Testimony of Stuart A. Newman, Ph.D.
Hearing on Human Cloning
Committee on Health, Education, Labor and Pensions
U.S. Senate
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My name is Stuart Newman. I have been a professor of Cell Biology and Anatomy at New York Medical College since 1979, where I teach medical and graduate students and direct a laboratory in developmental biology. This is the scientific field that studies embryo development, cloning, regeneration, and stem cells. My work on the development of form and pattern in animal embryos has been supported over the past 25 years by grants from the National Science Foundation and the National Institutes of Health. I am currently the recipient of two Federal grants.

Since my student days I have also been concerned with the uses to which scientific research is put. Having become convinced that scientists, who are beneficiaries of public resources, have a deep responsibility to anticipate what lies down the road in their own fields and to serve as a resource for the public on the complex issues around applications of scientific research, I joined with other scientists, social scientists, women's rights advocates, and environmentalists, to found the Council for Responsible Genetics in the late 1970s. The Council is now the Nation's oldest organization scrutinizing and interpreting the new genetic technologies, and has worked to educate the public on the scientific and social hazards of proposals to introduce inheritable genetic modifications into humans, including the allied technology of human cloning. I have placed into the record several documents from the Council that relate to the issues at hand, including the Genetic Bill of Rights, which

affirms, in part, that "All people have the right to have been conceived, gestated, and born without genetic manipulation."

I will state from the outset that I, and the Council for Responsible Genetics as an organization, unequivocally support a woman's right to make her own reproductive decisions. Therefore, while what I am here to tell you today calls into question technologies that manipulate, clone, and genetically alter human embryos, these views do not derive from any notion of the sanctity of the embryo, nor from attributing to it the status of a human being. Rather, our concerns derive from two distinct sources: (i) the irresponsible promotion of another scientifically questionable biotechnology, in conformity with what is now a recurrent pattern of playing to investors' hopes and patients' desperation; (ii) the destructive social consequences of moving down the technological path that begins with embryo cloning.

Specifically, cloning embryos for producing embryo stem cells will, by failing to deliver on its promises, inevitably lead to calls to extend the lifespan of clonal embryos so as to permit harvesting developmentally more advanced cells and tissues for research and potential therapies. The same well-intentioned imperatives that make some of you unwilling to deny patients who hope for relief by means of embryo stem cells will make you, or your successors, susceptible to demands for increased access to improved products of this work, up to and including full term clones from which to harvest organs.

I will try to lay out how this will happen. Embryo stem cells are derived from embryos that are less than two weeks old—the now proverbial "clump of cells in the bottom of a Petri dish." If derived from a clonal embryo resulting from transfer into an egg of a patient's somatic cell nucleus, the stem cells will be a genetic match for the nuclear donor. Transplants derived from such stem cells will be compatible with the immune system of

these patients. Please note, however, that this will be of little advantage to patients with type 1 diabetes, whose condition causes them to immunologically reject their own insulin-producing cells.

While such genetically matched cells may be tolerated by patients with other conditions, there are still likely problems. Two decades of research on embryo stem cells in genetically compatible mice has yielded a handful of studies with modest therapeutic results—in all cases less than what has been achieved with grafts of non-embryonic cells. Despite great efforts, embryo stem cells never become just one cell type or coherent tissue, but differentiate into disorganized mixtures of cell types. Most importantly, they are genetically unstable. If placed in adult mice they cause tumors. There is every reason to believe that human embryo stem cells, including those from cloned embryos, would cause cancer in human patients.

To overcome this, if it is indeed possible, will take years of research. Some say it's worth a try, and scientists and companies with patents on this technology are willing to make the attempt. However, science and medicine always gravitate toward better technologies. In fact, Dr. John Gearhart of Johns Hopkins University has isolated a different kind of human stem cell. These are derived from the developing gonads of 8-9 week human embryos, and could be obtained after elective abortion. Like the embryo stem cells, these so-called embryo germ cells can differentiate into all cell types. Most importantly, when transplanted into experimental animals they do not cause cancer.

