

FEDERAL REGULATION OF RECOMBINANT DNA TECHNOLOGY: TIME FOR CHANGE

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INTRODUCTION

Although the technique is only fifteen years old, genetic engineering involving recombinant DNA technology¹ has revolutionized biology. Genetic engineering has commercial and medical applications that may result in enormous social benefits. Perhaps as significant as its potential benefits, recombinant DNA research involves unique risks which create the possibility of a public health or an environmental disaster. Risk assessment in recombinant DNA technology is difficult because genetic engineering is such a new discipline that, beyond broad categorizations, we can only speculate about potential adverse effects. Many observers are concerned with the evolutionary consequences of an artificial genetic exchange between phylogenetically distant species, the production of new pathogens and substances for biological warfare, and eugenic manipulations.² Typical hypothesized biological disasters include the release into the atmosphere of harmful man-made organisms, organisms with new treatment-resistant properties, or new biological life forms with superior survival characteristics enabling them to displace existing beneficial organisms.³

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1. For definitions of the biotechnology terms used in this article, see *Glossary of Biotechnology Terms*, 1 HIGH TECH. L.J. 253 (1986).

2. See Levin, *Changing Views of the Hazards of Recombinant DNA Manipulation and the Regulations of these Procedures*, 7 RECOMBINANT DNA TECH. BULL. 107, 107 (1983).

3. See 185 SCIENCE 303 (1974) (letter entitled "Potential Biohazards of Recombinant DNA Molecules by the Committee on Recombinant DNA Molecules," from Paul Berg, Chairman, Assembly of Life Sciences, National Research Council, National Academy of Sciences). See generally Korwek and Cruz, *Federal Regulation of Environmental Releases of Genetically Manipulated Microorganisms*, 11 RUTGERS COMPUTER & TECH. L.J. 301, 308-10 (1985).

In this article I will review the Federal government's current matrix of regulation of recombinant DNA technology, and will examine alternative models of regulation to replace the fractured and unsatisfactory scheme now in effect. First, I will describe the scientific process of genetic engineering. Second, I will discuss the ways that various administrative agencies have tried to deal with the problems posed by genetic engineering in the absence of any meaningful legislative direction. This discussion will focus on the kinds of problems that develop when the regulation of recombinant DNA research is dispersed among several agencies with separate spheres of authority.⁴ Third, I will review unsuccessful Congressional attempts at developing a comprehensive legislative solution to cope with new biological risks. Finally, I will suggest an alternative regulatory scheme which would eliminate the most pressing problems found in the present regulatory structure and would provide for safe and optimal development of recombinant DNA technology.⁵

I. THE BIOLOGY OF GENETIC ENGINEERING

Recombinant DNA technology allows scientists to specifically alter or rearrange a cell's hereditary structure. Using such alterations, a scientist can change the cell's characteristics for scientific or industrial purposes. To help explain the benefits and risks involved in this evolving technology, a short summary of the biological basis of recombinant DNA technology follows.

The hereditary material in most living cells consists of molecules of deoxyribonucleic acid ("DNA"). A molecule of DNA is composed of a linear arrangement of four specific nucleoside bases—adenine (A), thymine (T), guanine (G), and cytosine (C)—strung together end-to-end. The hereditary information in the DNA is contained in the specific order of the nucleoside bases.⁶ This order defines the genetic code which specifies all the functions and characteristics of an organism.

The DNA genetic code is organized into units called genes, each comprised of one section of the DNA molecule.⁷ Each section usually consists of approximately one thousand bases, containing all the information needed to make one specific protein. This gene is "read" by the cell's transcription apparatus to make a unique messenger RNA molecule which is basically a copy of the information in the gene.⁸ The

4. See Proposal for a Coordinated Framework for Regulation of Biotechnology, 49 Fed. Reg. 50,856 (1984).

5. This article will not discuss the constitutional issues of prior restraint and freedom of investigation, which are also pressing problems.

6. B. LEWIN, GENES 22-26 (1983).

7. *Id.* at 3, 16.

8. *Id.* at 143.

information in this messenger RNA molecule determines the order in which amino acids are strung together by the cell's protein manufacturing apparatus. Protein is made up entirely of combinations of these amino acids. Thus, because the information contained in a gene specifies the order of amino acids in the manufactured protein, different genes contain different information codes for different proteins.

