Displaced Agendas: Current Regulatory Strategies for Germline Gene Therapy

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Recent developments in biotechnology are radically affecting the nature of reproduction and the manner in which we approach disease. In particular, germline gene therapy, or the insertion of genetic material into cells while they are developing and dividing, offers the promise of eradicating genetic defects in humans during embryonic development. In this article, the authors argue that the social and ethical implications of the developments in the field of germline gene therapy have not yet received adequate consideration. Unlike previous technologies which targeted already-developed cells, germline gene therapy can potentially correct and eliminate genetic deficiencies at the developmental stages of a cell. This raises issues of genetic enhancement beyond the therapeutic applications of this technology. However, the authors submit that an established pattern of subordinating social and ethical issues to technical and scientific debate in the regulatory arena is repeating itself in the case of discussions over germline gene therapy. The authors suggest that the American scientific regulatory process fails to fully meet the challenges of this technology, particularly because social and ethical issues are not formally considered in the existing process. They therefore suggest that American regulatory agencies should look to the approach taken by Europe with regard to germline gene therapy as an emerging technology, and that it may bo necessary to incorporate effective public debate over social and ethical concerns into a regulatory process which is primarily concerned only with the efficacy of new technologies.

Les développements récents en biotechnologie ont un impact sérieux sur la nature de la reproduction ainsi que sur notre conception de la maladie. En particulier, la thérapie génique germinale, soit l'insertion de matériel génétique dans des cellules en cours de développement et de division, ouvre la perspective d'éliminer les anomalies génétiques chez les êtres humains au cours du développement embryonnaire. Les auteures soutiennent que les questions sociales et éthiques soulevées par les progrès dans ce domaine n'ont pas encore été assujetties à une analyse adéquate. Contrairement à la technologie préalable ciblant des cellules déjà développées, la thérapie génique germinale peut potentiellement corriger et éliminer des déficiences génétiques lors du développement d'une cellule. Ceci soulève, au-delà des applications thérapeutiques de cette technologie, la problématique de l'amélioration génétique. Malgré cela, il apparaît que la tendance à subordonner les considérations sociales et éthiques au débat scientifique et technique dans le contexte de la réglementation se manifeste lors des discussious portant sur la thérapie génique germinale.

Les auteures avancent que le processus américain de réglementation scientifique ne répond pas aux défis posés par cette technologie, surtout parce que l'approche existante ne tient pas formellement compte des questions sociales et éthiques. Elles suggèrent par conséquent que les agences américaines de réglementation se tournent vers l'approche adoptée par l'Europe, qui, traitant la thérapie génique germinale comme une technologie nouvelle, reconnaît qu'il peut s'avérer nécessaire d'incorporer un débat public efficace sur les inquiétudes sociales et éthiques au sein d'un processus de réglementation qui, autrement, se préoccupe avant tout de l'efficacité des nouvelles technologies.

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Introduction

Scientific developments in the biotechnology age have introduced radical new technologies that are changing the nature of birth and reproduction as well as the way we approach disease. In recent years, these developments have included a variety of new reproductive technologies, cloning techniques, transgenics, gene replacement therapies, and hormonal manipulations. Proponents advocate these advances with enthusiasm, promising everything from total reproductive control and freedom from disease, to a higher state of human evolution. Others doubt the very wisdom of the interventions and advocate the imposition of tight restrictions on the pace of change. The social and ethical implications of these new technologies are profound: they not only hold potential and poorly understood risks, but they also hold the power to radically alter the genetic and cellular structure of human beings. The latest technology, and perhaps the most controversial, is germline gene therapy.

Germline gene therapy involves the insertion of genetic material into cells while they are still developing and dividing. The purpose is to replace faulty or missing genes.[1] The idea behind the therapy is to "fix" babies with genetic defects before they complete their development.[2] A recent proposal, for example, would involve genetic manipulation at the pre-implantation stage of embryonic development, the stage at which the embryo consists of only four to eight cells.[3] Genetic manipulation at this early stage is likely to affect most, if not all, of a developing foetus' cells. Thus far, the technology looks promising. Scientists involved in pursuing the technique point to preliminary data from animal models which suggest that germline gene therapy will be effective.[4]

The technology is far more radical and controversial than earlier gene therapy protocols. Somatic cell gene therapy, the prevailing technique to date, aims to replace flawed genes in already developed individuals and is targeted to particular classes of cells. Under this technology there is negligible risk that germ cells will be affected and that the trait will be passed on to progeny. However, in the case of germline ge-

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[1] See J.D. Watson *et al.*, *Recombinant DNA*, 2d ed. (New York: Scientific American, 1992) for advances in genetic research). See also Council for Responsible Geneties, "Position Paper on Human Germ Line Manipulation" (Fall 1992) at 1-3 [unpublished, archived with authors].

[2] "Genetics U.S. Experts Say Time to Think About Gene Therapy In Womb" *Gene Therapy Weekly* (12 October 1998), online: WL (HTHNEWS) [hereinafter "Gene Therapy in Womb"].

[3] For purposes of this article, the term "germline gene therapy" is used inclusively to refer to gene therapy directed expressly at the germ eells and gene therapy directed at the pre-implantation embryo. In directing gene therapy at the pre-implantation embryo, one has a theoretical opportunity to correct a genetic defect (or enhance) and to affect the germline. Later interventions, such as *in utero* gene therapy, also raise concerns about effects on the germline; however, in general *in utero* gene therapy has no intent to alter germ cells. Nevertheless, recent *in utero* gene therapy proposals indicate the movement toward earlier applications and raise concerns about germline effects.

[4] See R. Kolberg, "RAC Tiptoes into New Territory: In Utero Gene Therapy" (1995) J. NIH Research 37.

netic manipulation, it is expected that the procedure will affect the foetus' germ cells.[5] Scientists could therefore potentially "correct" a genetic deficiency in every embryo, thereby permanently eliminating the undesirable trait from future generations. At the same time though, the transferred genes could cause deleterious mutations that could also be passed on to progeny. Germline gene therapy offers a direct route to manipulating genetic expression in human beings, which raises significant questions about potential uses of the technique for the purposes of enhancement, well beyond any therapeutic goals.