On purely scientific grounds, embryo germ cells show greater promise than embryo stem cells. Now, if they were derived from clonal embryos they would be nearly perfect, again in a purely scientific sense. But interestingly, none of the advocates of permitting embryo cloning has raised the specter of growing clonal embryos for 8 to 9 weeks so that

genetically matched embryo germ cells could be harvested. These embryos would, of course, no longer be clumps of cells in a Petri dish, and some supporters of embryo cloning here might object. Right now it would be a hot potato, but once we have clonal embryos for a while and have gotten used to the idea, who would turn a deaf ear to calls by patients and their loved ones for these superior therapeutics?

And once stem cell harvesting from two-month clonal embryos was in place, who could resist the pleas to extend the time-frame so that liver and bone marrow could be obtained from six-month clonal fetuses to cure sufferers of life-threatening blood disorders such as beta-thalassemia, or so that brain lining cells could be harvested from near-term fetuses to treat Parkinson's sufferers?

I emphasize that all of this makes perfectly good scientific and medical sense. The only thing that stands in the way is a sense of propriety concerning the uses to which developing human embryos and fetuses may be put. Some of you may draw the line at the tiny clump of cells; others at the two-month embryo; still others somewhat short of full-term. Wherever each of you decides to leave this particular train, there will be others who will assert their right to take it to the next station. After Dolly the sheep was cloned, a British scientist suggested, tongue-in-cheek, that inactivation of brain-inducing genes could be used to produce headless full-term human clones for organ harvesting. To his surprise, Britain's most prominent embryologist publicly replied, "Why not?" Short of saying no to embryo cloning, any line that you draw will be a moving boundary. Few in this room would go along with the more extreme possibilities, but what about future generations growing up in a world in which producing clonal embryos for spare parts is medicine as usual?

Not only this, but the scientific publications that will ensue if embryo cloning proceeds will enable those reckless individuals who have announced their intention to make full-term

clones, and then genetically-"improved" clones, to do so. Those who think that handling clonal embryos as controlled substances in regulated laboratories will stop the transfer of the technology do not understand how science works.

This is my prediction: if embryo cloning is permitted, within a few years frustration over lack of progress in producing safe and effective therapeutics from embryo stem cells will lead to calls to permit harvesting of embryo germ cells from 2-3 month clonal embryos, and we may all find ourselves here again. The rest will be just a matter of time. But there are other possibilities. Stem cells derived from adult tissues and umbilical cord blood have already proved to be effective therapeutics in animal models and in clinical trials. There is less commercial interest around them since it is difficult to obtain patents on a patient's own cells. Correspondingly, however, these cells are immunologically compatible with the patient from whom they are derived. It will take much additional work to make this technology practical, but scientifically, and societally, I am convinced that this is the way to go.

APPENDIX I

Council for Responsible Genetics Statement on Embryo Research

June 2001

The Council for Responsible Genetics unequivocally supports a woman's right to make her own reproductive decisions. However, we oppose the utilization of human eggs and embryos for experimental manipulations and as items of commerce because of the potential for eugenic applications and health risks to women and their offspring.

The Council for Responsible Genetics therefore calls for a ban on the buying or selling of human eggs or embryos, and the manipulation of any and all human eggs or embryos by transfer of cells, nuclei, cytoplasm, mitochondria, chromosomes, or isolated DNA or RNA molecules of human or non-human origin.

This ban would apply whether or not the embryos are to be implanted and gestated and irrespective of the sources of funding, whether public or private.

No human embryo is to be produced solely for purposes of research.

APPENDIX II

THE GENETIC BILL OF RIGHTS

PREAMBLE

Our life and health depend on an intricate web of relationships within the biological and social worlds. Protection of these relationships must inform all public policy.

Commercial, governmental, scientific and medical institutions promote manipulation of genes despite profound ignorance of how such changes may affect the web of life. Once they enter the environment, organisms with modified genes cannot be recalled and pose novel risks to humanity and the entire biosphere.

Manipulation of human genes creates new threats to the health of individuals and their offspring, and endangers human rights, privacy and dignity.

Genes, other constituents of life, and genetically modified organisms themselves are rapidly being patented and turned into objects of commerce. This commercialization of life is veiled behind promises to cure disease and feed the hungry.

People everywhere have the right to participate in evaluating the social and biological implications of the genetic revolution and in democratically guiding its applications.

To protect our human rights and integrity and the biological integrity of the earth, we, therefore, propose this Genetic Bill of Rights.

