University of Richmond Law Review

Volume 19 | Issue 1 Article 2

1984

Regulation of the Biomedical Applications of Recombinant DNA Research

Robert L. Gully

Stephanie J. Bird

Follow this and additional works at: http://scholarship.richmond.edu/lawreview

 Part of the Medical Jurisprudence Commons

Recommended Citation

Robert L. Gully & Stephanie J. Bird, *Regulation of the Biomedical Applications of Recombinant DNA Research*, 19 U. Rich. L. Rev. 1 (1984).
Available at: http://scholarship.richmond.edu/lawreview/vol19/iss1/2

This Article is brought to you for free and open access by UR Scholarship Repository. It has been accepted for inclusion in University of Richmond Law Review by an authorized editor of UR Scholarship Repository. For more information, please contact scholarshiprepository@richmond.edu.

UNIVERSITY OF RICHMOND
LAW REVIEW

VOLUME 19 FALL 1984 NUMBER 1

REGULATION OF THE BIOMEDICAL APPLICATIONS OF RECOMBINANT DNA RESEARCH

*Robert L. Gully**
*Stephanie J. Bird***

I. INTRODUCTION

In recent years, the rapid expansion of knowledge in the field of molecular genetics resulting from the use of recombinant DNA (rDNA) techniques has been unprecedented. The expanded knowledge scientists have acquired through rDNA techniques has precipitated conspicuous breakthroughs in biomedical research involving the manipulation of human genetic material to diagnose and treat human disorders.[1] Application of this research may soon affect all aspects of our lives.[2] However, this newly-acquired ability

* Associate, Hunton and Williams; B.A., 1967, University of Texas; Ph.D., 1971, University of Minnesota; J.D., 1984, University of Texas.

** Visiting Scholar, Science, Technology & Society Program and The Center for Policy Alternatives, Massachusetts Institute of Technology; B.A., 1971, University of California, Los Angeles; Ph.D., 1975, Yale University.

1. Currently, four proposals have been or will be submitted to the National Institutes of Health for permission to attempt to insert rDNA into humans. *See* Chase, *Scientists Hope to Put New Genes in Victims of 2 Genetic Diseases*, Wall St. J., Jan. 26, 1984, at ___, col. ___. Investigators are attempting to place human growth genes in livestock. The National Institute of Health was asked to restrict this research, but has refused to do so. 49 Fed. Reg. 37,016 (1984). *See also* Gordon & Ruddle, *Integration and Stable Germ Line Transmission of Genes Injected into Mouse Pronuclei*, 214 SCI. 1244 (1981); Grouse, *Restriction Enzymes, Interferon, and the Therapy for Advanced Cancer*, 247 J. A.M.A. 1742 (1982); Marx, *Three Mice "Cloned" in Switzerland*, 211 SCI. 375 (1981); Spradling & Rubin, *Transposition of Cloned P Elements into Drosophila Germ Line Chromosomes*, 218 SCI. 341 (1982); Schmeck, *Injection of a Gene Cures Flaw in Cell*, N.Y. Times, Oct. 10, 1979, at A14, col. 1. *See generally* Motulsky, *Impact of Genetic Manipulation on Society and Medicine*, 219 SCI. 135 (1983).

2. *See generally* OFFICE OF TECHNOLOGY ASSESSMENT, U.S. CONGRESS, IMPACT OF APPLIED

to manipulate human genes raises broad ethical and legal questions. The issues raised by rDNA research are dissimilar to earlier questions regarding the use of genetically-engineered microorganisms in the laboratory and current questions related to the regulation of biotechnology.[3] Despite this dissimilarity, the rapidity with which biomedical developments have been achieved makes the resolution of these ethical and legal questions regarding rDNA techniques all the more urgent.[4]

A new technique developed through rDNA research permits a direct examination of the chemical organization of an individual's genetic material.[5] The most immediate application of this technique is its use in safe, accurate, and reliable genetic screening. Recently, genetic screening has been carried out for a few hereditary diseases, raising a variety of ethical and legal issues.[6] These concerns are likely to be extended and intensified since rDNA technology potentially permits screening for any hereditary factor.

GENETICS ON MICROORGANISMS, PLANTS, AND ANIMALS (1981); Teso, *The Promise of Biotechnology . . . and Some Constraints*, OECD OBSERVER, Sept. 1982, at 4. For additional comment, see Cooke, *Engineering a New Agriculture*, 85 TECH. REV. 22 (1982); Fox, *Genetic Engineering Industry Emerges*, CHEM. & ENG'G NEWS, Mar. 17, 1980, at 15; Marx, *Agricultural Applications of Genetic Engineering*, 216 SCI. 1306 (1982); Swaminathan, *Biotechnology Research and Third World Agriculture*, 218 SCI. 967 (1982); Yanchinski, *Chemical Giants Turn to Biotechnology*, NEW SCIENTIST, Nov. 6, 1980, at 349.

3. *See* Foundation on Economic Trends v. Heckler, 14 ENVTL. L. REP. (ENVTL. L. INST.) 20,467 (May 16, 1984) (National Institute of Health must prepare an environmental impact statement under the National Environmental Policy Act before changing its rDNA guidelines to permit the release of genetically-engineered microorganisms into the environment); STAFF OF HOUSE SUBCOMM. ON INVESTIGATIONS AND OVERSIGHT, COMM. ON SCIENCE AND TECHNOLOGY, 98TH CONG., 2D SESS., THE ENVIRONMENTAL IMPLICATIONS OF GENETIC ENGINEERING (Comm. Print 1984). *See generally* Sun, *Biggest Challenge Since the Double Helix*, 212 SCI. 28 (1981).

4. Although much remains to be learned in this field, knowledge is being acquired rapidly: in most areas of research, 'new' means something that has been found within the past five years but in molecular biology it often means something found within the past few months—or even last week. Time and time again in the past ten years, the speed with which events have unfolded has taken well-informed observers by surprise.

PRESIDENT'S COMMISSION FOR THE STUDY OF ETHICAL PROBLEMS IN MEDICINE AND BIOMEDICAL AND BEHAVIORAL RESEARCH, SPLICING LIFE: A REPORT ON THE SOCIAL AND ETHICAL ISSUES OF GENETIC ENGINEERING WITH HUMAN BEINGS 13 (1982) [hereinafter cited as PRESIDENT'S COMMISSION, SPLICING].

5. For a full description of the technique, see *infra* notes 25-32 and accompanying text. FDA approval has been sought for this diagnostic test. Letter from Edward N. Brandt, Assistant Secretary of Health, Department of Health and Human Services, to Congressman John D. Dingell (Sept. 13, 1984).

6. *See* PRESIDENT'S COMMISSION FOR THE STUDY OF ETHICAL PROBLEMS IN MEDICINE AND BIOMEDICAL AND BEHAVIORAL RESEARCH, SCREENING AND COUNSELING FOR GENETIC CONDITIONS 17-22, 93-94 (1983) [hereinafter cited as PRESIDENT'S COMMISSION, SCREENING].

This paper will explore some of the ethical and legal implications of the biomedical application of rDNA research and the adequacy of existing regulatory mechanisms to deal with them. The paper demonstrates that the existing mechanisms for regulating these diagnostic procedures do not adequately address the problems they present.

II. New Genetic Diagnostic Techniques Developed From rDNA Research

A. *Historical Background*[7]

Before 1978, physicans employed two laboratory techniques for identifying genetic disorders. Under the first technique, the physican could examine chromosomes[8] prepared from a patient's white blood cells to diagnose genetic problems associated with the presence of an additional chromosome[9] and to identify chromosomes damaged by environmental toxins.[10] The second technique employed biochemical assays to detect deficiencies in the products produced by particular genes.[11] This technique has been used to identify a limited number of genetic disorders.[12]

---

7. For a description of genetic diagnostic procedures and genetic disorders, see Note, *Father and Mother Know Best: Defining the Liability of Physicians for Inadequate Genetic Counseling*, 87 Yale L.J. 1488, 1490-94 (1978). *See also* Hsia, *The Law and Operation of Genetic Screening Programs*, in Genetics and the Law II 97 (A. Milunsky & G. Annas ed. 1980); Milunsky, *Prenatal Diagnosis of Genetic Disorders*, 295 New Eng. J. Med. 377 (1976).

8. The basic biochemical unit of genetic material is *DNA* (deoxyribonucleic acid), a double-stranded helical molecule composed of *nucleotides* (bases). The bases along one strand of the helix are paired with their complementary nucleotides on the second strand. The pair of complementary nucleotides is referred to as a *base pair*. A group of bases along the strand that code for a particular functional unit, often a protein, is called a *gene*. The sequence of bases along the strand determines the structure of the protein. When one or more nucleotides in the sequence are substituted or deleted, or when an additional base or bases are added, the structure of the protein produced is likely to be altered. These are referred to as a *gene substitution*, a *gene deletion*, and a *gene insertion*, respectively. Any such change can be manifested as a genetic disorder. Groups of genes are organized into structures called chromosomes. The total complement of chromosomes within the nucleus is called the *genome*. In humans, the genome consists of twenty-three pairs of chromosomes with one chromosome in each pair being of "maternal" origin and one of paternal origin. *See generally* J. Watson, The Molecular Biology of the Gene (3d ed. 1977).

9. *See* Milunsky, *supra* note 7, at 378.