Typically, the regulation of a new science in the United States gives priority to technical questions of risk and relegates social or ethical issues to subsidiary discussions.[6] This pattern is based on ingrained assumptions about scientific rationality and the ability of technical experts to distance themselves from social or political influence. When recombinant DNA techniques were introduced in the early 1970s, for example, initial public attention focused on the social, political and ethical ramifications of the technology. However, scientists and regulators quickly redefined the debate in terms of the safety and efficacy of the science.[7] Social considerations were gradually marginalized and often ignored. Similarly, expert assessments of the safety of bovine growth hormone were allowed to overwhelm the dissenting voices of farmers and social critics in the regulatory arena.[8] Another example was in the dispute over foetal tissue research, where researchers refocused the issue on the technical criteria which determine the definition of life instead of giving way to an ethical debate over foetal rights.[9]

A similar pattern is emerging in the case of research on germline gene therapy. Though currently at an early stage of development, this clinical technology has been the subject of debate among scientists and bioethicists for years. The concerns came into sharper focus, however, in September, 1998, when geneticist W. French Anderson, an advocate of gene therapy, presented a "pre-protocol" for *in utero* gene therapy to the National Institutes of Health ("NIH") Recombinant DNA Advisory Committee ("RAC"). At that time, it became clear that the research was moving quickly and inexorably toward actual clinical application. The subsequent response of the RAC suggests that social and ethical concerns will once again occupy only a limited place in regulatory discussions. The applicable regulatory agencies, the Food and Drug Administration ("FDA") and the NIH, are structured to focus on safety and efficacy rather than on social or ethical implications. Moreover, the RAC's role within the NIH

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[5] P.R. Billings & S.A. Newman, "Crossing the Germline" *Genewatch* 11:5-6 (January 1999) 1; Watson, *supra* note 1 at 569.

[6] See generally D. Nelkin, ed., *Controversy: The Politics of Technical Decisions* (Beverly Hills: Sage Publications, 1992).

[7] S. Krimsky, *Genetic Alchemy* (Cambridge: MIT Press, 1992).

[8] See E. Marden, "Recombinant Bovine Growth Hormone and the Courts: In Search of Justice" (1998) 46 Drake L. Rev. 617.

[9] See S. Maynard-Moody, "The Fetal Research Dispute" in D. Nelkin, ed., *supra* note 6, 82.

was recently reduced, its membership cut back, and its power diminished.[10] Ultimately, in this regulatory environment, it is likely that ethical debates will be marginalized as germline gene therapy proceeds toward application.

This pattern stands in striking contrast to proceedings in Europe on the same subject. The Europeans have allowed social and ethical issues to set the agenda for germline gene therapy. The Council of Europe decided that biotechnologies which modify the genome of any descendant are an affront to "human dignity" and are therefore socially and ethically unacceptable.[11] This decision effectively banned germline gene therapies in Europe based on social and ethical grounds alone.

This article examines the current regulatory regime with regard to the broad range of issues raised by germline gene therapy. Part I describes the technique of germline gene therapy and its current status. Part II reviews the convergence of scientific hubris, commercial interests, and the media hype driving the technology. Part III looks at the broad range of potential problems associated with the therapy. Finally, Part IV reviews the existing regulatory apparatus, and notes its limited ability to deal with the social and ethical issues that are bound to arise during clinical applications.

I. Germline Gene Therapy: The Potential for Permanent Change

The earliest gene therapy experiments, called somatic cell gene therapy, sought to treat disease by altering genetic material in an individual's affected cells.[12] These experiments began in 1991 with great fanfare. However, technical problems in delivering genetic materials to diseased cells have thus far limited the success of these experiments.[13] Germline gene therapy, on the other hand, aims to get around these prob-

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[10] See "Recombinant DNA Research: Proposed Actions Under the Guidelines" 61 Fed. Reg. 59,726, 59,727-28 (1996) [hereinafter "Proposed Actions"]. For later implementation of these changes, see "Recombinant DNA Research: Actions Under the Guidelines: Part II" 62 Fed. Reg. 59,032 (1997) [hereinafter "Actions Under the Guidelines"]. Some argued that the changes made to the RAC would actually benefit public debate. For example, FDA believes that it was the case-by-case review by the RAC that actually marginalized ethical discussion; FDA's hope is that the new focussed RAC will have more, rather than less, time for ethics.

[11] Council of Europe, *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*, E.T.S. No. 164 (1997), online: Council of Europe <http://www.coe.fr/eng/legaltxt/164e.htm> (date accessed: 22 October 1999) [hereinafter *Convention on Human Rights and Biomedicine*].

[12] See FDA, "Guidance for Human Somatic Cell Therapy and Gene Therapy" (Center for Biologics Evaluation and Research, March 1998) at 3. For a description of somatic cell and germline gene therapy, see generally, Watson, *supra* note 1.

[13] T. Friedman, "Human Gene Therapy" (1996) 2 Nature Medicine 144 at 145; N. Touchette, "Gene Therapy: Not Ready for Prime Time" (1996) 2 Nature Medicine 7 ("gene therapy, although having great long-term prospects, has been oversold to the public"). Even W. French Anderson admitted the ongoing lack of success with somatic cell gene therapy: see *Engineering the Human Germline Symposium* (Summary Report) (1998) online: Engineering the Human Germline Symposium

lems by manipulating the "pre-implantation embryo," the stage at which an embryo consists of between only four and eight undifferentiated cells. The genetic manipulation is intended to replace defective genes at this very early phase, thus transmitting healthy genes to every iteration of the dividing cells.[14] On the basis of animal studies, scientists have already indicated that this form of gene therapy could be an effective treatment for cystic fibrosis.[15] In 1998, a lobby of well known scientists including W. French Anderson and James Watson, the Nobel prize laureate for the discovery of the structure of DNA, publicly proposed extending genetic engineering techniques to the germline.[16]

It was shortly after this announcement that Anderson presented research "pre-protocols" to the NIH as a way, he claimed, to force a discussion of risks involved with the procedure. Indeed, the question of regulation has moved to centre stage. Anderson proposed to modify the genes of foetuses affected with adenosine deaminase deficiency ("ADA")[17] and an inherited blood disorder, known as severe alpha thalassemia,[18] by introducing viral carriers carrying replacement ADA and protein genes into the cells of an affected foetus.[19] Anderson made the proposal "with collaborators from the University of Nevada, the Reno Veterans Affairs Medical Center, the University of Southern California, the National Institutes of Health and a private company founded by Anderson, called Human Gene Therapy."[20] He claims that the technique will be ready to perform within several years.[21]

<www.ess.ucla.edu/huge/report.html> (date accessed: 22 October 1999) [hereinafter *Engineering the Human Germline*].

[14] See E. Tanouye, "Efforts to Repair Fetal Genes Spark Debate Over Risks, Ethics" *Wall Street Journal* (2 April 1996) B1.

[15] R. Kolberg, *supra* note 4. Scientific articles on germline gene therapy are a presence in the literature. See *e.g.* B. Gulbis *et al.*, "Protein and Enzyme Patterns in the Fluid Cavities of the First Trimester Gestational Sac: Relevance to the Absoptive Role of Secondary Yolk Sac" (1998) 4 Molec. Hum. Reprod. 857.