THE GENETIC BILL OF RIGHTS

1. All people have the right to preservation of the earth's biological and genetic diversity.

2. All people have the right to a world in which living organisms cannot be patented, including human beings, animals, plants, microorganisms and all their parts.

3. All people have the right to a food supply that has not been genetically engineered.

4. All indigenous peoples have the right to manage their own biological resources, to preserve their traditional knowledge, and to protect these from expropriation and biopiracy by scientific, corporate or government interests.

5. All people have the right to protection from toxins, other contaminants, or actions that can harm their genetic makeup and that of their offspring.

6. All people have the right to protection against eugenic measures such as forced sterilization or mandatory screening aimed at aborting or manipulating selected embryos or fetuses.

7. All people have the right to genetic privacy including the right to prevent the taking or storing of bodily samples for genetic information without their voluntary informed consent.

8. All people have the right to be free from genetic discrimination.

9. All people have the right to DNA tests to defend themselves in criminal proceedings.

10. All people have the right to have been conceived, gestated, and born without genetic manipulation.

Spring, 2000

APPENDIX III

THE COUNCIL FOR RESPONSIBLE GENETICS

POSITION PAPER ON HUMAN GERMLINE MANIPULATION

THE POSITION OF THE COUNCIL FOR RESPONSIBLE GENETICS

The Council for Responsible Genetics (CRG) strongly opposes the use of germline gene modification in humans. This position is based on scientific, ethical, and social concerns. Proponents of germline manipulation assume that once a gene implicated in a particular condition is identified, it might be appropriate and relatively easy to replace, change, supplement or otherwise modify that gene. However, biological characteristics or traits usually depend on interactions among many genes, and more importantly, the activity of genes is affected by various processes that occur both inside the organism and in its surroundings. This means that scientists cannot predict the full effect that any gene modification will have on the traits of people or other organisms.

In purely biological terms, the relationship between genes and traits is not well enough understood to guarantee that, by eliminating or changing genes associated with traits one might want to avoid, one may not simultaneously alter or eliminate traits one would like to preserve. Even genes that are associated with diseases and may cause problems in one context, can be beneficial in others.

There is no universally accepted ideal of biological perfection. To make intentional changes in the genes that people will pass on to their descendants would require that we, as a society, agree on how to classify “good” and “bad” genes. We do not have the necessary criteria, nor are there mechanisms for establishing such measures. Any formulation of such criteria would inevitably reflect particular current social biases. The definition of the standards and the technological means for implementing them would largely be determined by economically and socially privileged groups.

WHAT IS "GERMLINE MANIPULATION"?

The undifferentiated cells of an early embryo develop into either “germ” cells or “somatic” cells. The germ cells become the eggs or sperm of a developing organism and transmit its heritable characteristics. All other cells in the body are called somatic cells. While both types of cells contain genes, only the genes in germ cells are passed on to future generations.

Techniques are now available to change chromosomes of animal cells by inserting new segments of DNA into them. If this insertion is performed on specialized or differentiated body tissues, such as liver, muscle, or blood cells, it is referred to as somatic cell gene modification, and the changes do not go beyond the individual whose DNA is modified. If such changes are performed on sperm or eggs before fertilization, or on the undifferentiated cells of an early embryo, it is called germ cell or germline gene modification, and the changes are not limited to the individual organism. For when DNA is incorporated into an embryo's germ cells, or undifferentiated cells that give rise to germ cells, the altered gene or genes will be passed on to future generations and may become a permanent part of the gene

pool.

Deliberate gene alterations in humans are often referred to as “gene therapy.” The Council for Responsible Genetics (CRG) prefers to use the terms “gene modification” or “gene manipulation” because the word “therapy” promises health benefits, and it is not yet clear that gene manipulations are beneficial nor that the conditions for which proponents urge such interventions are always “illnesses.”

PROPONENTS' ARGUMENTS FOR ATTEMPTING GERMLINE MODIFICATION IN HUMANS

If one or both sex partners carry a version of a gene that could predispose their offspring to inherit a condition they want to avoid, genetic manipulation may seem like a way to prevent the undesired outcome. The earlier during embryonic development the targeted gene or genes are altered or replaced, the less likely is the resulting individual to be affected by the unwanted gene. While the immediate goal of such a modification might be to alter the genetic constitution of a single individual, modifications made at early embryonic stages would also affect the offspring of this future person.