10. For a brief description of the significance of this diagnostic approach, see Kolta, *Chromosome Damage: What It Is, What It Means*, 208 Sci. 1240 (1980).

11. *See* Milunsky, *supra* note 7, at 379.

12. *See* Golbus, *The Antenatal Detection of Genetic Disorders*, 48 Obstet. and Gynecol. 497 (1976).

These techniques have been employed to predict the likelihood of a couple giving birth to a child with a genetic disorder. Before 1960, genetic disorders had to be identified in the parents or earlier offspring, and a statistical projection made of the likelihood that the trait would appear in later children. In the early 1960's, the development of amniocentesis, a technique for obtaining amniotic fluid from the womb of a mother, made possible the chromosomal and biochemical analysis of fetal cells and amniotic fluid.[13] Thus, certain disorders could be detected *in utero*, eliminating some of the uncertainty in prenatal diagnosis. However, these prenatal diagnostic procedures were not infallible and amniocentesis itself still presents some minimal risks to the mother and infant.[14]

In the mid-1970's, the development of fetoscopy, a technique for obtaining blood directly from the fetus, permitted physicians to diagnose certain hemoglobin disorders directly in the fetus.[15] In addition, genetic diagnostic techniques were employed postnatally to identify genetic traits. Postnatal chromosomal analysis has been used to identify candidates for compulsory sterilization[16] and to predict the likelihood of violent tendencies in certain individuals.[17]

---

13. For a general description of the amniocentesis technique, see W. FUHRMAN & F. VOGEL, GENETIC COUNSELING 91-92 (2d ed. 1976).

14. The incidence of spontaneous abortions induced by amniocentesis is about 0.5% (one out of 200 cases). The NICHD National Registry for Amniocentesis Study Group, *Midtrimester Amniocentesis for Prenatal Diagnosis*, 236 J. A.M.A. 1471 (1976). This risk appears low, however, in a woman 35 years of age the risk of bearing an infant with Down's Syndrome is only one out of 365.

15. Kan, Golbus, Trecartin & Filly, *Prenatal Diagnosis of* B-*Thalassemia and Sickle Cell Anemia: Experience with 24 Cases*, 1977 LANCET 269. Hemoglobin is a molecule found in red blood cells which carries oxygen in the blood. Genetic disorders of hemoglobin occur in two types. One type involves a single base pair substitution in the globin gene. This disorder is referred to as a hemoglobinopathy, the most common example of which is sickle cell anemia. Several variants of this disorder occur. The trait is inherited in simple Mendelian fashion; hence the disease manifests itself in the homozygous condition, while the heterozygote is merely a carrier for the trait. (Mendelian inheritance simply states that some characteristics are derived from one parent while other characteristics are derived from the other parent. STEDMAN'S MEDICAL DICTIONARY 710 (5th unabr. lawyer's ed. 1982)). The second type of disorder results from deletions in the globin gene that cause a decrease in the amount of the globin molecule produced by the red blood cells. The α- and β-thalessemias are the most common examples of this disorder. *See* J. WATSON, *supra* note 8. *See also* Bank, Mears & Ramirez, *Disorders of Human Hemoglobin*, 207 SCI. 486 (1980). Before 1976, these disorders could not be diagnosed directly. Since 1976, the development of a new technique, fetoscopy, allows the hemoglobin to be examined prenatally from samples of fetal blood. However, fetoscopy has a five percent abortion rate. *See* Orkin, Little, Kazazian & Boehm, *Improved Detection of the Sickle Mutation by DNA Analysis*, 307 NEW ENG. J. MED. 32, 33 (1982).

16. *See* Wexler, *"Will the Circle Be UnBroken?," Sterilizing the Genetically Impaired*, in GENETICS AND THE LAW II 313 (1980).

17. *See* Jacobs, *Aggressive Behavior, Mental Subnormality and the XYY Male*, 208 NA-

Specific genetically-linked biochemical markers have been identified which are linked to an increased susceptibility to cancer,[18] depression,[19] and the toxic effects of industrial chemicals.[20]

In 1978, investigators applied techniques developed in rDNA research to detect a hemoglobin disorder from the DNA obtained from cells in the amniotic fluid.[21] The significance of this experiment was that, for the first time, a genetic disorder was diagnosed directly from the DNA, rather than indirectly from an analysis of the chromosomes or gene products. This technique is more sensitive than other methods of genetic diagnosis because it reveals small differences in the DNA of a gene itself rather than changes in the number or the appearance of chromosomes, or in the amount or structure of a gene product.[22] This new diagnostic ap-

---

TURE 1351 (1965) (seminal article on the topic). Evidence suggested that the presence of an additional Y sex chromosome in males was associated with a propensity for violence and antisocial behavior. This work is extremely controversial. For a detailed discussion of the research and its implications, see HASTINGS CENTER REPORT, SPECIAL SUPPLEMENT THE XYY CONTROVERSY, RESEARCHING VIOLENCE AND GENETICS (August 1980).

18. For example, relatives of patients with the rare genetic disorder, ataxia-telangiectasia, are five times more likely to die of cancer before age 45 than members of the public at large. For a provocative discussion of this observation and the ethical dilemmas posed by this knowledge see Kolata, *Testing for Cancer Risk*, 207 SCI. 967 (1980). *See also* Maugh, *Center Tests Look for a Passing Grade*, 211 SCI. 909 (1981) (reviewing the status in the regulatory process of eight tests for cancer based on specific gene products).

19. *See* Weitkamp, Stancer, Persad, Flood & Gultormsen, *Depressive Disorders and HLA: A Gene on Chromosome 6 That Can Affect Behavior*, 305 NEW ENG. J. MED. 1301 (1981) (demonstration that familial depression is linked to an HLA gene on chromosome six). *See generally* Maugh, *Is There a Gene for Depression?*, 214 SCI. 1330 (1981).

20. Currently at least two tests are available for detecting a potential hypersensitivity to toxic substances. One test is based upon a genetically-linked deficiency in glucose-6-phosphate dehydrogenase, a deficiency which is more prevalent in black males and Mediterranean Jews. This deficiency can lead to anemias upon exposure to chemicals such as napthalene. The other test is based upon detecting a genetically-linked deficiency in α -1-antitrypsin. This deficiency predisposes an individual to lung disorders and emphysema with exposure to lung irritants. The homozygous form of the trait is linked to emphysema. For a general discussion of the tests, see Holden, *Looking at Genes in the Workplace*, 217 SCI. 336 (1982). For a discussion of the legal and regulatory implications of these tests, see *Genetic Screening of Workers: Hearings Before the Subcomm. on Investigations and Oversight of the House Comm. on Science and Technology*, 97th Cong., 2d Sess. 45, 92-107 (1984) (testimony of Professor Mark Rothstein, College of Law, West Virginia University) [hereinafter cited as *Hearings, Genetic Screening*]; Peppleson, *Genes and Jobs*, 68 A.B.A. J. 1061 (1982); McGarity & Schroeder, *Risk-Oriented Employment Screening*, 59 TEX. L. REV. 999 (1981). For a discussion of the ethical implications, see Lappé, *Ethical Issues in Testing for Differential Sensitivity to Occupational Hazards*, 25 J. OCCUP. MED. 797 (1983).

21. Orkin, Alter & Altay, *Application of Endonuclease Mapping to the Analysis and Prenatal Diagnosis of Thalassemias Caused by Globin-gene Deletion*, 299 NEW ENG. J. MED. 166 (1978); Kan & Dozy, *Antenantal Diagnosis of Sickle Cell Anemia by DNA Analysis of Amniotic-Fluid Cells*, 1978 LANCET 910.

22. This point is essential for appreciating the sensitivity of the technique. The Restric-

proach is readily adaptable for identifying numerous other genetic problems, including many for which no other diagnostic procedure exists.[23]

B. *Genetic Diagnosis Using Restriction Enzyme Analysis of DNA*

1. A Simplified Description of the READ Technique

Restriction Enzyme Analysis of DNA (READ)[24] uses fetal DNA obtained from cells in the amniotic fluid. A restriction enzyme[25] breaks the DNA into fragments which are separated according to size. Probes of single-stranded radioactive DNA[26] are used to iden-

---

tion Enzyme Analysis of DNA (READ) technique can detect a single nucleotide difference in an individual's DNA. The other approaches look at second order and third order products that merely reflect the changes in the DNA.

23. *See* Kronenberg, *Looking at Genes*, 307 NEW ENG. J. MED. 50, 51 (1982); Motulsky, *Impact of Genetic Manipulation on Society and Medicine*, 210 SCI. 135, 137 (1983); PRESIDENT'S COMMISSION, SCREENING, *supra* note 6, at 40-41. The availability of other tests to diagnose genetic disorders depends upon the existence of a test that is sufficiently sensitive to detect small changes in the amount and/or the chemical structure of a particular protein (usually an enzyme). Since these proteins are only present in certain cell types in the body, another limitation is the ability to obtain a sufficient quantity of the specific cells needed for analysis. The hemoglobin disorders illustrate these limitations. *See supra* note 15. Before the advent of the new diagnostic technique, it was necessary to obtain hemoglobin from the fetus to detect alterations in the globin molecule. This hemoglobin is only present in sufficient amounts to analyze its protein sequence in blood cells. Thus in order to detect these disorders prenatally a technique had to be developed to remove blood from the fetus *in utero*. This procedure was not developed until the mid-1970's and even now carries a significant risk to both the mother and fetus. Even assuming that a sufficient quantity of the material from the appropriate cells can be obtained, many tests are not sensitive enough to detect the small changes in the protein that may significantly alter cellular functions. The new diagnostic technique avoids these problems since it analyzes the DNA directly. Only small amounts of DNA are required; moreover, the DNA can be obtained from any cell since identical DNA is present in all tissues of the body in equal amounts. If aditional DNA is required, the cells can be cultured. Since DNA replicates before each cell division, the amount of DNA doubles with each division in culture. Thus the new approach does not have the limitations in terms of requiring a specific cell type for analysis and large amounts of material. This approach is potentially available for detecting alterations of any single gene defect.