[16] See *Engineering the Human Germline*, *supra* note 13.

[17] ADA is an enzyme essential to the function of several cell types. In individuals with two dysfunctional ADA genes, the foetal immune system does not develop. As a result, the affected newborn will have a severe immune disorder and will thus be susceptible to infections and suffer high morbidity and mortality rates.

[18] Alpha thalassemia is a condition in which mature forms of hemoglobin are not properly produced, because a foetus lacks functioning alpha chain producing genes. As a result, the affected foetus generally will die around 20 weeks of development.

[19] J. Couzin, "RAC Confronts In Utero Gene Therapy Proposals" (1998) 282 Science 27. See also Billings & Newman, *supra* note 5.

[20] P.R. Billings & S.A. Newman, *supra* note 5 at 1-3.

[21] See "Just In Case You Think We're Making This Up", online: <www.users.globalnet.co.uk/~cahge/justin.htm> (date accessed: 28 February 2000).

The NIH considered the pre-protocols in January 1999 and postponed approval in view of the many questions that remain unanswered.[22] However, given the confluence of interests driving germline gene therapy, it may soon be a clinical reality.

II. The Interests Driving Germline Gene Therapy

As with so many areas of new technology, the progression toward germline gene therapy is driven by the convergence of scientific hubris, commercial interests, and media hype.[23]

A. Scientific Hubris

Many scientists and biomedical researchers herald the technology as a means of eliminating dreaded genetic diseases such as cystic fibrosis and ADA from the population. Together with patient advocates, they promise a day in which genetic disease will no longer be a reality.[24] Dr. Anderson, who has been a passionate advocate of developing gene therapies, has claimed that the techniques will revolutionize the nature of disease treatment, predicting that in the future, "[p]hysicians will simply treat patients by injecting a snippet of DNA and send them home cured."[25]

Other researchers have made equally hyperbolic promises about germline gene therapy. In June 1998, a group of practitioners met at a one-day symposium sponsored by UCLA's Science Technology and Society Program to foster public awareness of the emerging technology. John Campbell, a UCLA geneticist and moderator of the symposium, stated that

> Germline engineering may enable us to obtain the benefits of a century of genetic science. We now have the capacity to develop techniques to reliably and accurately introduce DNA constructs into germ cells and could begin to conceive and design genetic therapies to ward off diseases and improve the quality of human life.[26]

James Watson spoke of the new technique with equal enthusiasm: "Germline therapy will probably be much more successful than somatic [gene therapy]. We might as well do what we finally can to take the threat of Alzheimer's or breast cancer away from a family."[27] Lee Silver, a participant at the same symposium, similarly posited that "we now have the power to seize control of our evolutionary destiny."[28]

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[22] See RAC Statement (11 March 1999) online: Office of the Recombinant DNA Activities Homepage <http://www.nih.gov/od/orda/racinutero.htm> (last modified: 5 October 1999).

[23] E. Marden & D. Nelkin, "Cloning: A Business Without Regulation" (1999) 27 Hofstra L. Rev. 569.

[24] W. French Anderson, summarized in *Engineering the Human Germline*, *supra* note 13.

[25] Quoted in P. Dewitt, "The Genetic Revolution" *Time* 143:3 (17 January 1994) 46.

[26] *Engineering the Human Germline*, *supra* note 13.

[27] *Ibid.* at 9.

[28] *Ibid.* at 19.

Such statements reflect the belief that medicine must continually progress and embrace new technologies. Bioethicists L. Munson and L.H. Davis support this imperative:

> [M]edicine itself has a prima facie duty to pursue and employ germline gene therapy ... [W]e want to claim that members of the medical profession would be collectively derelict if research aimed at the therapeutic use of germline gene therapy were neglected without good reason.[29]

Similarly, ethicists John Fletcher and G. Richter claim that as the potential to diagnose genetic diseases becomes increasingly feasible, "[t]o refuse to pursue forms of gene therapy ... would be morally self-defeating at this juncture of human genetics."[30]

Proponents of germline therapy also tend to dismiss fears about the impact of the technology on society. James Watson reflected:

> I just can't indicate how silly I think is [the sanctity of the human gene pool]. I mean, sure, we have great respect for the human species. We like each other. We'd like to be better, and we take great pleasure in great achievements by other people. But evolution can be just damn cruel, and to say that we've got a perfect genome and there's some sanctity to it ... [is] utter silliness.[31]

Lee Silver has also touted the economic and social efficiency of a society in which there are "gen-rich" and "gen-poor" members. According to him, such genetic divisions would result in more fulfilling and productive lives for all involved.[32]

B. Commercial Interests

Commercial interests have converged with scientific hubris in promoting germline therapy. The economic stakes in this arena of technology are high. Currently, the United States has approximately 1,300 biotechnology companies employing 140,000 people. The product sales of genetically engineered products in 1997, including drugs and vaccines, were in the amount of $13 billion as compared to $7.7 billion in 1994, and there are 200 new products in final-phase trials or awaiting FDA approval. The total American investment in biotechnology R & D was approximately $9.1 billion in 1997.[33] Industry observers predict that the first gene therapy drug will be on the mar-

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[29] R. Munson & L.H. Davis, "Germ-Line Gene Therapy and the Medical Imperative" (1992) 2 Kennedy Instit. Ethics J. 137 at 153.

[30] J. Fletcher & G. Richter, "Human Fetal Gene Therapy: Moral and Ethical Questions" (1996) 7 Hum. Gene Therapy 1605.

[31] James Watson, quoted in *Engineering the Human Germline*, *supra* note 13.

[32] See "Just In Case You Think We're Making This Up", *supra* note 21 (quoting and analyzing Lee M. Silver's book *Re-making Eden* (New York: Bard, 1998)).

[33] See M.J. Malinowski & N. Littlefield, "Transformation of a Research Platform into Commercial Products: The Impact of United States Federal Policy on Biotechnology" in T. Caufield & B. Williams-Jones, eds., *The Commercialization of Genetic Research: Ethical, Legal and Policy Issues* (New York: Kluwer Academic/Plenum Publishers, 1999) 63. See also generally Pharmaceutical Manufacturers and Research Organization, *PhRma 1998 Industry Profile*' online: PhRma Publications

ket by 2000 and that by 2005 gene-therapy sales are expected to amount to $3.5 billion.[34]

With the growing focus on gene therapy, research in the area has enjoyed significant infusions of venture capital.[35] Members of the media have noted that, "if this area of science appears to be moving a bit fast for some members of the public, investors might say it isn't moving fast enough."[36] The driving motivation behind large commercial investments for pharmaceutical companies rests in a desire for "know-how ... so we can translate discoveries in the field into a concrete therapy, which Sandoz and Novartis would own and make money from."[37]

Economically, genetic enhancement is one of the most promising areas of gene therapy. Consumer demand for such therapies is already evident with the embrace of human growth factor therapy to "treat" shortness.[38] It has been predicted that "the demand for gene enhancement therapy will probably be very large, to give your children a better chance of success in the world."[39]

C. Media Hype

The media has picked up and amplified scientific and financial hype over this technology. When reporting on complex scientific issues, journalists often rely heavily on press releases from scientists and biotechnology firms[40] The result is often unbridled enthusiasm reflected in the headlines: "Genetic research leaves Doctors hopeful for Cures", "New Hope for Victims of Disease", "Genetics, the war on aging... [is]

<http://www.phrma.org/publications/industry/profile98/index.html> (date accessed: 3 December 1999).

