different reasons for the loss of momentum for legislation. First, RAC began to operate and its initially technical membership was broadened to include nonscientists. At the same time, scientific consensus began to grow that the dangers of inadvertent biohazard (as opposed to deliberate biological warfare engineering) were quite low. Gene exchange that took place in nature even without recombinant DNA was demonstrated. And the first successes in gene cloning, including the insulin and growth hormone genes, were announced.[18, 52] Those successes shifted some attention from possible risks to obvious benefits. Finally, the scientific community mounted a spirited lobbying effort against legislative action, spearheaded by Harlyn Halvorson, a former president of the American Society of Microbiology.[19]

Had the UCSF events become widely known as they occurred or soon after, they could well have undermined the RAC process even as it was just getting started. Or they might not have undermined confidence, if it were clear that the infraction was obviously inadvertent. Faith in scientific self-regulation was arguably the most important factor attenuating calls for legislation and stringent regulation—but this case might have played out as an example that scientists could not be trusted, or that the processes worked to surface and remedy even minor infractions. The impact of public disclosure of the inadvertent infraction might well have turned on how it was handled at least as much as what had actually occurred. An open and transparent process is generally more credible than a secret and opaque one. One thing is clear, however. In retrospect, heavy-handed regulation or inflexible statutory restrictions on recombinant DNA research would have been a serious error, as recombinant DNA research has proven enormously useful scientifically as well as and socially valuable. The putative biohazards have not proven substantial. The lesson here is not that the recombinant DNA guidelines did not work, only that they

influenced the conduct of science and that procedures for communicating them, investigating infractions, and enforcing compliance were incomplete.

APPENDIX B: THE CLINE CASE

This account of the Martin Cline case is mainly based on Larry Thompson's book *Correcting the Code*,[53] as supplemented by NIH case files[54] and old OTA files.

On July 10, 1980, Dr. Martin J. Cline infused 700 million blood cells treated with recombinant DNA into Ora Morduch, a 21-year-old Iraqi Kurdish Jew and patient activist living in Israel. The experiments took place at Hadassah University Hospital. The treatment was repeated the next day. Each treatment involved taking blood cells, incubating them with calcium phosphate in the presence of the DNA, radiating Ms. Morduch's bone marrow with 300 rads to kill native cells, and reinfusing the treated cells. On July 15 and 16, at the University Polyclinic in Naples, Italy, Dr. Cline administered a similar treatment to Maria Addolorata, a 16-year-old from Torino, except that a smaller body surface and lower dose of radiation were used (200 rads). The next day, the University of California, Los Angeles, IRB rejected Dr. Cline's proposed clinical protocol.

The IRB action culminated a 14-month struggle. In May 1979, Dr. Cline and his UCLA collaborators submitted a clinical protocol to the UCLA IRB proposing gene therapy for sickle cell disease and other hemoglobin disorders. This was based on a mouse experiment in which cells treated with recombinant DNA (by incubating them with DNA precipitated in calcium phosphate and rendered porous by electrical currents) were inserted into mice whose bone marrow had been entirely killed by radiation. The mice were also treated with the cell poison methotrexate that killed cells unless they had taken up the recombinant DNA—containing the globin gene linked to one that conferred resistance to methotrexate. Under this strong selection, the mice expressed low levels of the globin gene transiently.

Dr. Cline was chairman of the department of hematology at UCLA. The department had a history of several confrontations with UCLA's IRB. Moreover, the protocol was initially subject to both IRB review and the local Institutional Biosafety Committee, which oversaw compliance with recombinant DNA guidelines. The committees initially deferred to one another. Cline and collaborators decided to avoid the biosafety committee, and thus the recombinant DNA guidelines, by fragmenting the DNA before insertion into patients, so it would not longer be "recombined" in a vector. This modification, while avoiding a bureaucratic impediment, was arguably both more dangerous and less likely to provide benefit because chromosomes tend to incorporate such DNA fragments as large redundant arrays. Since one concern was gene regulation, and such tandem arrays are even less subject to control than single copies, this element could have introduced a new risk of unregulated gene expression. At the least, this needed testing. This protocol as proposed for human patients was never tested in animals, nor was the experiment without full-body radiation and without methotrexate selection, although these were essential features of the human experiments.

The IRB initially requested external expert review of the protocol, but Dr. Cline resisted, wishing to keep his ideas secret from scientific competitors. The back-and-forth led Dr. Cline to

propose the IRB seek advice from an expert panel. The four external consultants who reviewed the experiment were picked after Dr. Cline was allowed to reject direct competitors. All four consultants judged the experiment as premature.

In the experiments he conducted in Israel and Italy, Dr. Cline decided to go ahead and use recombinant DNA instead of cutting it into fragments as promised. He lacked facilities to fragment it, and did not personally know how to do it as proposed in the UCLA protocol. His promises not to use recombinant DNA had proved important in the review process at Hadassah University Hospital, and he had also told both patients no recombinant DNA would be inserted. This feature was again bureaucratically significant, but technically unsound.

Rumors about gene therapy having been tried in Israel percolated among research hematologists between July and October 1980. An NIH scientist also interested in gene therapy, W. French Anderson, heard about the rumors. He talked to the resident bioethicist at NIH's Clinical Center, John C. Fletcher, who decided to call Dr. Cline. He caught up with him by phone at a Montreal hotel. Fletcher told Cline about the rumors that Cline had attempted gene therapy in Israel, and he should come tell the facts to NIH officials if he had done so. At the end of an equivocal conversation, Cline denied having done such experiments.[53] On September 8, Charles McCarthy, director of NIH's office for overseeing human experimentation, wrote a letter to UCLA Chancellor Charles E. Young asking whether Dr. Cline had performed gene therapy experiments. In October, *Los Angeles Times* reporter Paul Jacobs broke the story on the front page, having checked with sources in Italy and Israel and with scientists who had been part of the rumor mill.

This began a series of investigations at UCLA and NIH, which culminated in May 1981, noting the first-ever documented transgression of the human subjects guidelines and also a violation of the recombinant DNA guidelines. Dr. Cline had by then resigned as department chair. The NIH reviewed his ongoing grants, terminated several, and required that future applications for clinical research, recombinant DNA research, and NIH funding should include the NIH committee's report on the investigation.[36]

Several factors cast doubt on Dr. Cline's own account of why he did the experiments: (1) he went abroad to do the experiments after being rebuffed at UCLA, (2) he did them knowing that in all likelihood the protocols would be rejected by the UCLA IRB, (3) he lied about using recombinant DNA to his collaborators and to the patients (setting aside the technically sound judgment that it was more likely to work), (4) he lied to John Fletcher about having done the experiments at all, and (5) he tried to convince his UCLA collaborators to keep mum about using recombinant DNA when the story broke.

Dr. Cline's contention that he acted with the best interests of the patients foremost in mind is undermined by his failure to tell either patient what he was really doing, his failure to produce evidence in advance about the possible harms that could come from overexpression of beta globin

in cells, the extremely incomplete animal model and human *in vitro* data, and his characterization of the trials as phase I.

Phase I trials are intended to test the safety and toxicity of drugs, usually by escalating dosages until side effects emerge in healthy patients. Testing for safety and toxicity in seriously ill patients is nonsensical, as their generally fragile health makes it impossible to know whether ill effects are due to the drug or the severe underlying disease. The Israeli case bears out this point: soon after the experiment took place, Ora Morduch entered the hospital in arrhythmic crisis and could have died. This was much more likely to be caused by excess iron in her heart muscle cells than Dr. Cline's treatments. But who could know? The Cline experiments taught nothing about the toxicity of the methods, and could never have been expected to do so.