24. For a general, but more specific description of the READ technique, see Kronenberg, *supra* note 23.

25. A restriction enzyme (or restriction endonuclease) is an enzyme that breaks down DNA at specific sites. Different restriction enzymes break (or recognize) the DNA at different sites. These cites are determined by the sequence of nucleotides in the DNA. The enzyme is named for the bacteria from which it is isolated. *See* Chang, Golbus & Kan, *Antenatal Diagnosis of Sickle Cell Anemia by Sensitive DNA Assay*, 1982 LANCET 1463.

26. A probe is a single stranded DNA molecule containing a part or all of a gene which is sought to be identified. The probe is constructed in the laboratory by synthesizing the sequence of nucleotides known to constitute or comprise part of the gene being studied. The

tify the fragments of DNA that comprise the gene of interest, for example, the globin gene.[27] If a part of the globin gene is absent,[28] or if a base-pair substitution[29] is present in the region of the gene recognized by the restriction enzyme,[30] the size of the DNA fragments comprising the globin gene will be different from that observed when DNA from a normal patient is analyzed. Thus, READ permits the detection of discrete changes in genetic material. This diagnostic technique has been used successfully to detect α- and β-thalassemias[31] as well as one form of sickle cell anemia[32] which

---

probe is made radioactive by the substitution of phosphorus 32. Less expensive, fluorescent probes have recently been developed. See Chang & Kan, *A Sensitive New Prenatal Test for Sickle Cell Anemia*, 307 NEW ENG. J. MED. 30, 31 (1982). In the READ technique, the DNA obtained from fetal cells is treated to separate the two strands of the DNA helix after the DNA is segregated by the size of the fragment. The radioactive probe binds the fragment of DNA containing the gene or part of the gene in the probe since the single strand of the probe DNA will bind to the complementary single strand of the fragment DNA.

27. *See supra* notes 8, 15 & 23.

28. *Id.*

29. *Id.*

30. The utility of the READ technique depends upon having a restriction enzyme that recognizes a site in a gene in which a change has taken place. The number of different restriction enzymes available (approximately 150) does not make this an insurmountable obstacle. *See* Kronenberg, *supra* note 23, at 51. Nonetheless, the technique can be modified to circumvent this limitation by looking at non-coding regions of the genes or regions of the DNA adjacent to the genes recognized by the restriction enzymes which have changes in them. The sequences of DNA within genes and adjacent to genes which do not code for a protein have a sequence which is specific for that location on the DNA molecule. Variations in the DNA sequence occur in specific genetic populations or associated with specific changes within the gene. Because these non-coding regions normally vary slightly in their base sequence throughout the general population, they are referred to as polymorphic regions of the DNA. These polymorphic regions are common in the genome and are inherited in a simple Mendelian fashion. (*See supra* note 15). Familial studies have revealed the linkage of specific genes and genetic disorders to specific polymorphisms. *See* Levin, *Jumping Genes Help Trace Inherited Diseases*, 211 SCI. 690 (1981). It is estimated that if as few as 165 polymorphic regions, evenly distributed through the genome, can be identified, scientists will be able to have a complete linkage map for all genetic disorders. *See* Botstein, White, Skolnick & Davis, *Construction of a Genetic Linkage Map in Man Using Restriction Fragment Length Polymorphisms*, 32 AM. J. HUM. GEN. 314 (1980). There is some argument about the strength of the linkage of a genetic disorder to a specific polymorphism. *Compare* Kan & Dozy, *supra* note 21, at 910 (95% frequency of linkage of sickle cell gene to Hpa I restriction enzyme polymorphism) *with* Bank, Mears & Ramirez, *supra* note 15, at 491-92 (60% frequency).

31. Thalassemia is a group of inherited disorders of hemoglobin metabolism in which there is a decrease in the net synthesis of a particular globin chain without a change in the structure of that chain. Alpha-thalassemia is the result of depressed synthesis of α-globin chains due to the presence of an abnormal gene. Likewise, β-thalassemia is the result of depressed synthesis of β-globin chains. STEDMAN'S MEDICAL DICTIONARY 1435 (5th unabr. lawyer's ed. 1982).

32. *See* Chang, Golbus & Kan, *supra* note 25 (sickle cell anemia); Chang & Kan, *supra* note 26 (sickle cell anemia); Little, Annison, Darling, Williamson, Camba & Modell, *Model*

previously could be detected only by using samples of fetal blood.[33]

2. Potential Applications of the Technique

The READ technique can be easily adapted to identify alterations in genes other than the globin gene.[34] However, two factors may limit the application of the technique to other genetic disorders. The first relates to how rapidly the probes used to identify fragments containing specific genes will become available. This factor represents only a minor obstacle to the expansion of the technique.[35] The second factor is the availability of altered sites within the gene which are close enough to the site recognized by a restriction enzyme to permit detection.[36] While this problem is formidable, it has already been partially circumvented through the identification of polymorphic regions[37] specifically linked to the gene which has been recognized by a restriction enzyme.[38] It has been suggested that one need identify only 165 such polymorphic genetic markers, that are equally distributed over the genome,[39] to detect any disease-producing gene.[40]

Parallel developments in other areas of biomedical research should facilitate the development of READ applications. Currently, the technique requires the use of DNA from fetal cells obtained by amniocentesis. In an unrelated area of research, a fluorescence-activated cell sorter[41] has been developed which permits the separation of maternal blood cells from fetal blood cells that

---

for Antenatal Diagnosis of B-*Thalassemia and Other Monogenic Disorders by Molecular Analysis of Linked DNA Polymorphisms*, 285 NATURE 144 (1980) (β-thalassemia); Orkin, Alter & Altay, *supra* note 21 (α-thalassemia); Orkin, Little, Kazazian & Boehm, *supra* note 15 (sickle cell anemia).

33. *See* Orkin, Little, Kazazian & Boehm, *supra* note 15.

34. *See supra* note 23.

35. *See* Levin, *supra* note 30, at 691. The number of genes whose sequence (or partial sequence) is known has increased enormously in the past three years. The National Institute of General Medical Sciences has established a computer library to store the sequences and to make them available to all investigators. The ability to synthesize genes has been simplified to an automated technique. *See* Alvarado-Urbina, Sathe, Liv, Gillen, Duck, Bender & Ogilvie, *Automated Synthesis of Gene Fragments*, 214 SCI. 270 (1981).

36. *See supra* note 25.

37. *See supra* note 30.

38. *Id.*

39. *Id. See supra* note 8.

40. *See* Botstein, White, Skolnick & Davis, *supra* note 30, at 315.

41. *See generally* Herzenberg, Sweet & Herzenberg, *Fluorescence-Activated Cell Sorting: A New Tool for Isolating Functional Cell Types*, 234 SCI. AM. 108 (Mar. 1976).

have crossed the placenta.[42] The cell sorter technique requires only twenty milliliters of maternal blood to isolate the fetal cells. By culturing these fetal cells,[43] sufficient fetal DNA can be made available for analysis.[44] Hence, it may soon be possible to use maternal blood for prenatal diagnosis with the READ technique, thus subjecting the mother and fetus to only a negligible risk.

The potential applications of READ are not limited to prenatal diagnosis. The technique also may be used to detect genetic disorders in adults; to screen for disorders such as Huntington's Disease, which do not manifest themselves until later in life;[45] and to detect genetic susceptibility to cancer, toxins, and other diseases.[46]

III. Ethical and Legal Implications of READ

READ dramatically extends the ability to diagnose genetic disorders. This potential carries with it attendant ethical and legal implications. The remainder of this paper attempts to identify

---

42. *See* Herzenberg, Biachi, Conn & Iverson, *Detection and Isolation of Fetal Cells from Maternal Blood Using the Fluorescence-Activated Cell Sorter (FACS)*, 1 Prenatal Diagnosis 61, 62 (1981). Currently, the technique is used to separate, identify, and collect cells of male infants from maternal blood.

43. *Id.* at 72.

44. *Id.* at 73.