[34] J. Lanthier, "It'll Take Longer to Clone Cash: Duplicating a Sheep Made Big Headlines But Investors Seeking Returns from Genetics Must be Patient" *Financial Post* (29 November 1997) 8. Another report predicts that the market for gene therapy could reach $45 billion by 2010. See L.M. Fisher, "Two Deals Extend the Financial Frontiers of Gene Therapy" *The New York Times* (10 January 1997) D5.

[35] Lanthier, *ibid.*

[36] Lanthier, *ibid.*

[37] E. Johnson, "Boehringer Networks to Get Ahead in Gene Therapy" (1997) 15 Nature Biotech. 12. See also L. Seachrist, "Bioethics Experts Sort Out Limits of Genetic Engineering" *Bioworld Today* (19 February 1998), online: WL (HTHNEWS) ("I don't believe we would be having the debate over genetic technologies if there weren't money to be made").

[38] See *e.g.* R.T. King Jr., "Study on Growth Hormone's Benefit in Boosting Height May Prolong Debate" *Wall Street Journal* (18 February 1999) B7; A. Toufexis, "A Growing Controversy: Debate Over Using Human Growth Hormone Injections to Make Short Children Grow Taller" *Time* 142:2 (12 July 1993) 49.

[39] Daniel Koshland, quoted in *Engineering the Human Germline*, *supra* note 13 at 10. See also comments of Sheila M. Rothman, quoted in V. Kiernan, "Cosmetic Uses of Genetic Engineering May Soon Be A Reality" *Chronicle of Higher Education* 44:6 (3 October 1997) A18 ("People are eager to use technology that they believe will improve their behavior, appearance or performance").

[40] See generally D. Nelkin, *Selling Science: How the Press Covers Science and Technology* (New York: W.H. Freeman, 1995).

the medical story of the century ... Genetic technologies will dramatically curtail heart disease, aging and much more."[41] A Gannett News Service story announced "Designer Genes in Store: Manipulative Therapy Just a Decade Away" and went on to suggest that "the ability to remove chance from our genetic hand of cards is closer than we think."[42] A professor of bioethics is quoted in another story: "Gene therapy for improving people is coming, and it will make it possible to improve your eyesight, your sex life, your hairline and your disposition."[43] An article in MSNBC On-line reported that the technology could make real the "promise of being born cured."[44] The article adds: "With gene therapy at the earliest stages, the likelihood of successfully rewriting the genetic code in all the relevant cells is much greater ..."[45]

III. Social and Ethical Issues

The development of germline gene therapy raises many questions about potential risks and especially those risks which may be imposed on future generations. Some critics, both scientists and bioethicists, express concern about the impact of germline gene therapy on the human gene pool, noting that a systematic elimination of genotypes may disrupt the delicate balance of dominant and recessive genes in the global gene pool.[46] They point to the fact that "bad" genes also serve useful purposes, noting for example that the gene that causes sickle cell anemia also confers partial resistance to malaria.[47] This begs the question: could genetic manipulations result in grave new disorders or genetic incompatibilities?[48] In this vein, biotechnology critic John Fagan has expressed that germline enginecring "will progressively corrupt the blueprint of our species with genetic errors." Accordingly, these errors "will irreversibly burden future generations with new genetic diseases, causing millions to suffer."[49]

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[41] A. Rosenfeld, "The Medical Story of the Century" *Longevity* (May 1992) 42.

[42] T. Friend, "Designer Genes In Store, Manipulative Therapy Just a Decade Away" *Florida Today* (4 November 1997), online WL (BUSNEWS).

[43] K. Danis, "Making Super Babies; Kids Bred to be Perfect May Lack Some of What Makes Us Human" *The New York Post* (20 December 1998), online: WL (BUSNEWS).

[44] G. McGee, "Designer Babies Raise Tough Questions" (1999) online: MSNBC Home <http://www.msnbe.com/news/229707.asp> (date accessed: 22 October 1999).

[45] *Ibid.*

[46] See D. Gianelli, "Fetal Gene Therapy Plan Stirs Fears Over Long-Term Safety" *American Medical News* (19 October 1998), online: WL (HTHNEWS) ("[Germline gene therapy] 'may unintentionally disturb the finely tuned function of one or several genes, ... interfere with the natural course of human evolution and have unforeseeable consequences on the survival of the species'").

[47] C. Joyce, "Should We 'Fix' Nature's Genetic Mistakes?" *USA Weekend* (24 April 1998) online: USA Weckend <http://www.usaweekend.com/98_issues/980426/980426forum_genes.html> (date accessed: 17 March 2000).

[48] D.C. Wertz, "Germ-line Gene Therapy Enters the Foreseeable Future" *The Gene Letter* (August 1998) online: GeneLetter <http://www.genesage.com/professionals/geneletter/archives/foresfuture.html>.

[49] J.B. Fagan, quoted in Editorial, "Will Cloning Beget Disasters?" *Wall Street Journal* (2 May 1997) A14.

There is a similar concern that the ultimate safety of germline genetic manipulations may be unknowable until many years after the treatment:

> Even if successful germline gene therapy can be done, it is difficult to design animal [models] that would predict potential late-stage complications in humans. For example, germ-line gene therapy might cure a patient of a fatal neurologic disease, but 20 to 30 years later a severe disabling polyneuritis might develop, one that did not occur in the preclinical toxicology tests.[50]

Scientist Dr. Gary Nabel has observed that correcting genetic flaws may carry some unassessed risk: "You may have a method offering a cure for an inherited disease, but it carries with it a finite risk of acquiring cancer later in life. We have no way of knowing ... what the risk will be over a patient's lifetime."[51]

These long-term risks impose ethical dilemmas. There is, for example, no way to integrate informed consent into applications of germline gene therapy. Ethicist John C. Fletcher has noted that those who would be most affected by germline gene therapy, the foetus and its offspring, cannot adequately give consent.[52] This would seem to imply that the consent process must be reframed.