The proper framework for the experiments is "compassionate use," referring to innovative therapy for patients with no better alternatives, and so even a small potential benefit can be acceptable. In this framework, the decisive factors are the unavailability of alternative treatments and the plausibility, even if small, of clinical benefit. The Cline experiments fail on both counts. Iron chelation therapy in conjunction with blood transfusion was being tested as Dr. Cline did his experiments. Indeed both patients eventually got and greatly benefited from those treatments, both surviving for more than a decade. Gene insertion was exotic and unlikely to work compared to chelation therapy.

Regarding the potential clinical benefit of inserting genes, the situation was at least as bad. First, exposing both legs to 300 rads of radiation (Israel) or 200 rads (Italy) could harm the patient and certainly could not help, except to "make room" for the infused cells, but this part of the protocol had never been tested. Second, credible evidence would have required either closely similar experimental data from animals or tissue culture evidence of gene expression using the same procedures on human cells. Yet even strong selection in the mouse experiments (total body radiation to kill all marrow cells followed by methotrexate selection) led to only low gene expression for a short time. Dr. Cline's clinical experiments in Israel and Italy involved a much smaller proportionate influx of cells and no selection. And although his Italian collaborator did indeed test gene expression *in vitro*, Dr. Cline did his experiments in patients before those results were known.

APPENDIX C: EXCERPT FROM UNIVERSITY OF CALIFORNIA V. ELI LILLY AND CO.

Source: *U.S. Patent Quarterly* 2d, Book 39, from "A. The '525 Patent" on pp. 1248–1254.

Some background information concerning research involving recombinant DNA must precede discussion of this issue. In the early 1970's when experiments in the area of recombinant DNA were first contemplated many people, including some scientists, were concerned that such experiments might pose medical threats to humans. Tr. at 1295. The National Academy of Sciences eventually "called for a broad moratorium on all recombinant experiments until they could be . . . better reviewed by the scientific community." Id. At a subsequent review of recombinant DNA research in 1975, it was suggested that experiments in that area might proceed if suitable guidelines were promulgated to govern the research. See Lilly Ex. 3547 at HG2 580773.

Consequently, the Recombinant DNA Molecule Program Advisory Committee, previously established by the Department of Health, Education, and Welfare's National Institutes of Health (NIH), held its first meeting to develop safety guidelines. Id. Those guidelines were issued by the NIH on June 23, 1976, and published in the Federal Register on July 7, 1976. Tr. at 1296, 1298; Lilly Ex. 3731 at 000004; Lilly Ex. 3547. "The NIH Guidelines establish [ed] carefully controlled conditions for the conduct of experiments involving the production of [recombinant DNA] molecules and their insertion into organisms such as bacteria." Lilly Ex. 3547 at HG2 580773. For example, the regulations classified types of biological containments (i.e., plasmids) and specified which ones could be used in certain recombinant DNA experiments. The regulations also governed the type of physical containment facilities (i.e., laboratories) in which scientists could conduct particular types of experiments. The safety guidelines mandated that no plasmid could be considered to fall within an approved classification until it had been certified by the NIH Recombinant DNA Advisory Committee. Tr. at 1301.

The guidelines also stipulated that any institution receiving NIH funds was to appoint a principal investigator. Under the guidelines, the principal investigator had certain responsibilities, including "supervising the safety performance of the staff to ensure that the required safety practices and techniques [were] employed" and "investigating and reporting in writing to the NIH Office of Recombinant DNA Activities and the institutional biohazards committee (or biosafety committee) any problems pertaining to operation and implementation of biological and physical containment safety practices and procedures, or equipment or facility failure." Lilly Ex. 3547 at HG2 580791. The guidelines governed the conduct of all NIH supported research in the area of recombinant DNA. The research UC was conducting on rat insulin the research that formed the basis of the '525 patent was NIH-supported. Consequently, UC was to operate within the strictures of the safety guidelines.

By January of 1977, the NIH only had certified the plasmids denominated pSC101 and pCR1 for experiments with mammalian DNA. Tr. at 1301. According to Rutter, UC scientists

delayed their recombinant DNA research, awaiting the NIH green light on use of a more advanced vector either pMB9 or pBR322. Tr. at 127. Rutter said UC representatives preferred to use pBR322. Id. Reportedly, that vector would be the most effective cloning agent. Id. On April 18, 1977, the NIH certified plasmid pMB9 as safe. Lilly Ex. 3554A at 177. On July 7, 1977, the NIH certified plasmid pBR322. Id.

Lilly contends that UC researchers knowingly used a plasmid not yet certified for use PBR322 in conducting its rat insulin experiments. Moreover, Lilly argues that UC researchers misrepresented the origins of their rat insulin data to the public, the NIH, the United States Senate and the PTO in order to conceal their misuse of plasmid pBR322. According to Lilly, the UC researchers' misuse of the plasmid and misrepresentations of the origins of their data are material to patentability of the '525 patent, and the misrepresentations of their data were intended to mislead the PTO. Thus, Lilly argues, a finding of unenforceability based on inequitable conduct is appropriate.

Clearly, UC's scientists used pBR322 in their research before the NIH had certified that plasmid for use. In January of 1977, working in Goodman's laboratory at the University, Ullrich began using pBR322 in his recombinant DNA experiments. Ullrich testified that he began using the plasmid after a colleague informed him by telephone that the NIH had approved pBR322 for use. Tr. at 79798; Lilly Ex. 3420 at HG 002878. The record indicates that prior to his use of pBR322, Ullrich informed Rutter that he had heard pBR322 was approved and that he intended to proceed with his experiments. Dr. Rutter concurred with Dr. Ullrich's plan, without further verification of the status of pBR322. Lilly Ex. 3420 at HG 002870.

Subsequently, during a February 4, 1977, meeting, certain UC researchers including Ullrich and Shine learned that although approval of pBR322 had been recommended, the NIH director's requisite certification of the plasmid as safe had not yet issued. Lilly Ex. 3420 at HG 00287172. Ullrich averred that he earlier had not been aware of the distinction between approval and certification. Tr. at 800. Thus, UC's premature use of pBR322 through February 4, 1977, was a violation of the NIH guidelines, but it was not necessarily an intentional violation.

The record, however, illustrates that UC researchers did not halt their use of pBR322 and/or the fruits of previous experiments with that vector after learning that pBR322 had not been certified. In fact, UC agrees that the experiments continued until at least March 3, 1977. Lilly Ex. 3420 at HG 002871. In its report to the Office of Recombinant DNA Activities (ORDA) concerning UC's premature use of pBR322, UC's biosafety committee stated:

At this [February 4] gathering, the investigators in Dr. Goodman's laboratory (including Drs. Ullrich and Shine) reportedly learned for the first time that there was some confusion about the status of pBR322 . . . However, the initial cloning experiments with pBR322 and insulin cDNA had been completed, and clones had been obtained. After February 4, no new clones were constructed, but those already obtained were grown up and examined for the presence of recombinant DNA.

There is no satisfactory explanation as to why the investigators in Dr. Goodman's laboratory continued experiments with these recombinant plasmids after February 4.