Proteins comprise most of the structural, regulatory, and metabolic components of a cell. Modifications in proteins can have profound effects on the cell's characteristics. Recombinant DNA technology enables scientists to perform such modifications in a very delicate fashion. Changing the sequence of nucleoside bases in a section of DNA within a gene will cause the gene to code a different sequence of amino acids, thus creating a different protein.⁹ A modification near a gene, on the other hand, will not change the type of protein produced, but can cause a cell to manufacture greater or lesser amounts of the protein.

The primary tool of DNA manipulation is called a vector. The vector is a small segment of DNA, usually a plasmid or virus, which can reproduce itself in the proper host, such as a bacterium or a particular cell line.¹⁰ The vector has specific sites into which a piece of DNA can be inserted to become part of the vector. Vectors can easily be transferred, grown, and subsequently re-isolated from the host, thereby generating many more copies of the vector. If a specific piece of DNA is inserted into the original vector, this technique can generate many copies of that DNA.

The process of selecting a piece of DNA, inserting this DNA into a vector, and reproducing many copies of this vector is called cloning. Cloning a gene, and subsequently modifying a gene that has been cloned, usually involves proteins called restriction enzymes, which cut a strand of DNA at very specific sites.¹¹ Using one restriction enzyme on a long piece of DNA, a scientist can cut the DNA wherever a specific sequence of bases appears in the long piece of DNA. This cutting generates a number of small fragments of DNA, all with the same end sequence. The scientist can then isolate one such fragment and insert into it a vector that has been cut with the same restriction enzyme. By transferring this modified vector into a host and reproducing the vector, the scientist clones this piece of DNA.¹²

To modify the cloned piece of DNA, the scientist can use restriction enzymes to cut out a small length of the DNA. He can also use

9. *Id.* at 42.

10. *Id.* at 300-02.

11. *Id.* at 50, 51.

12. *Id.* at 303-06.

chemicals which modify only individual bases in the sequence of the DNA piece he has cloned. This modified vector can then be cloned in a host. The effect of the modifications on the DNA can be studied by putting the vector into an appropriate host where the piece of DNA can be expressed and its expression studied. In industrial settings this cloning technique allows scientists to perform specific modifications on a gene so that the gene will code a protein that will perform some industrially advantageous function. For example, scientists have inserted a human growth gene into farm animals in order to grow larger livestock¹³ and researchers have proposed inserting ice-nucleating recombinant bacteria into potato plants in order to reduce their susceptibility to damage from frost.¹⁴

II. THE REGULATING AGENCIES

The regulation of recombinant DNA research is currently dispersed among several government agencies. The National Institutes of Health ("NIH") has taken the lead in promulgating substantive controls over recombinant DNA research. NIH policy has been influential because NIH possesses the technical expertise to understand the unique characteristics of biotechnology research. Yet NIH has only a limited ability to enforce its guidelines, and thus industry compliance with NIH standards has been largely voluntary. Regulatory power also rests in the hands of the Environmental Protection Agency ("EPA"), the Food and Drug Administration ("FDA"), and the United States Department of Agriculture ("USDA"). While all of these federal agencies have great experience with particular issues within their specific fields of expertise, they have only limited experience with the science of recombinant DNA technology.¹⁵

13. Jones, *Genetic Engineering in Domestic Food Animals: Legal and Regulatory Considerations*, 38 FOOD DRUG COSM. L.J. 273 (1983).

14. Milewski & Talbot, *Proposals Involving Field Testing of Recombinant DNA Containing Organisms*, 6 RECOMBINANT DNA TECH. BULL. 141, 143 (1983).

15. See generally OFFICE OF SCIENCE AND TECHNOLOGY POLICY: PROPOSAL FOR A COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY, 49 Fed. Reg. 50,855 (1984) (provides a concise index to U.S. law relating to biotechnology; clarifies policies of major U.S. regulatory agencies regarding biotechnology; describes a scientific advisory mechanism for assessment of biotechnology issues; explains how activities of federal agencies in biotechnology will be coordinated), CALIFORNIA ASSEMBLY OFFICE OF RESEARCH, BIOTECHNOLOGY: A REGULATORY REVIEW (1985) (reviews impact of recent formulation of federal regulatory policy and remaining regulatory uncertainties and jurisdictional conflicts upon California biotechnology industry).