Others concerned with the ethical implications of the technology point out that germline gene therapy could lead to dangerous eugenic practices.[53] If scientists are able to replace a defective cystic fibrosis gene in a developing foetus, we would be only one step away from replacing genes for physical and even character traits deemed to be socially undesirable. Critics fear that this will result in a new, more inimical class structure, in which the rich can buy their way into biological superiority.[54] A stunning example of this concern is illustrated by a recent report that an eleven year-old boy was receiving gene therapy treatments at a cost of U.S. $150,000 per year to increase his height. Four inches below average height, he was reportedly tired of being teased for being short. His father was quoted as embracing this effort: "You want to give your child that edge no matter what. I think you'd do anything."[55]

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[50] T. Gregory, "Clinical Applications of Molecular Medicine" *Patient Care* 32:18 (15 November 1998) 86, online: WL (HTHNEWS).

[51] Dr. Gary Nabel, quoted in R. Cooke, "Altering People: A Case of Ethics" *New York Newsday* (22 November 1994) B30.

[52] J.C. Fletcher, "Moral Problems and Ethical Issues in Prospective Human Gene Therapy" (1983) 69 Va. L. Rev. 515 at 542-43.

[53] Historian Daniel J. Kevles has demonstrated that eugenic dreams often arise from seemingly nentral medical capacities. See generally D.J. Kevles, *In the Name of Eugenics* (New York: Knopf, 1985).

[54] P.R. Billings & S.A. Newman, *supra* note 5. For an in-depth look at the social problems raised by enhancement therapy, see E. Parens, "Is Better Always Good?" (1998) 28:1 Hastings Center Report S1.

[55] *Supra* note 47.

Bioethicist William Gardner[56] has questioned whether genetic enhancement could be controlled once introduced:

> If genetic enhancement is feasible, it is likely that there will be demand for it because parents compete to produce able children and nations compete to accumulate human capital in skilled workers. If some parents or nations begin using genetic enhancement this will change these competitions in ways that increase the incentives for others to use it.[57]

The Council for Responsible Genetics, a group comprised of geneticists and molecular biologists, issued a statement warning that germline gene therapy could easily drift toward the creation of "designer babies": "If this first proposal is accepted, how much longer will it be before . . . any child who doesn't measure up to some arbitrary standard of health, behavior or physique is seen as flawed?"[58] This sentiment is echoed by disability groups who fear that they will be devalued or be seen as having "lives not worth living" if it were possible to eradicate their disability.[59]

Finally, critics claim that germline gene therapy represents an addiction to the notion of progress. The technology, they note, is not really necessary given alternative and available therapies. After all, the goal of eliminating diseased foetuses can be accomplished by prenatal diagnosis and selective abortion, or pre-implantation diagnosis and selective discard of affected embryos, without the added costs or moral quandaries involved in germline gene therapy.[60] As one scientist has concluded, "The simpler and safer technique of pre-implantation genetic diagnosis, already in clinical use, renders germline gene therapy for genetic diseases virtually pointless."[61]

Dr. Paul Billings, chief medical officer of the Department of Veterans Affairs in Texas worries that advocates of germline gene therapy may feel "[e]mboldened by a new, powerful array of techniques ... adhering to a theory of genetic determination of simple and complex human characteristics ..." and that they "seem ready to risk the lives of their subjects and generations to come."[62] For such critics, social and ethical concerns override the potential benefit of the technology and they wonder whether the technology is driven more by commercial interests than by social or individual needs.[63]

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[56] W. Gardner, "Can Human Genetic Enhancement Be Prohibited" (1995) 20 J. Med. & Phil. 65.

[57] *Ibid.* at 65.

[58] Quoted in "Gene Therapy in Womb", *supra* note 2.

[59] D. Nelkin & M.S. Lindee, *The DNA Mystique: The Gene as Cultural Icon* (New York: Freeman, 1995) at 174.

[60] B. Davis, "Germline Therapy: Evolutionary and Moral Considerations (1992) 3 Hum. Gene Therapy 361. See also A. McLaren, Letter to the Editor, "Problems of Germline Therapy" 392:6677 Nature (16 April 1998) 645.

[61] McLaren, *ibid.*

[62] P.R. Billings & S.A. Newman, *supra* note 5 at 4.

[63] See comments raised in K. Danis, *supra* note 43.

IV. Existing Regulation is Not Adequate to the Challenges Posed by the New Technology

Despite ethical concerns, reviews of the technology are likely to focus almost exclusively on technical considerations. This approach appears to be built into the regulatory structure. A 1996 Federal Register rule made clear that the FDA was to be the primary agency in charge of reviewing gene therapy applications.[64] The FDA's mandate, however, is limited to assuring the safety and efficacy of products. The agency is not authorized, nor is it equipped, to integrate social and ethical concerns into review procedures. Furthermore, it is unclear whether the FDA would even have regulatory jurisdiction in a case of enhancement therapy, as the agency's jurisdiction is limited to food, drugs, cosmetics, medical devices, and biologics. The NIH's responsibility for oversceing novel gene therapies is also limited. The NIH has jurisdiction only over proposals that are funded by the NIH or that take place in NIH-funded institutions. While the agency added the RAC in 1974 to integrate social and ethical concerns into genetic research funding decisions,[65] in 1996 it downgraded this Committee to an advisory body.

In addition to their structural or statutory limitations, hoth the FDA and the NIH are somewhat compromised by their dual roles as regulators and promoters of novel technologies. A pamphlet produced by the FDA and the NIH declares in its introduction that, "FDA and NIH share a common goal of promoting the development of useful, safe, and effective therapies for human disease."[66]

A. FDA Review

The FDA is one of the federal government's premier science-based agencies. Its mandate is to "ensure that (1) food is safe, pure, and wholesome; (2) cosmetics are safe; [and](3) human and animal drugs, biological products and therapeutic devices are safe and effective."[67] The FDA mantra in public meetings and discussions is that "sound science" underlies all regulatory decision making.[68] Its review of germline and

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[64] See "Proposed Actions", *supra* note 10. Note that cloning also has been assigned to FDA for regulatory review, though that technology also raises pressing ethical and social questions. For an evaluation of whether FDA's administrative authority really would cover cloning, see E. Price, "Does the FDA Have Authority to Regulate Human Cloning?" (1998) 11 Harv. J.L. & Tech. 619, online: WL (JLR).

[65] Krimsky, *supra* note 7.

[66] P.R. Burd, P.D. Noguchi & A.J. Grant, eds., *Forum 1996: Gene Therapy* (Rockville, Md.: Food and Drug Administration, 1996) at 3, online: Food and Drug Administration Homepage <http://www.fda.gov/cber/summaries/gtfor96.pdf> (date accessed: 1 February 2000).