45. Motulsky, *supra* note 23, at 137. The average age of onset of Huntington's disease (HD) is 41 years. HD is a progressive, debilitating disease that manifests itself in motor dysfunction and often in mental and psychological disorders. The duration of the disease from first symptoms to death averages 10 to 20 years. Treatment may ameliorate the symptoms for some patients for varying periods, but there is no cure. In the U.S., approximately one in 10,000-15,000 suffer from the disease, but the gene frequency, and thus those who will eventually have HD, is one in 4,000-10,000. Thus, in this country, about 10,000-25,000 have HD and an additional 20,000-50,000 are at 50 percent risk. It is a hereditary disease that is independent of gender, and the presence of the gene will invariably eventually result in the disease. Those who carry the gene and who will eventually have the disease cannot be distinguished from those who do not. In this context, the status of the carrier, and thus the meaning of the term, differs from that of carriers of recessive hereditary disease genes who do not have the disease but may have offspring who do. Those who have the gene for HD will get the disease; anyone with a parent who has HD is at 50 percent risk of having the gene, and conversely, anyone with HD has a 50 percent chance of passing it on to each child. Although the gene for Huntington's disease has not been identified, a polymorphic marker, genetically linked to Huntington's disease, has been identified. *See* Gusella, *A Polymorphic DNA Marker Genetically Linked to Huntington's Disease*, 306 Nature 234 (1983). Identification of the gene itself is only a matter of time.

46. *See* Shafritz, Shouval, Sherman, Hadziyannis & Kew, *Intergration of Hepatitis B virus DNA into the Genome of Liver Cells in Chronic Liver Disease and Hepatocellular Carcinoma: Studies in Percutaneous Liver Biopsies and Post-Mortem Tissue Specimens*, 305 New Eng. J. Med. 1067 (1981) (detection of viral hepatitis and hepatoma). *See also supra* notes 18 & 20.

some of these ethical and legal implications and to determine whether regulatory strategies exist to address them.

A. *READ and Prenatal Diagnosis*

One of the central ethical conflicts of any prenatal diagnostic technique is the extent to which information from that technique should influence the decision to bear a child. The legal aspect of this ethical conflict concerns the role of the state in effecting that decision, regardless of its basis. The availability of the READ technique complicates resolution of this conflict. Because the technique is sensitive, rapid, and reliable, it can provide more information, both significant and trivial, which may have an impact on the decision to bear a child. In addition, existing case law in the area of wrongful birth may impose a duty on physicians to provide this information. At the same time, because test results can be available within the first trimester, the state may be precluded from affecting the decision-making process.[47]

1. The Role of Information in the Decision to Bear a Child

Use of READ for prenatal diagnosis extends the ability to diagnose genetic disorders that may seriously impair postnatal viability of the fetus or that may endanger maternal health during pregnancy and childbirth. However, the technique can also be used to detect disorders that do not present a significant threat to either mother or newborn, or to identify genetic traits of unknown or neutral eugenic value. Thus, READ may increase the likelihood that abortion will be utilized to enforce genetic preferences rather than as a therapeutic procedure.

READ offers the only safe technique for diagnosing two forms of thalassemia.[48] Tests using the technique should soon be available for detecting growth hormone deficiency, phenylketonuria and Duchenne's muscular dystrophy,[49] and possibly for Lesch-Nyhan

---

47. *See* Planned Parenthood v. Danforth, 428 U.S. 52 (1976) (overturning a state law banning the use of saline amniocentesis as a technique for abortions. The Court held that the statute was related to the health of the fetus, not the mother.).

48. *See supra* note 31 & 32.

49. *Human Genetic Engineering: Hearings Before the Subcomm. on Investigations and Oversight of the House Comm. on Science and Technology*, 97th Cong., 2d Sess. 223, 242, 292 (1982) [hereinafter cited as *Hearings, Engineering*]. For a description of the disorders, see Annas & Coyne, *"Fitness" for Birth and Reproduction: Legal Implications of Genetic Screening*, 9 FAM. L. Q. 463 nn.9-10 (1975).

disease.[50] Each of these disorders either seriously threatens the mother or causes a painful or debilitating condition in the offspring that severely shortens its life-expectancy. No effective treatment exists for these disorders and, because of their serious and irremediable nature, it is reasonable to assume that the introduction of heretofore unavailable prenatal tests for these and similar disorders may increase the number of abortions of fetuses with such complications. However, concerns generated by this increase in the number of abortions must be balanced against the potential economic, social, and personal burdens that will be avoided if more fetuses suffering from these conditions are aborted.[51]

An additional factor should be considered. Procedures currently available can, at best, determine that the chance a fetus will be born with one of these disorders is one out of three.[52] Any decision to abort the fetus based upon that probability will inevitably result in the loss of two viable, unimpaired fetuses for every affected fetus. READ, however, can distinguish between those fetuses only *carrying* the trait and those fetuses that actually have the disorder,[53] thereby avoiding the abortion of two normal fetuses. But even if READ is utilized, the decision to give birth to a carrier of a deleterious genetic trait could increase the genetic load of that trait in the general population.[54]

READ offers the potential for identifying the presence or absence of *any* trait controlled by a single gene; thus, its potential

---

50. *See Hearings, Engineering, supra* note 49, at 223.

51. The cost of caring for an infant with Tay-Sachs disease is $20,000-40,000 per year. The total cost to society of caring for children with Down's Syndrome is 1.7 billion dollars per year. *See* H.R. REP. No. 498, 94th Cong., 2d Sess., *reprinted in* 1976 U.S. CODE CONG. & AD. NEWS 709, 727. *See also* Thompson & Milunsky, *Policy Analysis for Prenatal Genetic Diagnosis*, 27 PUB. POL'Y 25 (1979). *See generally* PRESIDENT'S COMMISSION, SCREENING, *supra* note 6, at 47-53 (a discussion of the policy implications of compulsory genetic screening; however, the discussion highlights many of the implications of genetic disease).

52. The other two positive results will only be carriers of the trait. *See* PRESIDENT'S COMMISSION, SCRENING, *supra* note 6, at 111-15. Genetic counselors usually consider a risk of one out of ten to be sufficiently high to recommend not having a child. *See* Carter, Roberts, Evans & Buck, *Genetic Clinic: A Follow-Up*, 1971 LANCET 281. *See also* Note, *The Constitutionality of Mandatory Genetic Screening Statutes*, 31 CASE W. RES. 897 n.2 (1981).

53. *See supra* notes 32-40 and accompanying text.

54. The genetic load is a measure of the frequency of a gene in the population. By increasing the number of carriers in the population the frequency of the deleterious gene increases and, also, the probability of a homozygous offspring with the disorder. Friedman suggests that, if the carriers for sickle cell anemia and cystic fibrosis could be identified with amniocentesis, fourteen million abortions over a span of forty years could eliminate the genes from the population. Friedman, *Legal Implications of Amniocentesis*, 123 U. PA. L. REV. 92, 107-08 (1974).

application extends beyond detecting genetic disorders which are debilitating from birth. For example, Huntington's disease is a severe, disabling genetic disease with a late onset[55] for which READ is likely to offer a safe test for prenatal detection.[56] The information obtained may be used to decide whether to bear a child with this genetic defect, just as in the case of the prenatal diagnosis of any serious genetic disorder. However, the relative significance of this information in making a meaningful decision in this instance differs from a similar decision regarding serious disorders that begin at or shortly after birth, because the economic, social, and personal consequences of the disease are manifestly different.

The ethical dilemmas posed by the READ technique become increasingly complex when one considers the potential of the technique to identify traits whose possible deleterious effects merely increase an offspring's susceptibility to a disease,[57] rather than actually causing the disease. READ should soon by available to test for the presence of a genetic defect which affects the production of an enzyme, α-1 antitrypsin.[58] Persons with this defect are more susceptible to pulmonary disorders such as emphysema,[59] although the degree of increased risk is a matter of great controversy.[60] The ethical problems posed by a decision to abort a fetus based upon the unquantified possibility of increased risk of disease are definitely more complex than those problems posed by a similar decision to abort based upon the certainty of delivering a non-viable genetically defective child. Furthermore, a decision to abort based upon neutral genetic traits revealed by READ[61] raises serious ethi-

---

55. *See supra* note 45.

56. *See* Gusella, *supra* note 45.

57. *See supra* note 20.

58. *See Hearings, Engineering, supra* note 49, at 292.

59. *Genetic Screening and Handling of High Risk Groups in the Workplace: Hearings Before the Subcomm. on Investigations and Oversight of the House Comm. on Science and Technology*, 97th Cong., 1st Sess. 151 (1981) (statement of Dr. Gilbert Omenn) [hereinafter cited as *Hearings, High Risk*].

60. About one in 10,000 persons have a deficiency of this protein and are predisposed to develop emphysema and other pulmonary disorders. *See supra* note 20. Carriers may also have a greater predisposition to lung disorders and sensitivity to airborne pollutants. Other genetic deficiencies in genes that control enzymes such as glucose-6-phosphate dehydrogenase and paroxnase may also predispose a worker to greater susceptibility to toxic substances and pesticides. Similarly, the aryl-hydrocarbon hydroxylase genes may control the breakdown of numerous carcinogens. The presence of particular genes, such as oncogenes, may indicate a greater susceptibility to cancer. *See Hearings, High Risk, supra* note 59, at 145-51.

61. A neutral genetic trait would be a genetic trait that has neither deleterious nor adaptive consequences for the organism. Eye color would be an example of a multigene neutral

cal concerns. A similar problem has already been confronted in regard to the ability to identify the sex of a fetus through amniocentesis.[62] If the number of such possibilities increases through the development of the READ technique, the dilemma created by this problem may demand legal resolution.