Lilly Ex. 3420 at HG 002872. Moreover, when questioned at trial, Ullrich did not deny use of pBR322 after learning that it had not been certified. Tr. at 824. We find that the record clearly supports Lilly's contention that UC knowingly violated NIH safety guidelines when its researchers continued to use pBR322 in recombinant DNA experiments even after learning that the plasmid had not yet been certified for use.

Additionally, neither Rutter nor Goodman officially reported the unauthorized use of pBR322 to the NIH after the time they became aware of the prohibited use. Rather, Rutter testified that he had an informal telephone conversation with Dr. DeWitt Stetten, NIH deputy director for science, and that he and Stetten ultimately decided against a formal disclosure of the incident. Tr. at 12930. In fact, Rutter testified that the conversation between Stetten and himself "was carried out in a deliberate way to convey the fact, but not to create a need to disclose . . . [t]o make a formal disclosure . . . There was no formal disclosure." Tr. at 246. Rutter also testified that during the conversation, Stetten and Rutter decided that the pBR322 clones would be destroyed. Id. at 131. This conversation reportedly occurred sometime between March 1619, 1977. Lilly Ex. 3420 at HG 002873.

Furthermore, neither Rutter nor Goodman informed UC's own biosafety committee of the misuse of pBR322. Rather, Dr. David Martin, then chairman of UC's biosafety committee, "heard rumors" of the incident through a technician in Rutter's lab sometime in May, 1977. Tr. at 227; Lilly Ex. 3420 at HG 002874. Martin then discussed the matter with Rutter and Goodman. Id. At a June 3, 1977, biosafety committee meeting, Martin reported the UC scientists' use of pBR322. However, an examination of the minutes of that meeting indicates that the committee was not informed fully of the events that had occurred. As UC stated in its committee report to the NIH, [t]he failure of the Biosafety Committee to notify the NIH of the pBR322 incident was primarily a consequence of the fact that the Committee itself was unaware of the details and import of the event. On the basis of the information the Committee had at that time, it was not aware that a violation had occurred. Lilly Ex. 3420 at HG 002874.

Thus, it is obvious that UC representatives did not formally report UC's researchers' violation of the guidelines to the NIH, nor did they provide a detailed explanation of the incident to UC's biosafety committee at its June 3, 1977, meeting. Events occurring later, however, brought the incident to the surface.

On September 9, 1977, Nicholas Wade, a Science reporter, called Dr. William Gartland (Gartland), director of ORDA, asking questions about UC's alleged use of an uncertified plasmid. Lilly Ex. 3731 at 000095. Wade stated that he was writing an article about the pBR322 incident an article that subsequently was published in the September 30, 1977, issue of the publication. Id. at 83, 87. Gartland apparently first learned of UC's inappropriate use of the plasmid during Wade's telephone call to him. Id. at 83.

On October 11, 1977, Gartland wrote Dr. James Cleaver, chairman of UC's biosafety committee, asking for an accounting of the incident. Lilly Ex. 3731 at 00008889. Cleaver responded on October 25, 1977, including in his response a memorandum authored by Goodman and Rutter detailing, as they recollected, the events surrounding the pBR322 incident. Lilly Ex. 3731 at 000090, 000092. In the memorandum, Goodman and Rutter stated that the decision was made to destroy the pBR322 clones. No date was affixed to this decision. Id. However, in the biosafety committee's January 20, 1978, report to the NIH in which the committee answered NIH questions about UC's misuse of pBR322 Rutter and Goodman said that Ullrich, the UC scientist actually working with the plasmid, told them that he disposed of the pBR322 clones on March 19, 1977. Lilly Ex. 3420 at HG 002873.

It is clear from the record that Ullrich did not destroy all the material associated with pBR322. He saved the purified DNA associated with the use of pBR322 plasmids, and Goodman and Rutter were aware that he did. In registered letters that Rutter and Goodman testified to having exchanged during the events in issue, they admitted that they chose to A [k]eep the cloned DNA since the experiments had already been performed . . . We believed that further sequencing of the DNA clones was acceptable since the hypothetical danger, if any, is not with the DNA itself." Lilly Ex. 3361 at HG 00069192; Lilly Ex. 3363 at WR 1072021; see also tr. at 231234, 11491153. Goodman's letter to Rutter was sent March 25, 1977; Rutter's letter to Goodman was sent March 22, 1977. These "smoking gun" letters could have had no purpose but to keep either of the writers from attributing the misuse to the other.

At trial, Rutter and Goodman testified that although the letters reflect that they chose to retain the cloned DNAs, they actually chose a different course of action. They contended that they destroyed all the cloned DNAs. Tr. at 302, 1111. When asked why he and Goodman did not amend their letters to reflect a different decision, Rutter responded:

Because acqtually we acted on the advice of DeWitt Stetten and destroyed the clones. It was unnecessary to adapt this guideline. We had carried out the activities which we had decided, namely, to destroy the clones for pBR322. Tr. at 302.

We believe the registered letters are reflective of Rutter and Goodman's contemporaneous level of concern over the pBR322 incident. We are far from convinced that the two would go so far as to mail identical registered letters to one another admitting to having taken a course of action that flew in the face of NIH regulations and, subsequently, upon abandoning that course of action, permit those letters to stand uncorrected in their respective files. Moreover, the earlier of these registered letters was dated March 22, 1977. Rutter's telephone conversation with Stetten was, at the latest, on March 19, 1977. Thus, the letters were exchanged after Rutter and Goodman had time to contemplate and decide their course of action and after the time Ullrich allegedly destroyed the tainted materials. In light of the persuasive nature of the registered letters and other evidence of record, we find Rutter and Goodman's trial testimony regarding the letters not credible.

In addition, Ullrich's trial testimony indicates that Goodman and Rutter did not decide to abandon use of the pBR322 DNA clones after they learned of pBR322's uncertified status. After Ullrich's recollection was refreshed by an examination of one of the registered letters, the following dialogue transpired:

Q. Does that refresh your recollection that you were, in fact, instructed by Drs. Goodman and Rutter to continue to work with the DNA even after you learned it was not certified?

A. I wouldn't use the word "instructed."

Q. Would you turn to Defendant's Exhibit

THE COURT: Wait just a minute. What word would you use?

THE WITNESS: It was probably the result of a discussion and an agreement among more than Drs. Howard Goodman and Rutter.

Tr. at 829.

We find by clear and convincing evidence that UC representatives continued to use at least the fruits of the uncertified plasmid in sequencing experiments well beyond the time they learned that such use was inappropriate. The Court believes such use is tantamount to use of the plasmid itself. Next, we must determine whether UC researchers misrepresented the origins of the rat insulin data data on which the '525 patent is based.

On May 9, 1977, Rutter submitted to the journal Science a manuscript in which UC researchers described the isolation of four pieces of rat insulin DNA. Lilly Ex. 3391; Lilly Ex. 3380. The pieces of DNA isolated and sequenced were denominated in the Science article as pAU1, pAU2, pAU3 and pAU4. The researchers stated in their manuscript describing their rat insulin work that they had used the bacterial plasmid pMB9 in their research efforts. Notably, pMB9 was not certified for use by the NIH until April 18, 1977.