[67] Agriculture, Rural Development, and Related Agencies Appropriation Bill, Senate Report No. 101-84, 135 Cong. Ree. 58874, 1st Sess. (1989) online: LEXIS (GENFED).

[68] See *e.g.* comments of Commissioner Jane E. Henney, M.D. at FDA Health Professional Organization Meeting, Bethesda, Maryland (8 February 1999).

somatic cell gene therapy is scientifically-oriented and focuses on factors such as safety and efficacy.

The FDA's technical focus is clear throughout its statements of policy. In an early document laying out the basis of FDA regulatory authority over gene therapies, the agency stated that

> [e]xisting FDA statutory authorities, although enacted prior to the advent of ... gene therapies, are sufficiently broad in scope to encompass these new products and require that *areas such as quality control, safety, potency, and efficacy* be thoroughly addressed prior to marketing.[69]

The FDA has authority over gene therapy under the *Federal Food, Drug and Cosmetic Act* ("*FFDCA*") and Section 351 of the *Public Health Service Act* ("*PHSA*"). In a 1993 statement on its approach to gene therapy products, the FDA made clear that it considers cellular products intended for use as gene therapy products subject to both these regulations:

> Gene therapy products are defined for the purpose of this statement as products containing genetic material administered to modify or manipulate the expression of genetic material or to alter the biological properties of living cells. Some gene therapy products [*e.g.*, those containing viral vectors] to be administered to humans fall within the definition of biological products and are subject to the licensing provisions of the PHS Act, as well as to the drug provisions of the act [*FFDCA*].[70]

Section 351(a) of the *PHSA* identifies a biological product as

> any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product ... applicable to the prevention, treatment, or cure of diseases or injuries of man.

The *FFDCA* defines "drug" to include

> articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and articles (other than food) intended to affect the structure or any function of the body of many or other animals.[71]

At the investigational stage, gene therapy products must be in conformity with 21 C.F.R. 312, which outlines procedures for clinical trials of Investigational New Drugs ("INDs").[72] Under the IND process,[73] gene therapies are subject to rigorous review for safety and efficacy. The aim of the IND review is to allow new drugs to be studied

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[69] "Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products" 58 Fed. Reg. 53,248 (1993) [emphasis added, hereinafter "Application of Current Statutory Authorities"].

[70] *Ibid.*

[71] *Food, Drug and Cosmetic Act*, 21 U.S.C. § 321(g)(1)(B) and (C) (1999).

[72] "Application of Current Statutory Authorities", *supra* note 69.

[73] See 21 C.F.R. § 312.2(a) (1999) ("[T]his part applies to all clinical investigations of products that are subject to section 505 [new drugs] of the Federal Food, Drug and Cosmetic Act ...").

while being made available to patients for treatment use.[74] Drugs in the IND process are subject to stringent requirements including detailed clinical protocols,[75] safety reports,[76] extensive record keeping,[77] and continuing supervision by an Institutional Review Board.[78] Moreover, any product subject to the IND process may be placed on a clinical hold by the FDA,[79] which means that the FDA may indefinitely delay or suspend a proposed clinical investigation if it is found that "[h]uman subjects are or would be exposed to an unreasonable and significant risk of illness or injury."[80]

The FDA's review process is firmly oriented around the tenets of expertise and risk evaluation. In a Guidance on the topic, the FDA set forth the regulatory considerations that govern approval of gene therapy products. These include adherence to the IND process, quality control, demonstration of reasonable safety, and careful product testing for bioactivity and potency.[81] Ethical issues are not explicitly included in these regulations.

Under the authority granted by the *PHSA* and the *FFDCA*, it is not clear whether the FDA would have any regulatory authority over enhancement applications of germline gene therapy.[82] Statutory authority elucidates the FDA's role in overseeing articles intended to diagnose, cure, mitigate, treat, or prevent disease. Thus, the agency is clearly involved when the technology is used for genetic disease. However, enhancement therapies do not fit into these categories and, as a result, the agency has no direct jurisdiction over manipulations aimed at affecting traits such as intelligence, personality or appearance.

The FDA has stated that because its authority extends over products for disease *or conditions* of human beings, it *would* regulate enhancement applications.[83] This posi-

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[74] See "Investigation New Drug, Antibiotic and Biological Drug Product Regulations: Treatment Use and Sale" 52 Fed. Reg. 19466 (1987).

[75] 21 C.F.R. § 312.23(a)(6) (1999).

[76] 21 C.F.R. § 312.32 (1998).

[77] 21 C.F.R. § 312.57 (1999), § 312.62 (1996), § 312.64 (1999).

[78] 21 C.F.R. § 312.66 (1987).

[79] 21 C.F.R. § 312.42 (1999).

[80] 21 C.F.R. § 312.42(b)(i) (1999).

[81] FDA, *Guidance for Industry: Guidance for Human Somatic Cell Therapy and Gene Therapy*, (1998) online: FDA, Center for Biologics Evaluation and Research <www.fda.gov/cber/gdlns/somgene.txt> (last modified: 8 October 1999).

[82] This argument was developed with respect to cloning by Price, *supra* note 64 at 641. Therein Price concludes that enhancement or reproductive choice applications of human cloning would not be subject to FDA regulation because they fall outside of the definitions of drug, medical device or biologic in the *FFDCA*.

[83] It could be also argued that germline gene therapy is simply a combination of a medical diagnostic technology, like genetic screening, and a fertility treatment, such as in vitro fertilization. In the past, the FDA has not regulated such procedures, a position that is consistent with the fact that the FDA is not permitted to regulate the practice of medicine. See W.L. Christopher, "Off-Label Drug Prescription: Filling the Regulatory Vacuum" 48 Food & Drug L.J. 247 at 250-56 (detailing the judicial indication that the FDA's supervision does not extend to regulation over the practice of medicine);

tion is, however, subject to debate. The FDA's authority has never extended to the regulation of medical interventions per se.[84] A gene alteration to enhance a foetus' qualities is a medical intervention, analogous to cosmetic treatments or reproductive technology such as cloning, and thus it is unlikely that the FDA would have jurisdiction.[85] Moreover, the agency acknowledges that off-label uses of approved drugs are permitted without further regulatory review in cases where they are instigated by a physician and where the risk to the patient is no greater than that found in the approved indication.[86] Thus, it becomes possible once the technology is approved for disease uses scientists could engage in "off-label" enhancement applications of germline gene therapy.