2. The Role of Courts in Affecting Dissemination of Information From READ

In recent years, courts have placed a duty upon physicians to provide pregnant women with information about their potential for bearing a genetically defective child so that the parents can make an informed decision about whether to terminate the pregnancy.[63]

---

trait. A number of such single gene traits have recently been reported such as a single gene that controls verbal ability. *Hearings, Engineering, supra* note 49, at 247.

62. *See* Fletcher, *Ethics and Amniocentesis for Fetal Sex Identification*, 301 NEW ENG. J. MED. 550 (1979) (an argument that a woman's reproductive interests include the right to elect to abort a fetus because of its gender). *Cf.* Powledge & Fletcher, *Guidelines for the Ethical Social and Legal Issues in Prenatal Diagnosis*, 300 NEW ENG. J. MED. 168, 172 (1979). Some doctors, when confronted with information about the sex of a fetus obtained from karyotypes of fetal chromosomes after amniocentesis, choose to withhold that information rather than have the information form the basis for a decision to elect an abortion. Hence, the physician assumes the burden of resolving the ethical dilemma. *See, e.g.*, Powledge, *Letter to the Editor*, 302 NEW ENG. J. MED. 524 (1980) (in response to Fletcher's argument). However, the physician may be unable to make such decisions with the information obtained from READ. In the first place, many disorders revealed with READ may not be as trivial clinically as the gender of the fetus. Moreover, a growing minority of courts place a duty upon a physician to provide parents with information upon which to base an informed decision about whether to seek an abortion in instances where the infant may not have a "meaningful" life. *See infra* notes 63-70 and accompanying text.

63. For a description of the wrongful birth cause of action, see Note, *supra* note 7. This Note played an important role in shaping the court's approach to this cause of action in Berman v. Allen, 80 N.J. 421, ___, 404 A.2d 8, 14 (1979). In *Berman* the physician failed to inform a 38-year-old mother of the availability of amniocentesis to diagnose Down's Syndrome. The *Berman* court allowed the parents of the subsequent mongoloid child to recover damages for mental and emotional anguish because the mother had been tortiously deprived of the option of making a meangful decision as to whether to abort the fetus. Since *Berman*, the New Jersey courts have expanded the cause of action. *See* Schroeder v. Perkel, 87 N.J. 53, 432 A.2d 834 (1981) (reversed and remanded lower appellate court's decision to grant a summary judgment in favor of a physician. The plaintiff charged that the physician misdiagnosed cystic fibrosis in her first child early enough to afford her the opportunity to decide whether to abort a second child.); Comras v. Lewin, 183 N.J. Super. 42, 443 A.2d 229 (1982) (reversed and remanded lower court dismissal of a suit charging a physician's negligent failure to make a timely diagnosis of pregnancy to permit a woman with diabetes to decide to have an abortion).

The courts in Virginia, California, and Washington have upheld a cause of action for wrongful birth. *See* Turpin v. Sortini, 31 Cal. 3d 220, 643 P.2d 954, 182 Cal. Rptr. 337 (1982) (failure to advise parents of possibility that fetus may be born congenitally deaf); Call v. Kezian, 135 Cal. App. 3d 189, 185 Cal. Rptr. 103 (1982) (failure to diagnose and test for

When a defective child is born, the physician's breach of this duty gives rise to a cause of action for the tort of wrongful birth. In developing this tort doctrine, the courts have neither defined the parameters of the standard of care owed by the physician, nor recognized the implications of the rapidly expanding developments in prenatal diagnosis and gene therapy. The continued expansion of this doctrine, in light of recent developments such as the READ technique, may have untold consequences for the practice of medicine and for the privacy interests of patients.

Courts applying the wrongful birth doctrine purport to do nothing more than extend the law of medical malpractice to prenatal diagnosis. The cases decided under the doctrine divide into three groups based upon the nature of the duty owed to the patient. In a majority of the cases the physicians were held liable for the failure to detect the genetic disorder in the fetus after undertaking to do so.[64] In a small number of cases, the physicans were held liable for failing to warn the patient of the risks and to advise her of the availability of tests to determine whether the risk would come to fruition.[65] In a single recent case, the California Court of Appeals[66] interpreted the tort of wrongful birth as requiring a physician to actually test for the presence of a disorder and advise the parents of the results of the test.[67]

In each of the three groups of cases, the court purported to hold the physician to the standard and degree of care and skill expected of the average practitioner in that specialty.[68] Yet, in the second

---

Down's Syndrone in middle-aged pregnant mother); Curlender v. Bio-Science Laboratories, 106 Cal. App. 3d 811, 165 Cal. Rptr. 477 (1980) (court held for an infant plaintiff born with Tay-Sachs Disease against physician and genetic test laboratory. The laboratory reported the wrong results of an initial screening of the plaintiff's parents' blood for Tay-Sachs trait. Apparently, in reliance upon the test, parents failed to elect further diagnostic tests using amniocentesis.); Naccash v. Burger, 223 Va. 406, 290 S.E.2d 825 (1982) (failure to discover Tay-Sachs Disease); Harbeson v. Parke-Davis, Inc., 98 Wash. 2d 460, 656 P.2d 483 (1983) (failure to tell of material risks of dilantin treatment to pregnant mother).

64. *See Turpin*, 31 Cal. 3d 220, 643 P.2d 954, 182 Cal. Rptr. 337; *Curlender*, 106 Cal. App. 3d 811, 165 Cal. Rptr. 477; *Schroeder*, 87 N.J. 53, 432 A.2d 834; *Comras*, 183 N.J. Super. A.D. 42, 443 A.2d 229; *Naccash*, 223 Va. 406, 290 S.E.2d 825.

65. *See Berman*, 80 N.J. 421, 404 A.2d 8; *Harbeson*, 98 Wash. 2d 460, 656 P.2d 483.

66. *Call*, 135 Cal. App. 3d 189, 185 Cal. Rptr. 103.

67. We hold here only that an attending physician is under a duty, when treating a middle-aged woman, to test for Down's Syndrome and to advise the parents of the results of the test, leaving to the parents the decision as to seeking an abortion or permitting the fetus to develop to the point of delivery.

Id. at 191, 185 Cal. Rptr. at 105.

68. In Washington, the standard of care used to measure physician negligence is not lim-

category of cases, where physicians failed to inform their patients of the availability of tests for birth defects, the standard appeared to relate more to the materiality of the information to the patient rather than to the standard of care in the relevant medical community.[69] The courts, however, have not defined materiality in any terms that would allow one to predict the circumstances under which a court might hold the likelihood of a particular disorder to be material. In addition, the courts have not indicated whether the existence of prenatal gene therapy or postnatal treatment or the degree of physical impairment to the infant would be relevant to the standard of care issue or merely to the damages issue.

Given the fact that the READ technique appears to be a highly accurate diagnostic tool that can be coupled with safe, perhaps even noninvasive procedures, it seems likely that its use will become widespread and accepted by the medical community. Because it may soon be possible to use the technique to test for a great variety of genetic characteristics, physicians may soon be able to identify many genetic conditions that could be deemed ma-

---

ited by the customs of practice in the community. Miller v. Kennedy, 11 Wash. App. 272, 522 P.2d 852 (1974), *aff'd per curiam*, 85 Wash. 2d 151, 530 P.2d 334 (1975) (physician has a duty to inform a patient about abnormalities in his or her body).

69. [W]e hold that parents have a right to prevent the birth of a defective child and health care providers a duty correlative to that right. This duty requires health care providers to impart to their patients material information as to the likelihood of future children being born defective, to enable the potential parents to decide whether to avoid the conception or birth of such children.

Harbeson, 98 Wash. 2d at ___, 656 P.2d at 491. *See also Berman*, 80 N.J. at ___, 404 A.2d at 14; Keogan v. Holy Family Hospital, 95 Wash. 2d 306, 622 P.2d 1246 (1980) (failure to inform patient with angina pectoris of further tests to diagnose a heart condition constituted negligence); Gates v. Jensen, 92 Wash. 2d 246, 595 P.2d 919 (1979) (holding that the failure to inform a patient of the availability of tests that would rule out glaucoma constituted negligence). The *Gates* court held that the physician's duty to inform the patient was limited to simple, inexpensive, and relatively risk free tests. *Gates*, 92 Wash. 2d at ___, 595 P.2d at 924. In *Keogan*, the court seemed to back away from these criteria: "Two of the tests available in this case, when considering the alternative of death by heart attack were relatively simple and risk free." *Keogan*, 95 Wash. 2d at ___, 622 P.2d at 1255. According to the court, the physician had a duty to inform the patient about the availability of angiography, an invasive cardiac diagnostic procedure with a risk of 0.2 to 0.3 percent. Angiography is only 80% effective as a diagnostic tool. *Id.* at ___, 622 P.2d at 1249.

The risks currently associated with amniocentesis used to obtain fetal cells for READ is less than 0.5 percent. *See supra* note 14. The effectiveness for detecting sickle cell anemia and thalessemia is very high. *See* Kronenberg, *supra* note 23, at 51. Assuming that the cell sorting technique can be adapted for use with this test, the risks would be negligible. The costs of using READ as a routine diagnostic technique are difficult to estimate at this time. The use of fluorescent probes would greatly reduce the cost. *See* Chang & Kan, *supra* note 26, at 32 (Chang and Kan believed that the test would soon be feasible to use in Ghana where 140,000 tests would be required per million pregnancies).

terial to a parent's decision to terminate or continue a pregnancy. The tort of wrongful birth may inadvertently impose a broad duty upon physicians to routinely screen for genetic disorders in order to avoid liability. The costs of such defensive medicine to health care consumers could be enormous.[70] Presumably, these costs could be avoided since a physician could merely inform the patient of the availability of the tests and have the patient waive the tests if she so desires.[71] However, this approach does not truly ameliorate the costs of defensive medicine because many, if not most, women confronted with even minimal risks are likely to opt for knowledge available through READ as long as the tests are relatively painless, non-invasive and inexpensive. Moreover, the waiver may not be viewed as voluntary if it was made because of the inability to pay.