Lilly contends that although UC researchers asserted that the work leading to the Science manuscript and, ultimately the '525 patent was done with plasmid pMB9, yet actually the work was done with the uncertified vector pBR322. Lilly argues that the DNA pieces described in the Science article really are those DNA clones obtained by UC's unauthorized use of pBR322. An examination of the evidence and trial testimony leads us to conclude that Lilly's position is well supported. We explain.

Ullrich maintained a laboratory notebook regarding his research activities and in that notebook he described his work with pBR322. See Lilly Ex. 3340. In his notebook, Ullrich specified which of the DNA clones showed a positive result from a hybridization experiment involving microorganisms transformed by the uncertified pBR322 plasmids containing rat islet

cDNA. Id. at HG 000445; tr. at 83437. Ullrich labelled each of the clones for identification purposes. Tr. at 83537. Significant to this discussion are the clones he labelled 113, 39 and 310.

Reference to these same clone numbers, i.e., 113, 39 and 310, was found on certain pages contained in a folder designated "INSULIN expt" from Howard Goodman's files. See Lilly Ex. 3354 at HG 002075. Ullrich admitted that the numbers 113, 39 and 310 "match with the numbers that we had seen before on the hybridization experiment." Ullrich further testified that several of the pages found in this folder contained his handwriting. Tr. at 84041. He also agreed that the page in this folder entitled "Summary of Insulin Clones" includes a diagram that describes where the pieces of DNA from pBR322 started and stopped. Tr. at 841.

At trial, Gilbert, in his expert testimony, relied on Ullrich's lab notes, the insulin experiment folder from Goodman's files, and a handwritten manuscript draft describing an experiment conducted in the plasmid pBR322. See Lilly Ex. 3365. Gilbert compared the sequence data from the unauthorized pBR322 research work with the sequence data reported in the Science article and concluded that the pieces of DNA reported in the article were derived from pBR322 research. Tr. at 1308, 131033. He stated that clone pAU1 listed in the Science article contained the same starting and stopping points as pBR322 clone 113; pAU2, the same as pBR322 clone 39; and pAU3, the same as pBR322 clone 310. Id. Moreover, Gilbert testified that pAU4 identified in the Science article corresponds to other sequence data reported in the pBR322 research. Tr. at 132122.

Gilbert was asked whether a second experiment, conducted in the same way as that with pBR322, likely would result in the isolation of clones having the same structure. Tr. at 1332. Gilbert answered that a researcher might isolate another clone having the same structure as that identified as 39. Tr. at 1333 34. However, he added that the same was not true of clones 113, 310 or that identified as pAU4 in the Science paper. Id. In these fragments, one would have expected variations in other experiments. Id. Even Ullrich declared it highly unlikely that the sequence reported in pAU4 would be duplicated by random chance. Tr. at 87374. UC expert Richards concurred with Ullrich's observation. Tr. at 206.

The Court finds Gilbert eminently qualified and credible. Significantly, we find that the evidence supporting his interpretation of the sequence of events is clear and convincing. Hence, we find that the duplications in the structure of pBR322derived clones and the structure of clones reported in the Science manuscript and the original '525 patent application are not products of random chance. Rather, we find that UC researchers used data derived from the pBR322 experiments in the aforementioned publications.

The Court also believes that comment on Rutter's testimony before the Senate subcommittee in November of 1977 is in order. After comparing the evidence of record against that testimony, we find that Rutter was not candid with members of the subcommittee. For example, Rutter testified that the experiments with the uncertified plasmid were not spurred by

commercial interests. Lilly Ex. 3554A at 219. Rutter also averred that none of the work in the plasmid had any relationship to Genentech, Inc. (Genentech).

Certain evidence of record counters Rutter's averments. The evidence indicates that UC representatives began collaboration discussions with both Genentech and Lilly shortly after learning that rat insulin DNA had been isolated in the uncertified pBR322. For example, on March 9, 1977 eight days after learning of UC's misuse of the plasmid and seven days after learning that an insulin clone actually had been obtained from pBR322 work Goodman contacted Lilly. Lilly Ex. 3400 at WR 10052. In his notes recording that conversation, Goodman wrote: "Have rat clone. Q. How? A. Don't want to say too much now, but can prove it." Lilly Ex. 3343A. Goodman met with Lilly personnel on March 14, 1977. Lilly Ex. 3349. In his notes of that meeting, Goodman wrote that he discussed a plasmid but that when someone asked him what plasmid, he answered, "Can't say." Id. at HG 001462. Additionally, Goodman's notes reflect that he told those present that what he wanted in exchange for what he had to offer included "money for lab" and "consulting." Id. at HG 001465.

Other evidence indicates that Goodman also approached Genentech during the same time period. On March 12, 1977, he met with Genentech representatives; Goodman's handwritten notes of that meeting indicate that Genentech offered Goodman "money for salaries, supplies, equipment, shares (common) . . . [and] consulting for me." Lilly Ex. 3347 at HG 001355. The record illustrates that Goodman called Genentech representative Ron Swanson at home the following day. Lilly Ex. 3348 at HG 001357. Goodman's notes of that telephone conversation state that Goodman "[h]inted [at] we were bringing something very valuable to the co & should be compensated for difference in kind between 'idea' & 'having [it]." Id. at HG 001357. Subsequently, other handwritten notes by Goodman illustrate that on March 15, 1977, he again called Genentech and reported the following: "Problem that in Boyer plasmid. Lay low. Not approved. Can't apply for patent yet." Lilly Ex. 3351 at HG 001364.

Significantly, although at trial Goodman could not recall when Rutter became involved in the Genentech negotiations, he did not dispute that Rutter did become involved. In fact, in Goodman's deposition of May 18, 1993, he testified that while Rutter was not present at the first of the Genentech negotiation meetings that he could recollect, Rutter was involved in all subsequent meetings. Tr. at 123738. Hence, contrary to Rutter's statements to the Senate subcommittee, we find that continued use of the fruits of the pBR322 research was driven by commercial interests and we find that those commercial interests were tied closely to Genentech.

UC asserts that even if the Court determines that the sequence data in issue did stem from work done in the uncertified plasmid pBR322, Lilly still cannot succeed in its inequitable conduct charge. Specifically, UC argues that Lilly cannot prove by clear and convincing evidence not only that UC's act was material to the prosecution of the '525 patent, but also that UC representatives committed the act with an intent to deceive the PTO examiner.

In *General Electro Music Corp. v. Samick Music Corp.*, 19 F.3d 1405 [30 USPQ2d 1149] (Fed. Cir. 1994), the patent applicant, Samick, sought expedited examination of its application because, Samick alleged, the claimed design was being infringed. Id. at 1406. In order to obtain expedited examination, Samick had to file a "petition to make special." Id.

At the time Samick filed its petition, the MPEP [Manual of Patent Examining Procedure] required that an applicant support a petition to make special with an oath or declaration alleging facts showing, among other things, "that he or she had made or caused to be made a careful and thorough search of the prior art or has a good knowledge of the pertinent prior art." Id. (quoting MPEP Section 708.02, II(5)). In light of this requirement, Samick, through its attorney, submitted a declaration stating that a prior art search had been conducted.

However, a jury determined that, contrary to Samick's attorney's declaration, Samick had not conducted a prior art search and, thus, that Samick intentionally had made a material false statement to the PTO. Id. at 1407. The Court entered judgment against Samick based on inequitable conduct rendering its patent unenforceable. Id. at 1408. The Federal Circuit affirmed. Id.