To its credit, the agency is clearly searching for a basis to oversee this radical technological advance.[87] In response to a query about the FDA's ability to include social and ethical considerations in decision making, Dr. Philip Noguchi, Director of the Division of Cellular and Gene Therapies in the Center for Biologics Evaluation and Research, made clear that the FDA does factor in a range of ethical issues stating that "we do that via presentations and discussion at the RAC [NIH] meetings. We have held joint meetings on in utero, genetic enhancement and the potential use of lentiviral vectors."[88] Yet, these meetings are not written into the FDA's policy on gene therapy, and the regulations do not provide the FDA with any explicit avenue for considering ethical issues on its own.[89]

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see also "Misuse of Prescription Drugs, Before the Subcomm. on Human Resources and Intergovernmental Relations, Comm. on Gov't Reform and Oversight" (1996) (statement of Michael Friedman, Deputy Commissioner for Operations, FDA) ("The history of the Act [FFDCA] indicates that Congress did not intend FDA to interfere with the practice of medicine."); 142 Cong.Rec. S12,024 (daily ed. 30 Sept. 1996) (statement of Senator Frist) ("While the FDA regulates medical devices and pharmaceutieals, it has no authority to regulate the general practice of medicine.").

[84] Price, *supra* note 64.

[85] The FDA is not permitted to regulate the practice of medicine. See E. Marden & D. Nelkin, "Cloning: A Business Without Regulation" (1999) 27 Hofstra L. Rev. 569 at 573-74. See also Price, *supra* note 64.

[86] See *Washington Legal Foundation* v. *Friedman*, 13 F.Supp.2d 51 (D.C. 1998).

[87] Indeed, in December 1994, Philip Noguchi and Amy Patterson of the FDA's Cell and Gene Therapies Division at the Center for Biologics Evaluation and Research, urged the RAC to establish a subcommittee to examine the issues surrounding "gene therapy in fetuses". See H. Gavaghan, "Future Perfect or Imperfect" (1995) 1 Nature Medicine 186 at 187.

[88] E-mail from Dr. Philip Noguchi to Emily Marden (16 April 1999).

[89] Because of general concerns that FDA is not equipped to integrate moral and ethical concerns, there is a move afoot to ensure RAC discussion of proposed novel gene therapy studies prior to FDA approval. See "Gene Therapy: RAC Public Discussion of Gene Therapy Protocols Prior to FDA Approval Will be Guaranteed by NIH" *F-D-C Rep.* ("The Blue Sheet") (30 Sept. 1998) [hereinafter "RAC Public Discussion"].

B. NIH Review

The NIH's supervision of germline gene therapy is constrained in a different way. The NIH does provide a forum for the consideration of the social and ethical issues raised by germline gene therapy through the RAC and its Gene Therapy Policy Conferences, but these outlets have a minimal regulatory impact. The NIH is *not* a regulatory agency *per se*; rather, it underwrites medical research. The agency reviews research and clinical protocols in the context of whether they deserve funding. In this sense, the NIH's "jurisdiction" is limited to NIH-funded protocols or protocols being carried out in NIH-funded institutions.[90]

The NIH did broaden its consideration of genetic research to include non-technical matters in 1974, in response to intense public controversy over recombinant DNA experiments.[91] At that time, the NIH established the RAC to assure adequate supervision of clinical research involving recombinant DNA.[92] The RAC was given the responsibility for reviewing protocols on both scientific and social grounds and the responsibility to recommend approval or disapproval to the NIH Director.[93] Toward this end, the RAC held regular public hearings which served as a forum for debate on a range of scientific, social and ethical issues. The group continued to play this role and to dictate NIH Policy on novel genetic science until 1996 when, pursuant to a new rule, the RAC's role was reduced.[94]

The RAC no longer has any formal role in approving or disapproving protocols. Its role is now advisory and instead of having systematic review powers over all new genetic technologies, the RAC serves as an advisor to the NIH Director only for those technologies deemed by at least three RAC members to require further review.[95] In addition, the RAC's membership has been reduced from twenty-five to fifteen members. The role of the Committee as a public forum has also been changed. The RAC now organizes Gene Therapy Policy Conferences ("GTPC") to discuss social and

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[90] Hypothetically, a privately funded researcher engaging in enhancement therapies may be able to avoid the regulatory process outright and just proceed with the application. In addition, a researcher could avoid the public debate generated by the RAC, by using private funding and submitting to FDA safety and efficacy evaluation alone. In fact, according to one FDA official, this situation has already arisen once.

[91] See National Institutes of Health, Office of Recombinant DNA Activities ("ORDA"), *Recombinant DNA Advisory Committee Charter*, online: Office of the Recombinant DNA Activities Homepage <www.nih.gov/od/orda/charter.htm> (last modified: 5 October 1999) [hereinafter *ORDA Charter*]; and Krimsky, *supra* note 7.

[92] See generally Krimsky, *supra* note 7.

[93] *Ibid.* See also *ORDA Charter*, *supra* note 91.

[94] See J. Beach, "The New RAC: Restructuring of the National Institutes of Health Recombinant DNA Advisory Committee" (1999) 54 Food & Drug L.J. 49. See also "Proposed Actions", *supra* note 10. For later implementation of these changes, see "Recombinant DNA Research: Action Under the Guidelines" 62 Fed. Reg. 4782 (1997); and "Actions Under the Guidelines", *supra* note 10.

[95] See "Proposed Actions", *supra* note 10. For later implementation, see "Actions Under the Guidelines", *supra* note 10.

ethical considerations in response to issues pertaining to gene therapy policy.[96] The idea behind the change was to streamline the regulatory process by separating the regulatory and monitoring responsibilities of the RAC. Dr. Harold Varmus, Director of the NIH, had hoped that the redirection of all regulatory concerns to the FDA would allow the RAC to focus on the broader implications of novel gene therapy proposals[97] including social and ethical considerations such as:

> (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 documents. (3) Identifying novel scientific and safety issues relevant to specific human applications of gene transfer ... (4) Publicly reviewing human gene transfer clinical trial data. (5) Identifying broad scientific and ethical/social issues relevant to gene therapy research as potential Gene Therapy Policy Conference Topics.[98]

However, limiting the RAC's role had the effect of concentrating regulatory review in the FDA where social and ethical issues are not formally considered.[99] One critic of germline gene therapy described the new RAC as mere window dressing: "The RAC has absolutely no standing in this debate. No power. No regulatory position. The FDA is the only player here."[100]

The RAC review of Anderson's pre-protocols in January, 1999 demonstrates the limits of the current regulatory structure. After hearing testimony from scientists, clinicians, families, policy makers, individuals, and groups of concerned citizens, the RAC concluded that "[a]t present there is insufficient preclinical data to support the initiation of clinical trials involving prenatal gene transfer."[101] Its report listed in detail 15 separate efficacy and risk issues that require additional data, including information on the specificity of genetic manipulations, the safety of clinical design, and the risk to the foetus and the mother. The RAC also appended to its list a set of unspecific concerns about informed consent issues and social and legal implications.[102] There was no indication of what these issues encompassed and how they might be addressed.

