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Human Embryo Research

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Summary

The FY1998 Labor-HHS-Education Appropriations Act, P.L. 105-78, enacted on November 13, 1997, prohibits the National Institutes of Health (NIH) from funding human embryo research in fiscal year 1998. This ban applies to all federally supported investigations involving the creation of a human embryo or embryos for research purposes, and studies in which a human embryo is destroyed, discarded, or knowingly exposed to risk of injury or death greater than that allowed for research on fetuses in utero as delineated in 45 CFR 46.208 (a)(2) and section 498(b) of the Public Health Service Act.[1] The expression "human embryo or embryos" include any organism not protected under 45 CFR 46 (Protection of Human Subjects) that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes (egg and sperm, female and male sex cell, respectively) or human diploid cells. Current research involving human embryos, done in the private and international sectors, pertains largely to the preimplantation embryo that results from in vitro fertilization.[2] It does not include human embryos or fetuses developing in the uterus or aborted human fetal tissue which are regulated as required in 45 CFR 46.201-46.211 (see CRS Report 95-886 for information on human fetal tissue research). In vitro fertilization is a medically assisted conception procedure in which mature oocytes (eggs) are removed from a woman's ovary and fertilized with sperm in a laboratory dish. Once fertilized, the embryo, when it has grown to a 32-cell embryo, can be transferred to the uterus and, if it implants, may develop to term and result in the birth of an infant. This report addresses some of the issues associated with human embryo research.

[1] The risk to the fetus must be minimal and the purpose of the research must be development of important biomedical knowledge which cannot be acquired by other means. Minimal risk is defined as that the probability and magnitude of harm or discomfort expected in the study are not greater than those ordinarily faced in daily life or the performance of routine physical or psychological tests, 45 CFR 46.208(a)(2), and 46.102.

[2] In vitro fertilization, the term *pre-implantation embryo* refers to the entity which exists during the first 14 days of development following fertilization. Peter Singer et al,. *Embryo Experimentation* (Cambridge University Press, 1990) p. xi, 4.

Background

In September 1994, a National Institutes of Health (NIH) Human Embryo Research Panel (NIH Panel) released a report which recommended that some areas of human mbryo research be acceptable to receive federal funds, including embryos created expressly for the purposes of research, under certain limited conditions.[3] The NIH Panel, made up of 19 individuals with expertise in basic and clinical research, ethics, law, social science, among other fields, also identified areas of human embryo research it considered to be unacceptable, or to warrant additional review. The Panel's report was unanimously (9 to 0) accepted by the Advisory Committee to the Director (ACD) of NIH on December 2, 1994. However, on that same day following the ACD meeting, President Clinton directed NIH not to allocate resources to "support the creation of human embryos for research purposes." The President's directive did not apply to research involving so-called "spare" embryos, those that sometimes remain from clinical IVF procedures performed to assist infertile couples become parents. Nor did it apply to human parthenotes, eggs that begin development through artificial activation, not through fertilization.[4] Animal studies of parthenotes have shown that they, in the early stages of development, can develop similarly to normal animal embryos. However, when transferred to the animal uterus, few have reached the stage of implantation.

The 103rd Congress and President Clinton had given NIH the authority to support human embryo research on June 10, 1993, with enactment of the National Institutes of Health Revitalization Act of 1993, P.L. 103-43 (Sec. 492A, or 42 USC 289a-1).[5] In response, NIH established the Human Embryo Research Panel to assess the moral and ethical issues raised by this research and develop recommendations for the agency's review and conduct of human embryo research. Following the President's December 1994 order to NIH not to allocate resources to "support the creation of human embryos for research purposes," the agency proceeded with plans to develop guidelines to support research using spare embryos. However, these plans were halted on January 26, 1996, with the enactment of P.L. 104-99, that prohibited NIH from using FY1996 funds human embryo research altogether. An identical ban was included in the Omnibus Appropriations bill that allocated funds for NIH in FY1997, P.L. 104-208, and a similar one applies to FY1998 funds.