We believe the decision in Samick illustrates that the Federal Circuit's application of the concept of inequitable conduct is not limited to situations in which the patent applicant intentionally misleads the PTO in the context of prior art. Rather, inequitable conduct may be found in a variety of circumstances in which the patent applicant has abandoned his duty of candor, good faith and honesty to the PTO.

We already have determined that certain of the data found in the '525 patent was the result of an experiment conducted in the uncertified pBR322 plasmid. Moreover, in its prosecution of the '525 patent, UC failed to report its use of that vector to the PTO examiner but rather reported use of pMB9 for the data in issue. In light of these findings, the Court must determine whether UC's misrepresentation to the PTO was material to the patentability of the '525 patent.

After considering the facts and the law, we find that there is a substantial likelihood that a reasonable examiner would have considered UC's unauthorized use of pBR322 important in his patentability determination. UC, as an institution that accepted funding from the NIH, was obligated to follow the guidelines issued by that agency; UC was aware of its obligation. Even after UC representatives admittedly learned of their premature use of the subject plasmid, they, nonetheless, continued, at the very least, to use the sequence data they secured from their tainted research. A reasonable examiner easily could have determined that without use of the unauthorized plasmid and the data therefrom, UC's application for the '525 patent would not have acquired its May 27, 1977, file date. Indeed, it is impossible to determine whether UC would have been the first to make patent application had its representatives followed the rules to which its competitors were bound.

The Court also must consider the issue of intent, though the issue need not detain us long. First, we consider UC's forbidden use of pBR322 long past its recognition of the uncertified status of that plasmid. Second, we reiterate our determination that UC representatives incorporated pBR322 data into the '525 patent application an incorporation that was not accompanied by candor or honesty in UC's prosecution of the '525 patent application. Considering the admissions contained in the exchange of letters between Rutter and Goodman, we find no room for doubt that UC's failure to reveal its unauthorized use of pBR322 was intentional. Moreover, the Court finds that such intentional failure necessarily was meant to deceive or mislead the PTO examiner. UC was aware of its violation of the NIH safety guidelines and apparently was concerned that the PTO would endorse neither its experimental use of uncertified pBR322 nor its use of the results of that experiment in the '525 patent application.

The United States Supreme Court has stated that

> . . . a patent is an exception to the general rule against monopolies and to the right to access to a free and open market. The far-reaching social and economic consequences of a patent, therefore, give the public a paramount interest in seeing that patent monopolies spring from backgrounds free from fraud or other inequitable conduct and that such monopolies are kept within their legitimate scope.

Precision Instrument Mfg. Co. v. Automotive Maintenance Mach. Co., 324 U.S. 806, 816 [65 USPQ 133] (1945). We are persuaded that endorsement of UC's conduct by enforcing the '525 patent would counter the public's interest. Hence, we hold that the '525 patent is unenforceable based on UC's inequitable conduct.

These regulations, however, did not pacify everyone. Public debate in Cambridge, Massachusetts about the safety of recombinant DNA research led to a determination that such research was banned from "the City of Cambridge until the citizens of Cambridge and the city council had convinced themselves that it was safe for the research to continue." Tr. at 1299. A citizens committee was appointed to investigate the matter and, in early 1977, the ban was lifted. Tr. at 12991300.

Rutter and Goodman were coprincipal investigators for the research in issue in the instant case. Lilly. Ex. 3420 at HG 002873. Rutter was then chairman of the Department of Biochemistry and Biophysics at the University of California. Tr. at 106; Lilly Ex. 3554A at 200. Goodman was then a professor in the Department of Biochemistry at the University. Tr. at 1106. During some of the time in which the subject research was being conducted, Goodman was out of the country on sabbatical leave. His absence, however, is not relevant to this discussion.

An institutional biohazard committee was established in each institution that received NIH funding. According to the guidelines, such a committee was responsible for, inter alia, certifying,

and recertifying annually, to NIH that the facilities, procedures, practices, training, and expertise of involved personnel had been reviewed and approved. Lilly Ex. 3547 at HG2 580781.

Hearings before qa subcommittee of the United States Senate were held in November of 1977 to examine the potential need for federal regulation governing all recombinant DNA research, including research not funded by the NIH. Lilly Ex. 3554A. At the hearings, Rutter testified about the pBR322 incident. Id. at 20024. Rutter told the subcommittee, inter alia, that the application for the '525 patent was not based on PBR322 research, id. at 21718, and that there were no commercial interests motivating UC to use the uncertified plasmid. Id. at 219.

The record suggests that Goodman actually became aware of the uncertified status of pBR322 on March 1, 1977. Lilly Ex. 3400 at WR 10052. Reportedly, on March 4, 1977, Goodman informed Rutter of the matter. Id.

The way in which ORDA became aware of the pBR322 incident is discussed infra at 7374.

In identical letters Rutter and Goodman exchanged with each other in March of 1977, discussed infra, they state that on March 5, 1977, Ullrich destroyed the "plasmid containing cells and kept only the purified DNA from the clones. . . ." Lilly Ex. 3361 at HG 000691; Lilly Ex. 3363 at WR 10720.

Gilbert also relied on Goodman's notes of a March 14, 1977, meeting with Lilly. Tr. at 131516; Lilly Ex. 3349. At this meeting, Goodman had drawn on the board a plasmid labeled in the same fashion as one in Goodman's insulin experiment folder. Lilly Ex. 3349 at HG 001462. In the experiment folder, the drawing appears under the title, "clone 113." Lilly Ex. 3354 at HG 002081. The Goodman Lilly meeting was on March 14, 1977. Hence, Gilbert concluded that the sequence listed in Goodman's insulin experiment had to exist before that date. Because Rutter testified that UC experiments with plasmid pCR1 were ineffective, tr. at 137, and because pMB9 was not even certified for use until April 18, 1977, the sequence described in Goodman's insulin experiment folder, and later drawn on the board at the Lilly meeting, had to be a pBR322 sequence. Tr. at 1328.

At trial, Lilly introduced certain drafts of research manuscripts found in UC's files. Lilly contends that although these manuscripts purport to arise from research conducted with certified plasmids, yet the data contained therein illustrate that the manuscripts actually were based on work done with the uncertified vector pBR322.

We agree with Lilly that the record illustrates that the data contained in these manuscripts originated in pBR322 research work. However, we already have found that the research work reported in the Science article and, ultimately, in the '525 patent, is based, at least in part, on work done in the uncertified plasmid. Thus, while the common threads in these manuscripts (e.g., identical sequencing errors, identical typographical errors) strengthen Lilly's argument that the

manuscripts all rely upon pBR322 research work, a detailed explanation of those documents and their corresponding features is unnecessary for purposes of this decision.

Genentech, a corporation located in California, is involved in other of the six cases consolidated in this Court for pretrial proceedings by the Judicial Panel on Multidistrict Litigation. See, supra at 12.

At trial, Goodman verified that the notes were in his handwriting. Tr. at 1219.

Evidence of record convinces us that Goodman was referring to pBR322 when he named the "Boyer plasmid." Ullrich testified that scientists in Herb Boyer's laboratory developed pBR322. Tr. at 79798. Moreover, other testimony reveals that the only plasmid with which UC researchers had achieved success by March of 1977 was the uncertified pBR322. Specifically, Rutter averred that UC was unsuccessful in its attempts to clone in plasmid pCR1. Tr. at 137. Furthermore, Rutter stated that UC researchers did not begin using vector pMB9 until after it was approved by the NIH. Tr. at 136. That approval was not received until April of 1977. Consequently, Goodman's midMarch 1977 reference to "Boyer plasmid" must mean pBR322.