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[96] "Proposed Actions", *supra* note 10. See also NIH Gene Therapy Policy Conferences ("GTPC"), online: Office of Biotechnology Activities <http://www4.od.nih.gov/oba/meeting.html> (date accessed: 17 March 2000).

[97] "Perils in Free Market Genomics" Nature 392:6674 (26 March 1998) 315.

[98] "Proposed Actions", *supra* note 10 at 729.

[99] 61 Fed. Reg. at 59,727. Apparently, the concentration of regulatory authority at FDA and the lack of systematic consideration of ethical issues at that agency has raised widespread concern. In September 1998, an industry trade publication reported that NIH and FDA were thinking of re-integrating RAC review into the regulatory process. See "RAC Public Discussion", *supra* note 89.

[100] Quoted in D.N. Gianelli, "Prenatal Gene Therapy Put on Hold—For Now" *American Medical News* (1 February 1999), online: WL (HTHNEWS).

[101] See NIH Gene Therapy Policy Conference: *Prenatal Gene Transfer: Scientific, Medical and Ethical Issues, Conclusions* (1999) online: Office of Recombinant DNA Activities Homepage <http://www.nih.gov/od/orda/gtpcconc.htm> (last modified: 5 October 1999).

[102] See *ibid.*

Those attending the meeting were certain that despite the social and ethical questions, the technology would ultimately be approved. Dr. Paul Billings of the Council for Responsible Genetics noted that the technology was "going to go ahead. It's just a matter of time."[103] Indeed, Dr. Anderson hopes to introduce a final proposal to the panel in the next few years.[104]

Ultimately, the regulatory process does not meet the challenges of the technology. John Robertson, professor of pediatrics, has observed that "[t]he effects of [germline gene therapy] would have reverberations for society, not just the individual patient, and our current framework for assessing risks and benefits doesn't account for societal risks."[105]

C. European Policy

Europe has taken a very different tack in determining the fate of germline gene therapy. As the United States moves toward a regulatory regime that focuses only on science and efficacy considerations, Europe has chosen to address germline gene therapy through the broader framework of international human rights law as a social and ethical issue.[106] The operating principle is that human beings share a genetic heritage which may change naturally, but which should not be purposively changed through human intervention. In Europe, the sense is that altering the germline would compromise human dignity.[107]

After almost a decade of study, the Committee of Ministers of the Council of Europe[108] adopted the *Convention for the Protection of Human Rights and Dignity of*

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[103] Quoted in Gianelli, *supra* note 100.

[104] *Ibid.* One of Anderson's colleagues in developing gene therapy predicted that "the technology to do germline gene therapy ... will become available in the next four to five years." See T. Friend, *supra* note 42.

[105] Quoted in L. Seachrist, "Prenatal Gene Therapy Could Require New Ethical Framework" *Bioworld Today* (12 January 1999), online: WL (HTHNEWS). See "Perils in Free Market", *supra* note 97 (noting the "sweeping significance" that germline gene therapy would have and the need for some form of regulatory review).

[106] For an interesting examination of different international perspectives on the ethical questions raised by gene therapy, see D.R.J. Macer *et al.*, "International Perceptions and Approval of Gene Therapy" (1995) 6 Hum. Gene Therapy 791.

[107] See J. Robertson, "Oocyte Cytoplasm Transfers and the Ethics of Germ-Line Intervention" (1998) 26 J.L. Med. & Ethics 211 at 216.

[108] The Council of Europe has 38 member states all of which are also members of the European Union. Established in 1949, the Council of Europe serves three main functions: it protects fundamental human rights and democratic pluralism, promotes European cooperation on solving social ills, and fosters appreciation of Europe's "multicultural identity" (Statute of the Council of Europe (5 May 1949) 87 U.N.T.S. 103, 104-105, arts. 1(a), (b); D. Pinto, "The Council of Europe in Action" in *Securing The Euro-Atlantic Bridge: The Council of Europe and the United States*, J.E. Mrox, D. Pinto & F. Rosentiel, eds. (New York: Institute for East-West Studies, 1993) 27).

the Human Being with Regard to the Application of Biology and Medicine.[109] The *Convention*, to which twenty-two nations are signatories, states that genetic manipulation may be undertaken for purposes of prevention, diagnosis, or therapy, but only if it does not aim to introduce a permanent modification in the genome.[110] This convention effectively rules out any uses of germline gene therapy.[111]

Conclusions

In this era of radical biotechnology, scientific advances present profound social and ethical dilemmas. Critics of germline gene therapy question the implications of tampering with the germline, the meaning of such interventions for human dignity, and the potential for eugenic abuse. There is the additional concern over how gene manipulation will affect future generations. Yet, driven by scientific hubris, commercial interests, and media hype, this technology is moving inexorably towards clinical application with minimal public discussion of these issues. Ultimately, the regulatory system, structured to address questions of safety and efficacy, effectively displaces any consideration of the social and ethical implications of scientific developments.

In the past, similar social issues have generated significant and often tumultuous public debate. For example, the consequences of the possible release of genetically engineered organisms into the environment were the focus of active public discussions during the 1970s. Concerns about harming future generations prompted widespread public opposition to nuclear power and the early development of *in vitro* fertilization provoked widespread ethical debate over the potential for eugenic abuses. In recent years, however, public involvement in technological decisions has radically declined, reflecting a broader shift from public activism to personal consumerism and the ascendance of commercial interests in the biosciences. There is a growing tendency to reduce ethical issues to technical questions and to defer to scientific expertise.

As a result, today, when scientists have the power to radically alter the human genetic structure, there is little public discussion or debate about the ethical and social consequences of this technology. There are few avenues through which bioethical concerns may be brought to the public arena in order to extend the public's knowledge and interest in these issues. In a world where biotechnology poses profound

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[109] *Convention on Human Rights and Biomedicine, supra* note 11, art. 13.

[110] For background on Europe's decision, see S. Murray, "As Science Races Forward, Lawmakers Try to Catch Up" *Wall Street Journal Europe* (4 March 1997), online: WL (WSJ-EURO). Europe has also sought to address social and ethical issues in regulating somatic cell gene therapy. See C.F. De Jager, "The Development of Regulatory Standards for Gene Therapy in the European Union" (1995) 18 Fordham Int'l L.J. 1303.

[111] See *Convention on Human Rights and Biomedicine, supra* note 11. Note also that as of June 1998, it appeared that Canada is considering outlawing forms of research including "gene alteration ... that involves human germline cells or human zygotes or embryos". See W. Kondro, "Leaked Document Indicates Canada's Future Stance on Human Research" (1998) Lancet 1868.

challenges to the biological and social order, it is time to consider developing new fora for public debate so that social and ethical concerns may play a more significant role in the review and regulation of science.