In creating the doctrine of wrongful birth, courts clearly have not anticipated the development of molecular genetics and its impact on prenatal diagnosis. The result of the interaction between the doctrine of wrongful birth and advancing molecular genetics could be a judicially-created genetic screening program. Genetic screening programs are not unique. In fact, most states have created such programs for particular genetic diseases.[72] The difference, however, lies in the fact that the judicially created programs would lack safeguards necessary to prevent the disclosure of information without consent. Patients have some statutory and legal remedies for unauthorized disclosure,[73] but considering the stigma

---

70. *See Keogan*, 95 Wash. 2d at ___, 622 P.2d at 1261. *See also* Griner & Glaser, *Misuse of Laboratory Tests and Diagnostic Procedures*, 307 NEW ENG. J. MED. 1336 (1982). Between 1973 and 1980, St. Paul Companies, the largest medical malpractice insurer, reported that the failure to diagnose was alleged in 25 percent of the medical malpractice suits. A 1976 HEW report revealed a similar figure. In this report, most malpractice claims in non-surgical suits, involved inadequate testing. *See* Furrow, *The Causes of Wrongful Life Suits: Ruminations on the Diffusion of Medical Technologies*, LAW, MED. AND HEALTH CARE, Feb. 1982, at 12. *But see* Capron, *Tort Liability in Genetic Counseling*, 79 COLUM. L. REV. 618, 666-72 (1979).

71. *See* Capron, *supra* note 70, at 671-72.

72. Seventeen states have established sickle cell anemia screening programs. Forty-two states have screening programs for phenylketonuria. Reilly, *Genetic Screening Legislation*, in ADVANCES IN HUMAN GENETICS 319, 353 (H. Harris & K. Hirschorn eds. 1975). *See generally* PRESIDENT'S COMMISSION, SCREENING, *supra* note 6, at 31-35. World-wide, over 350,000 Jewish adults have been screened for Tay-Sachs Disease. The program in the United States has significantly decreased the number of infants born with the disease. *Id.* at 19-20.

73. *See* Riskin & Reilly, *Remedies for Improper Disclosure of Genetic Data*, 8 RUT.-CAM. 480 (1977). The primary sanction for improper physician disclosure of data obtained in the professional relationship is delicensure, but only if the states provide this sanction. Some courts have awarded damaged for disclosure of confidential medical information. *Id.* at 491. Most state screening laws protect genetic data from unauthorized disclosure. *See, e.g.*, VA.

associated with many disorders and the type of information available from READ, a patchwork of remedies may not be adequate to protect patients' rights.

3. Impact of READ on a State's Ability to Affect the Abortion Decision

During the first trimester of pregnancy, a woman's privacy interest overrides any state interest in limiting abortion.[74] Similarly, the state cannot restrict a mother's right to an abortion during the second trimester unless the state is seeking to protect maternal health.[75] Amniocentesis is usually performed in the fifteenth or sixteenth week of pregnancy.[76] Chromosome and metabolic tests currently used for prenatal diagnosis require from three to eight weeks to process[77] and occasionally need to be repeated.[78] Hence, the results of prenatal testing are unavailable until late in the second trimester when the risks to maternal health from abortion can be substantial.

In contrast, the results of tests using READ are available in two weeks.[79] Since the risk to maternal health from abortion increases with fetal age, the early availability of the results of prenatal diagnosis using READ should make abortion safer for the mother while making any state interest in restricting access to abortions less compelling. More importantly, because the Supreme Court has held that the state cannot interfere with a mother's right to an

---

CODE ANN. § 32-112.23 (Cum. Supp. 1982).

74. *See* Roe v. Wade, 410 U.S. 113 (1973).

75. *See* Planned Parenthood v. Danforth, 428 U.S. 52 (1976).

76. Annas & Coyne, *supra* note 49, at 471.

77. Thompson & Milunsky, *supra* note 51, at 27.

78. Cell cultures for chromosomes and metabolic studies fail in about five to ten percent of the cases. *Id.* at 29.

79. Chang & Kan, *supra* note 26, at 31. A new genetic diagnostic procedure has been developed that permits prenatal testing in the first trimester. *See* Kazy, Rozovsky & Bakharev, *Chorion Biopsy in Early Pregnancy: A Method of Early Prenatal Diagnosis for Inherited Disorders*, 2 PRENAT. DIAGNOSIS 39 (1982). In this procedure, cells of fetal origin are removed from the chorionic villi at the site of placental implantation. These rapidly dividing cells are then cultured for use in chromosome and metabolic tests. The culture of these cells usually requires only two weeks. This procedure is being examined on an experimental basis in this country and in Europe. *See* Kolata, *First Trimester Prenatal Diagnosis*, 221 SCI. 1031 (1983). Preliminary evidence suggests that the test is safe and the cells are identical biochemically to those obtained by amniocentesis. *Id.* at 1033. Interestingly, in 1982 workers using READ already recognized the potential of adapting chorionic biopsy to diagnose hemoglobinopathies with this technique. *See* Orkin, Little, Kazazian & Boehm, *supra* note 15, at 36.

abortion during the second trimester except to protect maternal health,[80] the state may be powerless to restrict the decision to seek an abortion even when the procedure is used as a means of obtaining preferences for certain genetic traits. Therefore, unless the state can restrict access to the tests that provide the basis for that preference, it will be unable to regulate use of READ to screen for particular genetic traits.[81] It may even be unconstitutional for any state to attempt to interfere with a mother's access to information necessary to the abortion decision.[82] Thus, any attempt to limit prenatal diagnostic information absent a showing of a threat to maternal health may be unconstitutional.

B. *READ and Individual Rights*

The fact that the READ technique can be employed to obtain a genetic "fingerprint" from an individual to identify desirable or undesirable genetic traits has conflicting implications. On the one hand, the technique can be used to identify those persons particularly susceptible to an undesirable trait so that steps may be taken to protect them. On the other hand, the technique can be performed upon any blood sample without the patient's consent or knowledge. Thus, the possibility exists that information could be obtained and used in a discriminatory manner. The use of the results of genetic testing in the work place illustrates this conflict.

The capacity of READ to detect genetically-based heightened susceptibility to certain toxic compounds presents the opportunity to take corrective measures to protect those individuals from exposure to such toxins in the work place, either by reducing levels of exposure or by employing hypersensitive individuals in less hazardous work environments. However, this information could be used as a basis for employment discrimination.[83] Because the

---

80. *Danforth*, 428 U.S. 52.

81. *See supra* notes 47-62 and accompanying text.

82. "The decision to abort, indeed, is an important, and often a stressful one, and it is desirable and *imperative* that it be made with *full* knowledge of its nature and consequences." *Danforth*, 428 U.S. at 52 (emphasis added).

83. *See* Lappe, *supra* note 20. At least 59 companies, including Dupont, have or may initiate some form of screening program. Holden, *supra* note 20, at 336. New Jersey prohibits employment discrimination based upon atypical hereditary cellular or blood traits including the sickle cell trait. Florida and North Carolina prohibit employment discrimination based upon the sickle cell trait. *See Hearings, Genetic Screening, supra* note 20, at 97. West Virginia University Law Professor Mark Rothstein testified, at these hearings, that he believed it would be beyond OSHA's statutory mandate to promulgate standards regarding the

READ technique can be done on any blood sample, the testing could be performed without the employees' knowledge or consent and the information used as a basis for employment decisions.

The purported discriminatory use of information from genetic tests in the employment context has served as the basis for several recent discrimination suits. In *Smith v. Olin*,[84] summary judgment was granted to the defendant on a black worker's claim that he was fired discriminatorily because he had sickle cell anemia. The Fifth Circuit affirmed the lower court's decision without reaching the claim, agreeing with the lower court's findings that Smith's bad back was adequate reason for discharge from a laborer's position. In another case,[85] the Fourth Circuit has held that employment decisions based upon the possible susceptibility of female workers of childbearing age to toxic substances in the work place could be raised as a business necessity defense to a disparate impact claim[86] in a Title VII action. In order to assert such a defense, the court held that the employer could show that the action was required for employee or fetal safety and that the restrictions imposed served

---

use of genetic screening tests that would protect employment rights. *Id.* at 104. Rothstein further stated:

> [G]enetic and cytogenetic screening is a field in which the law has lagged well behind scientific developments. There is a strong potential that new scientific discoveries could be made in this field with a rapidity that would bring a variety of societal problems in their wake, and with which we are not presently prepared to deal.
>
> . . .
>
> The danger is that these techniques will be used prematurely, indiscriminately, and with harsh consequences for higher risk categories of workers.