It also is interesting to note that by agreement with UC the inventors are entitled to 50 percent of the net profits derived from any royalties or fees received from patent rights.

Lilly contends that UC's inequitable conduct in procurement of the '525 patent should render the '740 patent unenforceable as well. However, we believe UC acted inequitably in the prosecution of the '740 patent itself, as discussed infra. Therefore, we need not consider whether UC's conduct associated with the '525 patent should hinder its ability to enforce another patent in suit.

A NOTE ON SOURCES

This paper was written on short notice, over two successive weekends, in order to meet NBAC's pressing deadlines. I have relied heavily on others' accounts of many of the events, and I am indebted to them. John C. Fletcher (University of Virginia) kindly shared copies of public NIH files bearing on the Cline case,[54] and Rebecca Lawson (Office of Recombinant DNA Activities, NIH) quickly found and copied files on the UCSF and Harvard recombinant DNA guideline cases.[30, 55] Laura Bishop of the National Reference Center for Bioethics Literature did several literature searches on very short notice and emailed the results. Susan Poland from the Kennedy Institute of Ethics at Georgetown University took a late Friday road trip to secure the federal court documents. These generous gestures were immensely helpful in reconstructing the events. I have e-mailed and called many of the principals to ask for corrections to or comments on published accounts and the public record.

With more time, more primary sources could have been reviewed and cited. The accounts are accurate to the extent required here, I believe, because several scholars and policy analysts

have worked hard to construct accounts, and those involved in the debates concur that the accounts are generally accurate. The facts of the UCSF insulin-cloning incident were subject to a formal federal trial, but some findings remain under appeal. For NBAC's deliberations about the merits of moratoria, however, further detail may not be necessary.

The main source for the UCSF cloning story was Stephen Hall's beautifully written and lively book *Invisible Frontiers: The Race to Synthesize a Human Gene*,[1] although some of the facts did not come out until the University of California-Eli Lilly litigation in 1995 (see appendix—and footnote 31). Letters from William Rutter and his attorney Rachel Krevans of Morrison & Foerster and from Kirke Hasson (on behalf of Howard Goodman) helped separate the agreed from the contested facts in the UCSF cloning incidents. The broader history of the recombinant DNA debate is recounted by Bernard Talbot,[20] Sheldon Krimsky,[17] John Lear,[16] and Judith Swazey, et al.[19] Many relevant background documents were collected for the *Recombinant DNA Technical Bulletin* maintained by NIH. James Watson and John Tooze selected many of the seminal documents for *The DNA Story*.[15] And finally, Donald Fredrickson has reviewed part of this history in previous articles,[18, 56] and is working on a book. OTA's 1981 report, *Impacts of Applied Genetics,* includes an excellent brief history of the recombinant DNA controversy and the early origins of commercial biotechnology,[52] although, surprisingly, it does not mention the guideline infractions. The first *Federal Register* guidelines notice also has an expansive and detailed history of events leading up to them.[57]

For background on review of gene therapy, several sources were particularly useful. LeRoy Walters chaired numerous relevant oversight groups for over a decade—the 1984 OTA workshop panel, the Human Gene Therapy Working Group, the Human Gene Therapy Subcommittee, and the Recombinant DNA Advisory Committee. He and coauthor Judy Palmer devoted the better part of a chapter in their recent book to the history of how human gene therapy has been reviewed at NIH and the Food and Drug Administration, and that is the best place to start for a chronology.[41] Scope Note 24, by Mary Carrington Coutts, summarizes the salient literature up to 1991.[58] Eve Nichols's book for the Institute of Medicine and a 1984 OTA report review the process before the first real protocols appeared.[59, 60] And *Splicing Life*, the report by the President's Commission, was the first major public policy statement and remains among the most significant.[39] The recent changes in gene therapy review, with NIH's RAC only reviewing protocols that raise novel issues are stated in official government notices.[3, 61] No discussion of gene therapy is complete without noting the sober December 1995 report that urged more attention to scientific foundations and less to hype.[62]

The best and most detailed account of the Cline case is contained in chapters six and seven of Larry Thompson's book *Correcting the Code*,[53] which was guided by interviews with Cline, his collaborators abroad, the patients and their families, and numerous NIH officials. His account goes well beyond the NIH case file. [36, 37, 54, 63] The early events in human gene therapy are summarized well by John Fletcher.[64] The human gene therapy account in this paper is partly based on files collected for the 1984 report *Human Gene Therapy*,[60] but much more detailed accounts

have been published since. A compendious volume on gene therapy was written by *Chicago Tribune* reporters Jeff Lyon and Peter Gorner.[65]

The tortuous history of fetal research and embryo research is reviewed most concisely and effectively by Constance Pechura,[66] and summarized through early 1994 by the Institute of Medicine.[67] Alta Charo analyzes the results of NIH's Human Embryo Research Panel,[13] and how its findings were rejected by President Clinton. The closely parallel experience of the Human Fetal Tissue Transplantation Research Panel is reviewed by Childress,[12] and the *de facto* moratorium on fetal research due to the absence of an Ethics Advisory Board in DHHS is documented by OTA.[68] The earlier history of fetal research is summarized well by Dorothy Lehrman in a report for the Association of American Medical Colleges,[69] and touched on by a 1989 Institute of Medicine report.[70]

The role of bioethics commissions has generated its own small literature. Michael Yesley comments on the National Commission from his perspective as its executive director.[6] The President's Commission was the subject of a symposium a year after it closed its doors,[71] and many articles have been written about it. The most useful recent synthetic literature comes from a 1995 Institute of Medicine report that contains pertinent background papers, including especially useful ones by Dan Brock[72] and Bradford Gray.[73] Background on federal, state, and international bioethics commissions is collected in the 1993 OTA report[7] which contributed directly to the establishment of NBAC. It includes the legislative language creating the National and President's Commissions and the Biomedical Ethics Board and Advisory Committee, as well as the 1976 and 1979 EAB charters. The point about the separate functions of public deliberation and consensus building versus protocol review and guideline preparation are covered in greater detail, [74, 75] as well as difficulties in steering a research program and attempting policy deliberation in the same group.[76]

A 1996 report, *Understanding Risk*, is highly commended for thinking about how to incorporate risk assessment into public policy.[77]

The following is a record of direct contacts through May 3, 1997.

Phone or face-to-face conversations:

Charles Weiner, MIT, 25 March
Bernard Talbott, NCRR, 25 March
William Gartland, NIDR, 25 March
Judith Swazey, Acadia Institute, 24 March
LeRoy Walters, 24 March
Rebecca Lawson, ORDA, 25 March
John Fletcher, 21 March
Larry Thompson, 2 April
Stephen Hall, New York Times, 3 April
Walter Gilbert, Harvard University, 3 April

Amy Hamilton, Eli Lilly & Co., 9 April
[confidential source, Genentech, 3 April]

Letters:

Kirke Hasson, Pillsbury, Madison & Sutro LLP, 29 April
William Rutter, Chiron Corporation, 30 April
Rachel Krevans, Morrison & Foerster, 30 April

E-mail from:

Axel Ullrich, Max Planck Institute for Biochemistry, Martinsried, Germany, 21 March
Donald S. Fredrickson, National Institutes of Health, 21 March
Barbara Culliton, Editor, *Nature Medicine,* 24 March
Charles Weiner, MIT, 24 March
Larry Thompson, FDA, 25 March
John Fletcher, University of Virginia, 20 March
Laura Bishop, NCRBL (who did literature searches at the National Reference Center for Bioethics Literature, Georgetown University), 26 March
LeRoy Walters, 7 April
Peter Seeburg, Center of Molecular Biology (ZMBH), University of Heidelberg, 11 April

E-mailed to:

Martin Cline, UCLA, 20 March

References

1. Hall, S.S., *Invisible Frontiers: The Race to Synthesize a Human Gene,* New York: Atlantic Monthly Books, 1987.

2. *The Compact Edition of the Oxford English Dictionary,* Oxford, UK: Oxford University Press, 1971.