A. National Institutes of Health

The NIH Guidelines for Research Involving Recombinant DNA Molecules ("Guidelines") are the most important source of standards and procedures regulating recombinant DNA research.¹⁶ The NIH Guidelines list four types of experiments believed to have the greatest potential for harming human health: (1) deliberate formation of genes which code for potent vertebrate toxins, (2) deliberate transfer of drug resistance, (3) deliberate transfer of recombinant DNA into human subjects, and (4) deliberate release into the environment of genetically engineered organisms. Prior NIH approval is required for research that involves these type of experiments.¹⁷

In 1974, the National Institutes of Health chartered the Recombinant DNA Advisory Committee ("RAC") to develop recommendations for the regulation of recombinant DNA research. RAC developed the Guidelines for Research Involving Recombinant DNA Molecules, which NIH issued on June 23, 1976.¹⁸ The 1976 Guidelines presumed that since the possibility of harm could not be properly evaluated, all recombinant DNA technology was considered dangerous. As research on recombinant DNA progressed, knowledge about the risks of such research increased. In light of this data, NIH revised the Guidelines in 1978 to allow for more lenient policies and procedures for conducting recombinant DNA experiments.¹⁹ Since the 1978 modification, the Guidelines remain largely unchanged. NIH's policy for modifying the Guidelines since 1978 is directed at strictly controlling only those experiments involving unique organisms.²⁰

The revised 1978 Guidelines contain a long list of non-unique organisms exempted from regulation. The relevant criteria used by NIH in determining whether or not to exempt an organism include (1) an evaluation of the seriousness of the risks posed by the organism, and (2) whether there exists cost-effective and unobtrusive methods for guarding

16. See Karny, *Biotechnology: The Regulatory and Legislative Environment*, 5 RECOMBINANT DNA TECH. BULL. 127, 127 (1982).

17. Department of Health and Human Services, National Institutes of Health, Guidelines for Research Involving Recombinant DNA Molecules, 49 Fed. Reg. 46,266, 46,268 (1984) [hereinafter cited as 1984 Guidelines].

18. Recombinant DNA Research Guidelines, 41 Fed. Reg. 27,902 (1976) [hereinafter cited as 1976 Guidelines].

19. Department of Health, Education, and Welfare, National Institutes of Health, Recombinant DNA Research Revised Guidelines, 43 Fed. Reg. 60,080 (1978) [hereinafter cited as 1978 Guidelines]. Karny, *Regulation of Generic Engineering: Less Concern about Frankensteins, but Time for Action on Commercial Production*, 12 TOLEDO L.R. 815 (1981).

20. Unique organisms contain new traits in each new combination of DNA. *Evaluation of the Risks Associated with Recombinant DNA Research*, 4 RECOMBINANT DNA TECH. BULL. 166, 168 (1981).

against potentially dangerous experiments with that organism.²¹ For example, NIH had exempted such safe, non-unique microorganisms as *E. coli*, yeast, and *B. subtilis* from the Guidelines' requirements. The exemption of these organisms was justified on the grounds that they had a relatively long history of laboratory manipulation, that a thorough genetic mapping of their known traits existed, and that their attenuation was such as to minimize any potential danger.²²

Although the Guidelines are now more flexible with regard to the types of experiments which can be conducted and the conditions under which those experiments can take place, special safety precautions are still required for certain kinds of research. For example, research work dealing with the cloning of toxic genes,²³ the release of recombinant DNA in the environment, and the introduction of antibiotic resistant genes into microorganisms not known to acquire the genes naturally must still be approved by NIH on a case-by-case basis.²⁴

NIH has also modified laboratory containment requirements for large-scale work. When the Guidelines were originally formulated in 1976, certain categories of recombinant DNA experiments were temporarily prohibited so that information concerning potential hazards could be collected. As a part of the 1978 revisions, a specification was incorporated into the Guidelines which prohibited experiments involving more than 10 liters of culture.²⁵ The only exception to this rule was for

21. See Karny, *supra* note 19, at 127; *Procedures for Review of Large Scale Experiments*, 5 RECOMBINANT DNA TECH. BULL. 51 (1983); McGarity & Shapiro, *Public Regulation of Recombinant DNA Gene Therapy*, 3 J. LEGAL MED. 185 (1982); *Evaluation of the Risks Associated with Recombinant DNA Research*, 4 RECOMBINANT DNA TECH. BULL. 166, 168 (1981).