Id. at 99-100. *See generally* Ashford, Spadafor & Caldart, *Human Monitoring; Scientific Legal and Ethical Concerns*, 8 HARV. ENVT'L L. REV. 263 (1984) (containing a thorough discussion of problems and issues associated with screening in the work place).

It should be noted that the physician has an enforceable duty not to reveal confidential information. *See generally* Riskin & Reilly, *Remedies for Improper Disclosure of Genetic Data*, 8 RUT.-CAM. L.J. 480 (1977). The primary sanction for improper physician disclosure of data obtained in the progessional relationship is delicensure, but only if the states provide this sanction. *Id.* at 491. Some courts have awarded damages for disclosure of confidential medical information. *Id.* Most state screening laws protect genetic data from unauthorized disclosure. *See, e.g.*, VA. CODE ANN. §§ 32.1-69 (Repl. Vol. 1979).

84. 555 F.2d 1283 (5th Cir. 1977).

85. Wright v. Olin Corp., 697 F.2d 1172 (4th Cir. 1982).

86. Employment practices that have a disproportionate adverse impact on certain groups violate Title VII. *See* McDonnell Douglass v. Green, 411 U.S. 792 (1973); Griggs v. Duke Power Co., 401 U.S. 424 (1971). As a defense to a disparate impact claim, an employer may show that the employment practice was justified because it was necessarily related to job performance, and thus, a business necessity. *See* Albemarle Paper Co. v. Moody, 422 U.S. 405 (1975); Comment, *The Business Necessity Defense to Disparate-Impact Liability Under Title VII*, 46 U. CHI. L. REV. 911 (1979).

that purpose.[87]

A number of genetic traits have been linked to susceptibility to pollutants and toxic substances in the work place.[88] Some have a higher incidence in specific racial groups[89] or may be gender-specific. Presumably an employer could justify an employment policy that had a disparate racial or gender impact if he could show that the policy was necessary and efficacious for the operation of the business. Only three states currently have laws prohibiting employment discrimination based upon the results of sickle cell screening tests.[90]

Assuming that an employer can test for susceptibility to toxic substances, it is unclear what limits the courts will place upon the dissemination of the data. Recently, the District of Columbia Circuit Court of Appeals ruled that an employer had to turn over all information relevant to health and safety in the work place to a labor union, including employee medical records, as part of the employer's duty to bargain in good faith.[91] However, the court did require that all names be deleted from the medical records.[92] The court held that such a limited disclosure did not violate an employee's right to medical confidentiality.[93]

Conceivably, genetic testing to reveal the presence of genes controlling an individual's susceptibility to diseases, including cancer,[94] could be required as a condition to the individual's obtaining insurance. Information about other genetic traits could also be used to justify voluntary or compulsory sterilization[95] and as a basis for withholding the right to obtain an education[96] or to marry.[97]

---

87. *Wright*, 697 F.2d at 1189.

88. *See supra* note 60.

89. *See supra* note 20.

90. *See supra* note 83.

91. Oil, Chem. & Atomic Workers Local Union No. 6418 v. NLRB, 711 F.2d 348 (D.C. Cir. 1983) (females restricted in job access as a part of a fetal vulnerability program).

92. *Id.* at 363.

93. *Id.*

94. *See supra* note 18; *see also* Cooper, *Cellular Transforming Genes*, 218 SCI. 80 (1982); Marx, *The Case of the Misplaced Gene*, 218 SCI. 983 (1982).

95. *See* Wexler, *supra* note 16, at 313. The Supreme Court has upheld a Virginia statute permitting eugenic sterilization. Buck v. Bell, 274 U.S. 200 (1927).

96. Several states require susceptible individuals to have a blood test for sickle cell anemia before entering school. *See, e.g.*, MASS. GEN. LAWS ANN. ch. 76, § 15A (West 1982); N.Y. EDUC. LAW § 904 (McKinney 1982).

97. A test for sickle cell anemia is required in New York for any individual who is not Caucasian, Indian or Oriental. N.Y. DOM. REL. LAW § 14-aa(1) (McKinney 1977). However, the results of the test are not to be used as a sole basis to deny a marriage license. *Id.* § 13-

IV. The Inability of the Existing Regulatory Systems to Deal with the Issues Raised by READ

The complex and diverse nature of the issues raised by the READ technique typify those issues which can be raised by other biomedical applications of rDNA research.[98] In some aspects, these issues differ from those that typically confront the regulatory process. The problems presented by READ are not due to the inherent risks of the procedure itself. Instead, the problems stem from the myriad ethical and legal dilemmas engendered by the scientific knowledge made available through the technique, and by the potential use or abuse of that knowledge. Clearly, the regulation of knowledge is far more perplexing than the attempt to limit the risks involved in a substance, drug, or medical procedure, even when an accurate assessment of the risk is difficult or impossible to obtain. Thus, the regulatory strategies employed to protect human safety may not necessarily be consistent with the ethical standards of society.

A. *Regulation of Diagnostic Devices Under the Food, Drug, and Cosmetic Act*

The Medical Device Amendments of 1976,[99] to the Food, Drug, and Cosmetic Act give the Food and Drug Administration (FDA) authority to regulate medical devices, including all *in vitro* reagents used to diagnose disease in man.[100] These amendments divide all medical devices into three classes based upon the degree of regulation required to provide reasonable assurance of the device's safety and effectiveness.[101] Class I and II devices are regulated ge-

---

aa(2).

98. *See* President's Commission, Splicing, *supra* note 4, at 51-79.

99. 21 U.S.C. §§ 360(c)-(k) (1982).

100. 21 U.S.C. § 321(h) (1982). "In vitro diagnostic products are those reagents, instruments and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health . . . . Such products are intended for use in the collection, separation and examination of specimens taken from the human body." 21 C.F.R. § 809.3(a) (1983).

101. 21 U.S.C. § 360c(a) (1982). A Class I device is one for which the generic controls authorized by the Act are sufficient to assure safety and effectiveness and which is not purported or represented to be for use in "supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health." *Id.* § 360c(a)(1)(A)(i)-(ii). A Class II device is one for which normal safeguards against adulteration and mislabeling are inadequate to assure safety and effectiveness, but for which sufficient information exists to establish performance standards. *Id.* § 360c(a)(1)(B). A Class III device is one for which there is insufficient information to determine whether controls are

nerically and do not require premarket approval. Class III devices require FDA approval before marketing.[102] The manufacturer of a new device can obtain premarket approval by providing "reasonable assurance" that such a device is safe and effective "under the conditions of use prescribed, recommended or suggested" in the proposed label.[103]

The reasonable assurance of safety standard is met by establishing that "[t]he probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use outweigh any probable risks."[104] The risks in this balancing test are confined to risks of injury or illness to the patient resulting from the use of the diagnostic procedure.[105] The FDA requires the demonstration of clinically significant results to establish that the device is effective.[106]

Within the regulatory framework described above it would be difficult for the FDA to withhold approval of a READ-utilizing test that could be demonstrated to yield clinically significant results. The initial application for approval of a test employing the technique would be classified as a Class III device because the test was not delivered into commerce before May 28, 1976 and is not substantially equivalent to another device classified as Class I or II.[107] The risks to the patient associated with READ are essentially similar to those associated with amniocentesis. These risks are generally considered negligible if the procedure is performed early in the second trimester. The benefits to health depend upon the type of information sought by the particular test. The benefits of tests for serious and clinically significant genetic disorders outweigh the

---

sufficient to provide reasonable assurance of safety and effectiveness, which cannot be classified as a Class II device and which is purported to be used in "supporting or sustaining human life or for use which is of substantial importance to preventing impairment of human health" or which "presents a potential unreasonable risk of illness or injury." *Id.* § 360(a)(1)(C) (i)-(iii).

102. *Id.* § 360c(a)(1)(C).

103. *Id.* § 360e(d)(2)(A)-(B). In addition the applicant must show good manufacturing procedures and accurate labeling. *Id.* § 360e(d)(2)(C)-(D). The safety and effectiveness of the device are to be determined "(A) with respect to the persons for whose use the device is represented or intended (B) with respect to the conditions of use prescribed, recommended, or suggested in the labeling . . . and (C) weighing any probable benefit to health . . . against any probable risk of injury or illness from such use." *Id.* § 360c(a)(2)(A)-(C).

104. 21 C.F.R. § 860.7(d)(1) (1983).

105. *Id.*

106. *Id.* § 860.7(e)(1).

107. 21 U.S.C. § 360c(f)(1) (1982).

small risks of amniocentesis. However, in the case of tests for neutral genetic traits, it could be argued that there is no benefit to health, and hence the test should be considered unsafe compared to the minimal risks of amniocentesis.[108]

Arguably, a test for a seemingly neutral trait could have beneficial value to some groups of individuals. Moreover, given the minimal risks of the diagnostic procedure, an FDA decision not to approve the test could be construed as interfering with a patient's right to medical autonomy and/or her constitutional right to be free from restraints in obtaining an abortion.

In deciding whether to approve a diagnostic device the Medical Device Amendments clearly do not permit the FDA to consider concerns relating to the misuse, unauthorized use or impact of a technique on medical practice and society.[109] The Act, however, does allow the sale, distribution or use of an approved device to be restricted.[110] For example, the FDA has used section 360j(e)(1)[111] to propose restrictions on the use of an *in vitro* test for detecting neural tube defects by screening for the presence of alpha-fetoprotein in maternal blood. The test lacks specificity unless coordinated with other diagnostic tools and confirmed through amniocentesis. The FDA based its proposed restrictions on the likelihood that the test's inherent lack of specificity would give parents false warnings as to the possibility that their child could have a neural tube defect. The FDA reasoned that the alerted parents would opt for unnecessary abortions rather than utilize the follow-up tests necessary to confirm the initial diagnosis.[112] All of the un-

---

108. *See supra* note 14.