3. Office of Recombinant DNA Activities, *Appendix M: The Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA Molecules into the Genome of One or More Human Subjects,* Bethesda, MD: National Institutes of Health, U.S. Department of Health and Human Services, 1997.

4. German Embryo Protection Act, Gesetz zum Schutz von Embryonen, October 24, 1990, *Hum Reprod,* 6:605-606, 1991.

5. National Commission, *Research on the Fetus: Report and Recommendations,* Washington, DC: National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Department of Health Education and Welfare, 1975.

6. Yesley, M.S. The use of an advisory commission, *Southern California Law Review,* 51(September):1451-1469, 1978.

7. U.S. Congress, *Biomedical Ethics in U.S. Public Policy,* Washington, DC: Office of Technology Assessment, 1993.

8. Ethics Advisory Board, *The Request of the Centers for Disease Control for a Limited Exemption from the Freedom of Information Act,* Washington, DC: U.S. Department of Health and Human Services, 1980.

9. Ethics Advisory Board, *Report and Conclusions: HEW Support of Research Involving Human* In Vitro *Fertilization and Embryo Transfer,* Washington, DC: U.S. Department of Health, Education and Welfare, 1979.

10. Ethics Advisory Board, *Report and Recommendations: Research Involving Fetoscopy,* Washington, DC: U.S. Department of Health, Education and Welfare, 1979.

11. Ethics Advisory Board, *The Request of the National Institutes of Health for a Limited Exemption from the Freedom of Information Act,* Washington, DC: U.S. Department of Health and Human Services, 1980.

12. Childress, J.F., Deliberations of the Human Fetal Tissue Transplantation Research Panel, in *Biomedical Politics*, K.E. Hanna (ed.), Washington, DC: National Academy Press, 1991, 215-240.

13. Charo, R.A., The hunting of the snark: The moral status of embryos, right-to-lifers, and third world women, *Stanford Review of Law and Policy,* 6(2):11-37, 1996.

14. U.S. Congress. This language appears in HR 2127, appropriations for FY1996, section 510, and HR 3755, section 512, appropriations for FY 1997. They govern appropriations under Public Law 104-91, as noted in HR 2880, section 128, 1996.

15. Watson, J.D., J. Tooze, *The DNA Story,* San Francisco: W.H. Freeman, 1981.

16. Lear, J., *Recombinant DNA: The Untold Story,* New York: Crown, 1978.

17. Krimsky, S., *Genetic Alchemy: The Social History of the Recombinant DNA Controversy,* Cambridge, MA: MIT Press, 1982.

18. Fredrickson, D.F., Asilomar and recombinant DNA: The end of the beginning, in *Biomedical Politics,* K.E. Hanna (ed.), Washington, DC: National Academy Press, 1991, 258-292.

19. Swazey, J.P., J.R. Sorenson, C.B. Wong, Risks and benefits, rights and responsibilities: A history of the recombinant DNA research controversy, *Southern California Law Review,* 51(September):1019-1078, 1978.

20. Talbot, B., Introduction to recombinant DNA research, development and evolution of NIH *Guidelines,* and proposed legislation, *University of Toledo Law Review,* 12(Summer):804-814, 1981.

21. Singer, M., D. Soll, Guidelines for hybrid DNA molecules, *Science,* 181(September 21):1114, 1973.

22. Berg, P., D. Baltimore, H.W. Boyer, et al., Potential biohazards of recombinant DNA molecules, *Proc Nat Acad Sci* U S A, 71(July):2593-2594, 1974.

23. Berg, P., D. Baltimore, H.W. Boyer, et al., Potential biohazards of recombinant DNA molecules, *Science,* 185(July 26):3034, 1974.

24. Berg, P., D. Baltimore, S. Brenner, R.O. Roblin, M. Singer, Summary statement of the asilomar conference on recombinant DNA molecules, *Proc Nat Acad Sci* U S A, 72(June):1981-1984, 1975.

25. Berg, P., D. Baltimore, S. Brenner, R.O. Roblin, M. Singer, Summary statement of the Asilomar Conference on Recombinant DNA Molecules, *Science*, 72(June 6):991, 1975.

26. Stetten, D., Letter to David Martin of University of California, San Francisco, Deputy Director, NIH, 1977.

27. Goodman, H.M., W.J. Rutter, Memo to Dr. James Cleaver, chairman, Biosafety Committee, University of California, San Francisco, Department of Biochemistry and Biophysics, UCSF, 1977.

28. Cleaver, J.E., Letter to William J. Gartland, Director, Office of Recombinant DNA Activities, NIH, and committee report in response to NIH questions communicated by Dr. W.J. Gartland to Dr. J.E. Cleaver on December 1, 1977, Chair, Biosafety Committee, University of California, San Francisco, 1978.

29. Wade, N., Recombinant DNA: NIH rules broken in insulin gene project, *Science*, 197(September 30):1342-1345, 1977.

30. Office of Recombinant DNA Activities, Case file on William Rutter, University of California, San Francisco. National Institutes of Health, 1978.

31. *University of California v. Eli Lilly and Co.*, MDL Docket No. 912, No IP-92-0224-C-D/G, decided December 11, 1995, U.S. Patent Quarterly, 39 USPQ2d(July):1225-1258, 1976, esp. 1248-1254. ("The U.S. Court of Appeals for the Federal Circuit rendered its decision in this case on July 22, 1997. Please refer to Docket 96-1175 for the decision.")

32. Thomas, C.A., The fanciful future of gene transfer experiments: Genetic interaction and gene transfer, Brookhaven, NY: Brookhaven Symposia in Biology, No. 29, 1977, 348-358.

33. Thomas, C.A., Letter to Dorothea S. Miller, Grants Administrator, NIH, 1977.

34. Dach, L., Letter and Freedom of Information Act request, Environmental Defense Fund, 1977.

35. Minutes of meeting, Executive Recombinant DNA Committee, NIH, 1978.

36. Talbot, B., Memorandum for the record on *Background and Committee Recommendations* regarding the *Report of NIH Ad Hoc Committee on the UCLA Report Concerning Certain Research Activities of Dr. Martin J. Cline*, Executive Secretary, NIH Ad Hoc Committee of the UCLA Report Concerning Certain Research Activities of Dr. Martin J. Cline, 1981.

37. Fredrickson, D.S., Statement of the Director, NIH, Accompanying the Release of the Report Concerning Martin J. Cline, M.D., Office of the Director, NIH, 1981.