22. Department of Health and Human Services, National Institutes of Health, Guidelines for Research Involving Recombinant DNA Molecules, 48 Fed. Reg. 24,564, 24,567 (1983) [hereinafter cited as 1983 Guidelines].

23. A toxic gene codes for the biosynthesis of molecules that are lethal for vertebrates at an L.D.₅₀ of less than 100 nanograms per kilogram of body weight. The term L.D.₅₀ indicates that out of a group of test subjects given an identical dose of the toxin, 50% will die within a specified time period. Genes in this category include those which code for botulinum toxins, tetanus toxin, diphtheria toxin and neurotoxins. 1984 Guidelines, *supra* note 17, at 46,268.

24. See 1983 Guidelines, *supra* note 22, at 24,557-58; see also Sun, *Cline Loses Two NIH Grants*, 214 SCIENCE 1220, 1220 (1981). A professor at the University of California at Los Angeles lost at least two of four NIH grants because he prematurely conducted the first gene therapy experiments on human beings. Although NIH had forbidden him from conducting clinical tests in the United States on patients with certain blood disorders, his research team injected new genetic material into Israeli patients suffering from the same disorders.

25. A "culture" includes both the organisms and the medium used to support them. See Milewski, *Large-Scale Procedures Under the NIH Guidelines*, 5 RECOMBINANT DNA TECH. BULL. 88, 88 (1982).

experiments utilizing organisms with recombinant DNA sequences that were rigorously characterized and not considered harmful.²⁶

Representatives of private industry have pressed for a relaxation of the large-scale experiment provisions contained in the Guidelines.²⁷ In September, 1980, the Recombinant DNA Advisory Committee determined that it would no longer review detailed information on large-scale containment facilities, but instead would delegate this responsibility to local institutional biosafety committees ("IBCs").²⁸ The IBCs amount to mini-RACs at local levels responsible for much of the review functions originally performed by NIH. In recommending this change, RAC concluded that the use of rigorously characterized organisms in large-scale recombinant DNA production processes was similar to large-scale, non-recombinant DNA fermentations, which industry had been performing for many years with an excellent safety record.²⁹ To date, however, experimental procedures involving manipulation and growth of recombinant DNA organisms in greater than 10 liter volumes are still prohibited by the Guidelines.³⁰

The legal basis of NIH's power to impose compliance with the Guidelines is unclear. There are two basic theories: first, that NIH's authority to enforce compliance derives from the private obligation created by the contract between each NIH funding grantee and the agency, and second, that NIH has independent statutory authority to force compliance by grantees. Recently, the Circuit Court of Appeals for the District

26. A rigorously characterized organism has a genetic map which indicates the order of and distances between DNA sequences. It can be deduced by various experimental methods. See B. DAVIS, MICROBIOLOGY, 246-47 (2d ed. 1973). As already noted, nonharmful organisms are those which have no pathogenic qualities.

27. For example, Dr. Allan Waitz of Schering-Plough Corporation initially suggested that experiments involving ten liters of culture should be handled exclusively by local biosafety committees. *Meeting of the Large-Scale Review Working Group of the Recombinant DNA Advisory Committee*, 6 RECOMBINANT DNA TECH. BULL. 19, 21 (1983).

28. Milewski, *supra* note 25, at 89. An IBC oversees all recombinant DNA work performed at a particular institution for compliance with the NIH Guidelines. It must comprise at least five members collectively possessing the expertise to assess the safety of the recombinant DNA experiments. Two members must be otherwise unaffiliated with the institution, and must represent the community's interest with respect to health and environmental matters. Minutes of IBC meetings and certain other documents must be made available to the public upon request. The IBC must be registered with NIH. See 1984 Guidelines, *supra* note 17, at 46,267. Section I-D-2 defines "Institutional Biosafety Committee" as a committee that meets the requirements for membership specified in Section IV-B-2 and has the responsibilities specified in Section IV-B-3.