Potential Uses for Human Embryo Research

Human embryo research currently is done in the United States and other countries, including Canada, the United Kingdom, and Australia. In the United States, this research

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[3] NIH, *Report of the Human Embryo Research Panel*, 27 September 1994.

[4] Fertilization is the fusion of sperm and egg (gametes) nuclei. In humans, for two weeks following fertilization, the product of conception undergoes preembryonic development and is known as the conceptus. From the third through eighth weeks after fertilization, the conceptus is called an *embryo*, and from the ninth week through birth, a *fetus*. Elaine Marieb, *Human Anatomy and Physiology* (The Benjamin/Cummings Publishing Co., Inc. 1989) pp. 956-957.

[5] This law ended the so-called de facto ban on federal human IVF funding which had been in effect since a Department of Health and Human Services Ethics Advisory Board (EAB) concluded in 1979 that IVF research was acceptable from an ethical standpoint.

is supported with private funds and performed principally at the more than 300 in vitro fertilization (IVF) clinics throughout the country. The major objective of much of this research has been to enhance the efficiency of IVF. The NIH Panel also found that research on preimplantation embryos created in an IVF setting had the potential to lead to a number of scientific and medical advances, including enhanced understanding and potential treatment of infertility, genetic disease, and cancer.

Improving IVF - Infertility, or the inability of a couple to conceive a child after at least one year of regular intercourse without contraception, affects at least 2.8 million U.S. couples.[6] Approximately half of these couples eventually conceive with some form of treatment, such as IVF or other assisted reproductive procedures, and interestingly, in a significant number of cases, some couples conceive independently of treatment.[7] Since the birth of the first IVF baby in 1978 in England, there have been more than 16,000 IVF births worldwide.[8] However, the overall live birth rate — 14% for each IVF treatment cycle in the United States and 12.5% in England[9] — is very low. Investigators at IVF clinics have focused most of their embryo research efforts on trying to improve the low efficiency of IVF. Such work suggests that in some cases, there may be problems with embryos themselves (e.g., genetic defects), and in others, problems associated with the culture conditions or uterine problems that prevent implantation.

Currently, investigators rely on donated spare embryos for research. The overall percentage of normal embryos in IVF clinics considered to be "spare" is about 13%.[10] These embryos include those donated for research by couples because they are no longer needed for implantation, or they are considered to be abnormal. However, researchers identify insufficient availability of "normal" embryos as a major barrier to improving the IVF procedure. Embryos that are unsuitable for implantation have limited value for research purposes; many of them have chromosomal abnormalities. The NIH Panel suggested that federal funding of such research might lead to improvements in culture conditions, or to the development of noninvasive diagnostic tests to distinguish embryos with greater developmental potential.

Preventing Pregnancy Loss - Even with natural conception, where eggs are fertilized in the body as a result of intercourse and embryos implant naturally in the uterus, up to 60% of embryos are believed to fail to implant or miscarry once they have implanted. A large proportion of these losses are thought to be caused by genetic defects in embryos, such as chromosomal and single-gene deformities; one-third or more may be

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[6] Machelle M. Seibel, "A New Era in Reproductive Technology," *New England Journal of Medicine*, 31 March 1988, p. 828-834.

[7] H.W. Jones, and J. P. Toner, "The Infertile Couple," *NEJM*, 2 December 1993, p. 1710-1715.

[8] Carol Lawson, "Celebrated Birth Aside, Teen-Ager Is Typical Now," *New York Times*, 4 October 1993, p. A18.

[9] R.M.L. Winston, and A. H. Handyside, "New Challenges in Human In Vitro Fertilization," *Science*, v. 260, 14 May 1993, p. 932-936.