One use proposed for germline modification has been to “cleanse” the gene pool of “deleterious” genes. For example, Daniel E. Koshland, Jr., a molecular biologist and the former editor-in-chief of Science, has written, "keeping diabetics alive with insulin, which increases the propagation of an inherited disease, seems justified only if one ultimately is willing to do genetic engineering to remove diabetes from the germline and thus save the anguish and cost to millions of diabetics” (2). Another goal of germline manipulation may be to avoid the need for repeated somatic gene modifications.

Some people also suggest that germline modification would enable couples to “enhance” certain characteristics of their offspring. In the article referred to above, Koshland raises the possibility that germline alterations could meet future “needs” to design individuals "better at computers, better as musicians, better physically."

WHAT IS THE TECHNICAL FEASIBILITY OF MODIFYING THE HUMAN GERMLINE?

Both somatic and germline modification are widely performed on laboratory animals for research purposes. Beginning in 1990, somatic gene modifications have been performed on humans, and the FDA is reviewing additional experimental protocols in increasing numbers (3).

No published reports have yet appeared on germline modification in humans, but articles proposing such procedures are appearing with increasing frequency (4, 5). In mice and other animals that have been employed as models for human biology, germline modification has actually proved technically easier than somatic modification. The cells of early embryos incorporate foreign DNA and synthesize the corresponding functional proteins more readily than do most differentiated somatic cells. In the first widely-reported successful experiment using the germline technique, an extra gene that promoted the synthesis of growth hormone was introduced into fertilized mouse eggs and the unusually high levels of the hormone made the mice grow to twice their normal size. Germline techniques are also being used to

modify farm animals in attempts to increase yields of meat or enhance its nutritional quality, to cause them to produce pharmaceuticals in their milk, and to make their organs more suitable for human transplantation

Given what has been accomplished in animals and the availability of in vitro fertilization, there appear to be no technical obstacles to initiating germline modification experiments in humans.

WHAT ARE THE TECHNICAL PITFALLS?

Current methods for germline gene modification of mammals are inefficient, requiring the microinjection of DNA into numerous eggs before one egg is successfully modified. Furthermore, introduction of a foreign gene into an inappropriate location in an embryo's chromosomes can have unexpected consequences. For example, the offspring of a mouse that received an extra copy of a normally present gene, while appearing unaffected at birth, developed cancer at 40 times the rate of the unmodified strain of mice (6). In another experiment, disruption of a normal gene by insertion of foreign DNA into mouse embryos resulted in mice that lacked eyes, the semicircular canals of their inner ears, and in anomalies of the tissue that mediates the sense of smell (7). This second case highlights the fact that the techniques used for making germline modifications can produce developmental disruptions in the manipulated embryo itself.

Techniques to introduce foreign DNA into eggs, however, are constantly being developed and will eventually be portrayed as efficient and reliable enough for human applications. For example, it may soon be possible to place a gene into a specified location on a chromosome while simultaneously removing the unwanted gene. This will increase the accuracy of the procedure, but it will not eliminate the possibility of creating genetic changes or combinations that will be harmful to the modified embryo and its descendants. Such inadvertent damage could be caused by technical error, but more importantly, it could also arise from biologists' inability to predict how genes or their products interact with one another and with the organism's environment to give rise to biological traits. It would have been impossible to predict, a priori, for example, that someone who has even one copy of the gene associated with the blood protein known as hemoglobin-S would be protected against malaria, whereas a person who has two copies of this gene would develop sickle cell disease.

This unpredictability applies with equal force to germline genetic modifications intended to correct presumed disorders and to those introduced to enhance desired characteristics.

SOCIAL AND ETHICAL IMPLICATIONS OF GERMLINE MANIPULATION

The attempt to improve the human species biologically is known as eugenics, and formed the basis of a popular movement in Europe and North America during the first half of the twentieth century. In the 1920’s and 1930’s, eugenics was advocated by prominent scientists across the entire political spectrum, who represented it as the logical outcome of the most advanced biological thinking of the period. In the United States, eugenic thinking resulted in state laws permitting forced sterilization of individuals regarded as inferior because they were variously disabled or “feeble minded or paupers.” In Europe, the Nazis took up these ideas, and their extermination programs led to widespread revulsion against the concepts of

eugenics.