29. Milewski, *supra* note 25, at 90.

30. Responsibility for reviewing protocols, evaluating the biology of the host-vector system, determining if the DNA is well-characterized and free of harmful sequences, inspecting physical facilities, and setting containment levels has been delegated to the local IBCs. *Id.* at 90.

of Columbia has held that NIH approval of genetic engineering experiments is an explicit condition which must be satisfied before a scientist can receive federal funds for recombinant DNA research. This indicates that courts may consider NIH's authority to be contractual in nature.³¹ Moreover, since a court may enjoin a party who defies an explicit regulatory condition governing receipt and expenditure of federal funds, NIH may have remedies unavailable in the normal contractual context.³²

However, earlier commentators stressed that the Guidelines were administrative rules,³³ which meant that NIH was required to comply with the provisions of the Administrative Procedure Act ("APA").³⁴ However, when the Guidelines were first published in 1976, NIH argued that they were not rulemaking proposals, although it did invite public comment and participation in their drafting. Subsequent revisions to the Guidelines have been preceded by notice, a comment period, public rulemaking proceedings, and a decision document that explains the basis for the decisions reflected in the revision. Thus, NIH's compliance with the informal rulemaking requirements of Section 553 of the APA suggests that the Guidelines may most accurately be described as rules.³⁵

Even if the Guidelines are substantive administrative rules, Edward Korwek has suggested that NIH's authority to enforce compliance stems from contractual obligations which are derived from the rules.³⁶ The Guidelines do specify required terms and conditions of funding contracts. The fact that NIH grants covered by the Guidelines originally required a memorandum of understanding and agreement also supports this theory.³⁷ Korwek did emphasize that this theory is only speculative, however, since NIH failed to state its legal authority at any time during the development of the Guidelines.

Although NIH regulations have force with respect to any institution receiving NIH grants, they do not directly apply to commercial enterprises conducting recombinant DNA research without NIH funds.³⁸

31. *Foundation on Economic Trends v. Heckler*, 756 F.2d 143, 155 n.7 (D.C. Cir. 1985).

32. *Id.*

33. Karny, *supra* note 19, at 820.

34. 5 U.S.C. §§ 551-8913 (1982).

35. Karny, *supra* note 19, at 821.

36. Korwek, *The NIH Guidelines for Recombinant DNA Research and the Authority of FDA to Require Compliance with the Guidelines*, 35 FOOD DRUG COSM. L.J. 636 (1980). The agency believes that its authority is derived from the Public Health Service Act which provides that the Agency may enter into contracts. 42 U.S.C. § 241(a)(7) (1982). This provision would also tend to support the contention that contract theory is the source of NIH's power to require compliance.

37. Korwek, *supra* note 36, at 636.

38. The revised Guidelines do provide for both voluntary compliance by private industry and for protection of proprietary data contained in applications to NIH. See 1984 Guidelines, *supra* note 17, at 46,273.

Since many companies and individuals perform recombinant DNA research without government grants, a large amount of recombinant DNA research is being conducted by enterprises that are not legally constrained by the crucial provisions of the Guidelines. Even though many companies voluntarily comply with the Guidelines,³⁹ it is unfortunate, given the great pressure to sacrifice safety in order to minimize costs and delays, that commercial enterprises facing fierce competition in the rapidly developing genetic engineering market are not directly subject to this important set of Federal regulations.

Despite this gaping loophole, enterprises that license biotechnology developed with NIH grants may be required to comply with the Guidelines. Many businesses acquire production technology by licensing it from federally-funded research institutions; thus, compliance with NIH may be an explicit obligation of the licensee under the licensing contract. However, it is unclear whether NIH has the authority to require compliance with the Guidelines regardless of the intent of the parties.

For example, in 1982 Stanford University and the University of California were granted a patent for a recombinant DNA process developed with NIH support (the "Cohen-Boyer" patent).⁴⁰ The contracts between Stanford and its licensees required that any licensee must "intend to comply" with the containment provisions in the Guidelines.⁴¹ Apparently, this contractual provision was incorporated into Stanford's license agreements at the recommendation of NIH.⁴² However, as emphasized by Dr. Bernard Talbot and as conceded by other interested

39. McGarity & Bayer, *Federal Regulation of Emerging Genetic Technologies*, 36 VAND. L. REV. 461, 502 (1983); see also Comment, *Regulating the Environmental Release of Genetically Engineered Organisms*: Foundation on Economic Trends v. Heckler, 12 FLA. ST. U.L. REV. 891, 900 (1985).