[10] This figure was based on a study of IVF in England, which may or may not be comparable to what happens in the U.S. Winston, *New Challenges in Human In Vitro Fertilization*.

grossly abnormal.[11] Other causes of pregnancy loss occur during implantation, when at about a week after fertilization, the embryo normally begins to implant into the wall of the uterus. The NIH Panel concluded that federally funded studies in this area might lead to greater understanding of this process and eventually to the development of therapies to prevent implantation failure and other causes of pregnancy loss.

Preimplantation Genetic Diagnosis - Preimplantation diagnosis of embryos is a technique used experimentally since 1992. It was developed to help couples who are at high risk of passing on a serious genetic disease. It has been used with IVF for couples who are fertile but who had a child born with a genetic condition and know they are at risk of having a second affected child. IVF with preimplantation genetic diagnosis permits doctors to identify embryos that are unaffected with a specific genetic abnormality before transfer to the uterus.[12] In this procedure, one or two cells can be removed from an IVF embryo at the 8- to 16-cell stage for biopsy, without affecting subsequent development of the embryo.[13] Genetic material, deoxyribonucleic acid (DNA), in the biopsied cells can then be amplified[14] and analyzed for the presence or absence of the defect. Embryos from which biopsied cells are determined to be unaffected can be transferred to a woman's uterus for implantation in the same day as the biopsy. At the time of the NIH Panel assessment, 29 healthy children had been born worldwide as a result of this technique, and 11 pregnancies were ongoing.[15] It has been applied successfully to a number of diseases including cystic fibrosis, Lesch-Nyhan syndrome, Duchenne muscular dystrophy, and Tay-Sachs disease.

The NIH Human Embryo Research Panel

The NIH Panel released its report on September 27, 1994. The Panel determined that "sufficient arguments existed to support the permissibility of certain areas of research involving the preimplantation human embryo within a framework of stringent guidelines." The Panel identified three major factors that led to its affirmation of certain kinds of embryo research: (1) the promise of human benefit from embryo research is significant and carries great potential benefit to infertile couples, to families with genetic conditions, and to individuals who need effective therapies for a variety of diseases; (2) even though the preimplantation human embryo warrants serious moral consideration as a developing form of human life, it does not have the same moral status as infants and children, because it lacks most qualities considered relevant to the moral status of persons, including sentience (capacity for sensation or feeling), and there is a very high rate of natural mortality at the preimplantation embryo stage; and (3) without federal funding and

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[11] R.G. Edwards, "Causes of Early Embryonic Loss in Human Pregnancy," *Human Reproduction*, v. 1, no. 3, 1986, p. 185-198.

[12] Winston, *New Challenges in Human In Vitro Fertilization*.

[13] Reproductive Technologies, P.O.S.T. Briefing Note 48, January 1994, British Parliamentary Office of Science and Technology.

[14] Amplification of genetic material of interest is done using a method known as polymerase chain reaction, or PCR. PCR amplifies DNA of any origin and can increase the amount of DNA sequence hundreds of millions of times and more. B. Eisenstein, *NEJM*, Jan. 18, 1990, p. 178-183.

[15] *NIH Human Embryo Research Panel Report*.

regulation of preimplantation embryo research, this research will continue to be done in the private sector without consistent ethical and scientific scrutiny.

The NIH Panel determined that embryos donated by couples in IVF programs are acceptable sources for research, whether the embryos are transferred to the uterus or not. The Panel also concluded that, because research involving the fertilization of eggs is required to answer crucial questions in reproductive medicine, it is ethically permissible to fertilize donated eggs expressly for research purposes. However, this should be allowed, they said, only if the research cannot be validated any other way, or when a compelling case is made that the research is required to validate a study that has potential outstanding scientific and therapeutic value.[16] The Panel identified a number of types of embryo research they considered to be acceptable for federal funding, including studies directed at improving the likelihood of a successful pregnancy, preimplantation genetic diagnosis studies, and research on the fertilization process. However, this research should be allowed only if it adheres to certain standards, including: it must be conducted by scientifically qualified individuals; it should involve the minimum number of embryos required; and it should be done with the informed consent of the donors of embryos or oocytes and sperm. The Panel recommended that all such embryo research proposals also be reviewed by a national advisory body for the first 3 years at a minimum.