38. Randall, C., B. Mandelbaum, T. Kelly, Letter to President Jimmy Carter from General Secretaries of the National Council of Churches, the Synagogue Council of America, and the United States Catholic Conference, reprinted in the President's Commission report, *Splicing Life,* 1980, 95-96.

39. *Splicing Life: The Social and Ethical Issues of Genetic Engineering with Human Beings,* Washington, DC: President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, 1982.

40. Subcommittee on Investigations and Oversight, Committee on Science and Technology, U.S. House of Representatives, *Human Genetic Engineering,* Washington, DC, 1982.

41. Walters, L., J.G. Palmer. *The Ethics of Human Gene Therapy,* New York: Oxford University Press, 1997.

42. Anonymous, Human gene marker/therapy clinical protocols, *Hum Gene Therapy*, 8(March 20):629-654, 1997.

43. Kessler, D.A., Regulation of somatic-cell therapy and gene therapy by the Food and Drug Administration, *N Engl J Med,* 329(October 14):1169-1173, 1993.

44. Council of Europe, *Recommendation 934 (1982) on Genetic Engineering,* Strasbourg, Germany: Council of Europe, Parliamentary Assembly, 1982.

45. Council for International Organizations of Medical Sciences, The Declaration of Inuyama and Reports of the Working Groups, *Hum Gene Therapy,* 2(Summer):123-129, 1991.

46. Bankowski, Z., A.M. Capron (eds.), *Genetics, Ethics, and Human Values: Human Genome Mapping, Genetic Screening, and Gene Therapy,* Proceedings of the XXIV CIOMS Conference, Tokyo and Inuyama City, Geneva: Council for International Organizations of Medical Sciences, 1990.

47. Capecchi, M.R., Appendix E: Background information on homologous recombination, in L. Walters, J.G. Palmer (eds.), *The Ethics of Human Gene Therapy,* New York: Oxford University Press, 1997, 186-196.

48. Rubinstein, D.S., D.C. Thomasma, E.A. Schon, M.J. Zinaman, Germ-line therapy to cure mitochondrial disease: Protocol and ethics of *in vitro* ovum nuclear transplantation, *Camb Q Healthc Ethics,* 4:316-339, 1995.

49. Macklin, R., Universality of the Nuremberg Code, in *The Nazi Doctors and the Nuremberg Code*, G.J. Annas, M.A. Grodin (eds.*)*, New York: Oxford University Press, 1992, 240-257.

50. Falkow, S., J.H. Grosa. Letter to A.E. Adelberg, Department of Human Genetics, Yale University, University of Washington, 1977.

51. Ullrich, A., J. Shine, J. Chirgwin, et al. Rat insulin genes: Construction of plasmids containing the coding sequences, *Science*, 196(June 17):1313-1319, 1977.

52. Office of Technology Assessment, U.S. Congress, *Impacts of Applied Genetics: Micro-Organisms, Plants, and Animals,* Washington, DC: 1981.

53. Thompson, L., *Correcting the Code: Inventing the Genetic Cure for the Human Body*, New York: Simon & Schuster, 1994.

54. Office of Recombinant DNA Activities, Risks OoPfR, Case file on Martin Cline, National Institutes of Health, 1981.

55. Office of Recombinant DNA Activities, Case file on Charles Thomas, Harvard University, National Institutes of Health, 1978.

56. Fredrickson, D.S., A history of the recombinant DNA guidelines in the United States, *Recomb DNA Tech Bull,* 2(July):87-90, 1979.

57. Fredrickson, D.S., Part II: Department of Health, Education and Welfare, National Institutes of Health, Recombinant DNA Guidelines, *Fed Regist*, 41(July 7):27902-27943, 1976.

58. Coutts, M.C., *Scope Note 24: Human Gene Therapy,* Washington, DC: National Reference Center for Bioethics Literature, Georgetown University, 1991.

59. Nichols, E.K., *Human Gene Therapy,* Cambridge, MA: Harvard University Press, 1988.

60. Office of Technology Assessment, U.S. Congress, *Human Gene Therapy—Background Paper*, Washington, DC:1984.

61. Office of Recombinant DNA Activities, Notice of Proposed Actions Under the *NIH Guidelines for Research Involving Recombinant DNA Molecules*, Bethesda, MD: National Institutes of Health, 1997.

62. Orkin, S.H., A.G. Motulsky. Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy, Bethesda, MD: National Institutes of Health, 1995.

63. Krause, R.M., B. Talbot, Report of the NIH Ad Hoc Committee on the UCLA Report, 1981. (Chairman, NIH Ad Hoc Committee on the UCLA Report (RMK) and Executive Secretary (BT). Other committee members: Susan Gottesman, Harry Keiser, Mortimer Lipsett, Charles McCarthy, and Richard, Riseberg (Counsel).)

64. Fletcher, J.C.,.Moral problems and ethical issues in prospective human gene therapy, *Virginia Law Review,* 69:515-546, 1983.

65. Lyon, J., P. Gorner, *Altered Fates: Gene Therapy and the Retooling of Human Life*, New York: W.W. Norton, 1995.

66. Pechura, C.M., Fetal and embryo research: A changing scientific, political, and ethical landscape, in *The Ethics of Research Involving Human Subjects,* H.Y. Vanderpool (ed.), Frederick, MD: University Publishing Group, 1997, 371-400.

67. Institute of Medicine, *Fetal Research and Applications: A Conference Summary*, Washington, DC: National Academy Press, 1994.

68. Office of Technology Assessment, U.S. Congress, *Infertility: Medical and Social Choices,* Washington, DC:1988.

69. Lehrman, D., *Summary: Fetal Research and Fetal Tissue Research*, Washington, DC: Association of American Medical Colleges, 1988.

70. Institute of Medicine, *Medically Assisted Conception: An Agenda for Research*, Washington, DC: National Academy Press, 1989.

71. Weisbard, A.J., J.D. Arras, J. Katz, et al., Symposium: Commissioning morality: A critique of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Cardozo Law Review,* 6(Winter):223-355, 1984. (This is a collection of several different articles by these authors.)

72. Brock, D.W., Public moral discourse, in *Society's Choices: Social and Ethical Decision Making in Biomedicine,* R.E. Bulger, E.M. Bobby, H.V. Fineberg (eds.), Washington, DC: National Academy Press, 1995, 215-240.

73. Gray, B.H., Bioethics commissions: What can we learn from past successes and failures?, in *Society's Choices: Social and Ethical Decision Making in Biomedicine*, R.E. Bulger, E.M. Bobby, H.V. Fineberg (eds.), Washington, DC: National Academy Press, 1994, 261-306.

74. Hanna, K.E., R.M. Cook-Deegan, R.Y. Nishimi. Finding a forum for bioethics in U.S. public policy, *Politics and the Life Sciences,* 12(August):205-219, 1993.

75. Hanna, K., R.M. Cook-Deegan, R.Y. Nishimi, Bioethics and public policy: Still seeking a forum, *Politics and the Life Sciences*, 13(February):102-105, 1994.

76. Hanna, K.E., The ethical, legal, and social implications program of the national center for human genome research: A missed opportunity?, in *Society's Choices: Social and Ethical Decision Making in Biomedicine*, R.E. Bulger, E.M. Bobby, H.V. Fineberg (eds.), Washington, DC: National Academy Press, 1995, 432-457.

77. National Research Council, *Understanding Risk: Informing Decisions in a Democratic Society*, Washington, DC: National Academy Press, 1996.