Today, public discussion in favor of influencing the genetic constitution of future generations has gained new respectability with the increased possibility for intervention presented by in vitro fertilization and embryo implantation technologies. Although it is once again espoused by individuals with a variety of political perspectives modern eugenic programs are now defended as driven by individual need and "choice." But the doctrine of social advancement through biological perfectibility underlying the new eugenics is even more potent than the older version: its supporting data seem more scientifically sophisticated, and the alignment between the State, through its support of the market, and the individual exercising so-called free choice, is unprecedented. The result could be similar to the organized eugenics programs so avidly embraced prior to the Second World War.

It is important to recognize that the dream of eliminating "harmful" gene variants (such as those associated with cystic fibrosis or Duchenne muscular dystrophy) from the entire human population could be realized only over time scales of thousands of years, and then only with massive coercive programs of germline manipulation monitored by special genetic police. Such programs would be neither feasible nor morally acceptable. In practice, then, any presumed beneficial effects of germ line modification would affect only individual families and are not likely to yield a public health benefit unless accompanied by unacceptable compulsion. This is in contrast to harmful genetic effects, which are likely to be widely disseminated given patterns of human reproduction and migration.

Even without access to germline modification, people could avoid having a child who manifests a trait they do not want to pass on. Prenatal diagnosis and abortion are available options; so are obtaining eggs, sperm or embryos from people who do not carry the trait in question; and so indeed is adoption. As disability rights advocates have pointed out, most disabilities are acquired and not inherited, and we have in no way exhausted the social measures that could be implemented to enable people with disabilities to live ordinary lives. Given that there are alternatives for avoiding the inheritance of "unwanted genes", the main selling point of germline modification over the long term would appear to be the prospect of "enhancement" of desired traits—designer children.

While, as noted above, unsuccessful attempts at germline modification can profoundly perturb ordinary biological function and introduce new, harmful genetic variants into the gene pool, even "successful" attempts will for the first time bring production of human beings into the realm of designed items. Like all such items, these human specimens will be subject to the fashions of the times.

These considerations make the social and ethical problems raised by germline gene modification very different from those raised by genetic manipulations that target specific nonreproductive tissues and organs of individual patients, as with somatic cell gene modification.

Health conditions targeted in clinical trials of somatic gene modification include cystic fibrosis, lung cancer, malignant melanoma, breast cancer, brain cancer, and muscular dystrophy. Such trials are being conducted at many major medical research institutions.

Violations of regulations and conflicts of interests in these trials have been pervasive (8,9), and have led to deaths of research subjects. Like the testing of new pharmaceuticals, somatic manipulations affect only the individual who undergoes them. However, these treatments are not strictly analogous to other therapies that incur individual risks. Radiation, chemotherapy or drug treatments can be stopped if they prove harmful to patients, while some forms of somatic gene modification cannot. Subjects thus forfeit their right to withdraw from a research study because the intervention cannot be stopped, whether it proves harmful or not. **While it appears that somatic gene modification techniques will be used increasingly in the future, the CRG urges that they be used with great caution and only for life-threatening conditions.**

While a policy of proceeding with caution may be suitable for somatic gene modifications, the goal of which is to cure or alleviate health problems of existing individuals who are able to consent to the intervention, such a policy is not appropriate for germline modification. Many of the ethical arguments against germline modification are similar to those that pertain to somatic cell modification. In addition the following arguments lead us to unequivocally oppose germline modification:

(1) Germline modification is not needed in order to save the lives, or alleviate the suffering, of existing people. Its target population are ”prospective people” who have not even been conceived.

(2) The cultural impact of treating humans as biologically perfectible artifacts would be entirely negative. People who fall short of some technically achievable ideal would be seen as “damaged goods”, while the standards for what is genetically desirable will be those of the society's economically and politically dominant groups. This will only increase prejudices and discrimination in a society where too many such prejudices already exist.

(3) There is no way to be accountable to those in future generations who are harmed or stigmatized by wrongful or unsuccessful germline modifications of their ancestors.

The Council for Responsible Genetics therefore calls for a permanent ban on germline gene modification.

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