Areas of research considered by the Panel to warrant additional review include studies which would use fetal oocytes for fertilization and investigations involving the development of embryonic stem cells (which could potentially improve bone marrow transplantation) from embryos fertilized specifically for this purpose. In addition, cloning by blastomere separation or blastocyst splitting without transfer to a patient's uterus were considered in need of further review.[17] The Panel did not determine if such proposals were acceptable or not acceptable, but suggested that they not be federally funded for the foreseeable future, unless there was an extraordinary demonstration of scientific or therapeutic justification, as well as review by an ad hoc advisory body.

The Panel also found various types of embryo research to be unacceptable for federal funding and advised that they not be funded for the foreseeable future. Included was research involving fertilization of fetal oocytes with transfer, cloning followed by transfer to a woman's uterus, and studies which would attempt the transfer of parthenogenetically produced human eggs. Significant ethical concerns were cited as the grounds against funding.

The Moral Status of the Human Embryo

The subject of research on human embryos presents profound ethical and policy issues. The central issue relates to the moral status of the human embryo, a controversy which originates largely from differences in deeply held religious and philosophic views.

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[16] One Panel member dissented from the Panel's conclusion about the second condition.

[17] In blastomere splitting, at the two- to eight-cell embryo stage, each cell is separated and cultured individually where they divide and form smaller-than-normal embryos, which can then be transferred to the uterus. In blastomere separation, a single embryo at the blastocyst stage is mechanically split into two and both halves are transferred to the uterus, where, identical twins could develop.

Opponents of human embryo research believe that a human embryo is a human being, and that it must be accorded the moral status of a person from the time of fertilization. Some holding this view argue strongly that human embryos should therefore be the subject of no research, while others support research if the embryo will be the direct beneficiary.

Supporters of embryo research believe that very early embryos, those up to the implantation stage of development, do not have the same moral and legal status as persons. While they acknowledge that embryos are irrefutably genetically human, they believe embryos do not have the same moral relevance, because of the lack of specific capacities, including consciousness, reasoning and sentience.[18] They argue that it is morally acceptable to perform limited research on embryos, particularly because of the potential therapeutic and scientific benefit the research holds for persons. For example, they believe it is ethically acceptable to investigate early development of embryos until 14 days after fertilization, the period during which implantation is believed to take place. Many holding this view, including the NIH Panel, believe that the importance of the potential knowledge obtained from this research must be considered. Opponents, however, argue that this goes against the principle that human beings should be treated as ends but never simply as means.

Pending Legislation Involving Human Embryos

Legislation was introduced on January 27, 1998, S. 1574 (Campbell), that would prohibit the "conduct of research for cloning a human being or otherwise creating a human embryo by any person. The bill cited as the "Human Cloning Prohibition Act," also prohibits federal funds from being obligated or expended to knowingly conduct or support research to clone a human being or otherwise create a human embryo. Violators of this law would be subjected to civil penalty of up to $5,000 for each violation. S. 1574 has been referred to the Committee on Labor and Human Resources. In addition, H.R. 922 (Ehlers), the "Human Cloning Research Prohibition Act," was reported to the House on August 1, 1997 (H.Rept. 105-239, Part I), by the House Committee on Science (amended). This bill would prohibit federal funds from being obligated or expended for research that includes the use of human somatic cell nuclear transfer technology to produce an embryo (for more information on human somatic cell nuclear transfer and cloning, see CRS Report 97-335).

[18] Presentation by Bonnie Steinbock, Ph.D. Dept of Philosophy, State University of N.Y., Albany, NIH Human Embryo Research Panel meeting, 3 February 1994.