109. *See generally* 21 U.S.C. § 360j(e)(1) (1982).

110. The Secretary may by regulation require that a device be restricted to sale, distribution, or use—(A) Only upon the written or oral authorization of a practitioner licensed by law to administer or use such device, or (B) Upon such other conditions as the Secretary may prescribe in such regulation; if, because of its potentiality for harmful effect or the collateral measures necessary to its use, the Secretary determines that there cannot otherwise be reasonable assurance of its safety and effectiveness.

Id.

111. *Id.*

112. 45 Fed. Reg. 74,158-60 (1980). In the United States between 0.1 and 0.2 percent of all live births have neural tube defects (e.g., spina bifida). A fetal protein, related to the fetal immunological system, alpha-fetoprotein (AFP), is an indicator of the presence of a neural tube defect. AFP will appear at elevated levels in the maternal blood in about 50 of 1,000 mothers at 14 weeks of pregnancy. However, only one out of 1,000 of the mothers will be carrying a fetus with a neural tube defect. Following a second blood test about 30 of these mothers still showing an elevated level of AFP will have to undergo sonograms to

desirable effects used to justify the restriction related directly to the effectiveness of the test.[113] Despite these concerns, the FDA ultimately decided to approve the test without restriction.[114]

Since, in most instances, tests using READ will be considered both safe and effective, section 360j(e) restrictions probably will not be placed on the tests. Thus, it appears that the existing FDA regulatory mechanisms will not permit the agency to consider all of the possible problems surrounding this technique.

B. *Regulation of Genetic Screening Under the Occupational Safety and Health Act*

Congress enacted the Occupational Safety and Health Act (OSH Act)[115] "to assure as far as possible every working man and woman in the Nation safe and healthful working conditions . . . ."[116] The OSH Act imposes a "general duty" on every employer to furnish each employee with a work place "free from recognized hazards."[117] Furthermore, with regard to toxic materials or harmful physical agents, the Occupational Safety and Health Administration (OSHA) must set standards which assure "[t]o the extent feasible, on the basis of the best available evidence that *no employee* will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life."[118] Any

---

eliminate false positive results caused by twins and improper estimation of fetal age. This usually reduces the number of at risk mothers to 15 per 1,000. Amniocentesis is usually performed at 22 weeks of gestation to measure AFP in the amniotic fluid. Of ten mothers with elevated AFP in the amniotic fluid only one will be carrying a normal child. *Id.* at 74,158-59.

113. The proposed restrictions addressed the concerns of some critics of the test that its general use will overburden the allocation of the limited medical resource of amniocentesis. *Id.* at 74,161 (1980). *See generally* PRESIDENT'S COMMISSION, SCREENING, *supra* note 6. The FDA however did not include this concern among its justifications for restricting the test under 21 U.S.C. § 360j(e). 45 Fed. Reg. 74,159 (1980).

114. 48 Fed. Reg. 27,780 (1983); *see* Sun, *FDA Draws Criticism on Prenatal Test*, 221 SCI. 440 (1983).

115. 29 U.S.C. §§ 651-678 (1982).

116. *Id.* § 651.

117. Section 654, entitled "Duties of employers and employees," reads in part:

> (a) Each employer—
>
> (1) Shall furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death or serious physical harm to his employees . . . .

21 U.S.C. § 654(a)(1) (1982).

118. *Id.* § 655(b)(5) (emphasis added). The term "occupational safety and health standard" is defined as: "[A] standard which requires conditions, or the adoption of one or more

standard must prescribe the use of "appropriate forms of warning" to ensure that employees are "apprised of all hazards" to which they are exposed.[119] The standard may prescribe the type of medical examinations or other tests which the employer must make available to employees exposed to hazardous materials.[120]

READ, which can accurately diagnose susceptibility to "toxic materials or physical agents,"[121] may constitute a method of assuring a safe or healthful work environment. Certainly, it could be argued that the technique is a means of ensuring that no employee suffers material health impairment from exposure to such hazardous materials.

Assuming that the use of the READ technique, or one like it, were required in an OSHA standard,[122] the OSH Act does not protect employees from dismissal if they are more susceptible to a hazardous material present in the work place. In fact, the District of Columbia Circuit Court of Appeals recently held that the "general duty"[123] clause in the OSH Act does not protect employees from dismissal based upon susceptibility to hazardous materials.[124]

---

practices, means, methods, operations, or processes, reasonably necessary and appropriate to provide safe or healthful employment or places of employment." *Id.* § 652.

119. *Id.* § 655(b)(7).

120. *Id.*

121. Woo, Alpha-1 Antitrypsin Deficiency and Pulmonary Emphysema: Identification of Recessive Homozygote by Direct Analysis of the Mutation Site in the Chromosomal Genes, Cold Spring Harbor Symposium on the Application of Recombinant DNA to Human Disease (1982). *See supra* note 20.

122. Dr. Bernard Goldstein of the Environmental Protection Agency has predicted that within five to ten years rDNA techniques (presumably the READ technique) will be employed to detect health effects in individuals exposed to toxic substances. *See* 15 ENV'T REP. (BNA) 1059 (1984).

123. *See supra* note 117 and accompanying text.

124. American Cyanamid Co. v. Oil Chem. and Atomic Workers Int'l Union, 9 O.S.H. REP. (BNA) 1596 (1982), *aff'd*, 11 O.S.H. REP. 2193 (D.C. 1984). Thirteen women were required to submit to sterilization in order to keep their jobs working in an area with high levels of lead which might cause birth defects. Five women submitted to sterilization, but all thirteen lost their jobs. The commission granted American Cyanamid's motion for summary judgment in suit alleging discriminatory employment policies. The dissent of Commissioner B. Cottine stated that the general duty clause in the Occupational Safety and Health Act, 29 U.S.C. § 654(a)(2), could be used to prevent this type of employment policy. *American Cyanamid*, 9 O.S.H. REP. at 1601 (Cottine, Comm'r, dissenting). *See also Hearings, Genetic Screening, supra* note 20.

C. *Regulation of READ Under the Toxic Substances Control Act*

The Toxic Substances Control Act (TSCA)[125] regulates some applications of rDNA research employed in biotechnology.[126] Under section 5 of TSCA, the manufacturer of a new "chemical substance" must notify the Environmental Protection Agency (EPA) of its intention to manufacture or process such a substance.[127] This section appears to require the manufacturer of DNA probes and restriction enzymes used in the READ technique to notify the EPA before beginning manufacture.[128] However, the TSCA specifically excludes from the definition of the term "chemical substance": "any food, food additive, drug, cosmetic, or device (as such terms are defined in section 201 of the Federal Food, Drug, and Cosmetic Act) when manufactured, processed or distributed in commerce for use as a food, food additive, drug, cosmetic or devise."[129] *In vitro* reagents are included in the definition of a "device" under 29 U.S.C. section 321(h) of the Food, Drug and Cosmetic Act.[130] Thus, it would appear that the TSCA prevents the EPA from considering the issues associated with READ. If the concerns surrounding the use of this technique merit regulatory attention, new mechanisms will have to be designed to specifically deal with the special complexity produced by this technology.

V. CONCLUSION

The issues associated with READ illustrate the complications that may be encountered as rDNA research generates new biomedical techniques that may be applied to treat and alter human genes. The inability of existing regulatory strategies to address these issues suggests that further inadequacies may be encountered

---

125. 15 U.S.C. §§ 2601-2629 (Supp. 1981).

126. It has been suggested that some of the industrial applications of biotechnology could be regulated under the Toxic Substances Control Act. McGarity & Bayer, *Federal Regulation of Emerging Genetic Technologies*, 31 VAND. L. REV. 461, 505-06 (1983) (the legal authority to regulate genetically engineered microorganisms would turn upon the agency's ability to establish that a microorganism is a "chemical substance" under § 2602).

127. 15 U.S.C. § 2604(a) (Supp. 1981). The term "chemical substance" is defined as: "[A]ny organic or inorganic substance of a particular molecular identity including—(i) any combination of such substances occurring in whole or in part as a result of a chemical reaction or occurring in nature . . . ." *Id.* § 2602(2)(A).

128. The term "manufacture" is defined to mean "to import . . ., produce, or manufacture." *Id.* § 2602(7).

129. *Id.* § 2602(2)(B)(vi).

130. 29 U.S.C. § 321(h) (Supp. 1981).

in regulating other biomedical applications of rDNA technology. READ does not directly endanger human health, however, it does have the potential for misuse and the invasion of an individual's privacy interests. In this respect, the lack of any effective in-place mechanism to ensure consideration of these problems is troublesome.

Clearly, as new biomedical applications of rDNA develop, careful consideration will have to be given to the effectiveness of existing regulatory strategies. However, because of the rapidity with which advancements can and are being made in the field of rDNA research, prospective examination of potential problems is needed to ensure that society is willing and able to accept the benefits and burdens of this research.