40. Goldstein, *A Footnote to the Cohen-Boyer Patent and Other Musings*, 5 RECOMBINANT DNA TECH. BULL. 180, 180 (1982).

41. The provision from the Stanford license agreement reads in pertinent part:

4. Compliance with Laws, Regulations and Standards

* * *

4.2 With respect to operations by the U.C. LICENSEE in the United States, its territories and possessions, LICENSEE specifically expresses its intent to comply with the physical and biological containment standards set forth in the NIH Guidelines for Research Involving DNA Recombinant Molecules, dated 21 November, 1980, or any other subsequent amended version of U.S. Government guidelines or regulations pertaining to such activities in effect during the term of this Agreement. LICENSEE further agrees to cooperate with government agency(ies) authorized to monitor compliance with such containment standards.

Stanford Patent License, reprinted in 1 BIOTECHNOLOGY L. REP. 63, 63 (1982).

42. See Affidavit of Dr. Bernard Talbot, Acting Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health 4 (Sept. 6, 1984).

parties,⁴³ there is no language in the present Guidelines which specifically mandates compliance with NIH provisions by licensees.⁴⁴

The Guidelines have been adopted by other federal agencies and their grantees, and are used fairly widely in the private sector.⁴⁵ The substantial interest in voluntary compliance with the Guidelines prompted NIH in January, 1980, to draft a provision encouraging industry participation.⁴⁶ This provision established procedures protecting proprietary information submitted for NIH review.⁴⁷ Despite the uncertainty concerning the origins of NIH authority to regulate recombinant DNA research, the Guidelines remain the de facto standard for most biotechnological research.

B. Food and Drug Administration

Over the past seven years, the Food and Drug Administration's regulation of health-related consumer products has increased extensively, causing many biologically produced drugs and recombinant DNA techniques to be subject to FDA approval. Beginning in 1979, the FDA claimed that its authorizing statute, the Federal Food, Drug, and Cosmetic Act,⁴⁸ particularly section 201(p)(1), permitted it to require pre-marketing approval for new drug products and methods of production. Previously, only active ingredients in new drugs required such approval.⁴⁹ The FDA's position implied that drugs produced biologically by DNA hybridization rather than by conventional means would be subject to the full battery of required FDA tests before being approved for sale on the market. The FDA's interpretation of the Act was first accepted by the Second Circuit in 1980 in *Premo Pharmaceutical Laboratories, Inc. v.*

43. According to Dr. Talbot, HEW-NIH Institutional Patent Agreements ("IPA's") were never revised to require that licensees of recombinant DNA creations provide an assurance of compliance with the physical and biological containment standards set forth in the Guidelines. *Id.* at 4-6.

44. Mr. Jeremy Rifkin, director of the Foundation on Economic Trends, suggested that the Guidelines should be modified to cover private companies "who are signatories of the license agreements with NIH funded institutions where said agreements contain clauses requiring the licensee to adhere to the NIH Guidelines involving recombinant DNA experimentation." Department of Health and Human Services, National Institutes of Health, Recombinant DNA Research: Actions Under Guidelines, 50 Fed. Reg. 9,760, 9,767 (1985).

45. McGarity & Shapiro, *Public Regulation of Recombinant DNA Gene Therapy*, 3 J. LEGAL MED. 185, 190 (1982).

46. 1983 Guidelines, *supra* note 22, at 24,564.

47. *Id.*

48. 21 U.S.C. §§ 301-392 (1982 & Supp. II 1984).

49. *Pharmadyne Laboratories, Inc. v. Kennedy*, 466 F. Supp. 100, 104 (D.N.J.), *aff'd on other grounds*, 596 F.2d 568 (3d Cir. 1979).

*United States*⁵⁰ and was ultimately upheld by the Supreme Court in *United States v. Generix Drug Corporation*.⁵¹ After *Generix*, it is clear that new recombinant DNA versions of previously approved drugs are considered "new drugs" subject to pre-marketing clearances by the FDA. In order to provide guidance to current or prospective manufacturers of new biological drug products, the FDA has developed a series of documents recommending issues that manufacturers should consider in recombinant DNA production processes.⁵²

In addition to its regulation of new drugs and methods of drug production, the FDA also is considered to have jurisdiction over gene therapy through its power to regulate clinical pharmaceutical testing. For example, if DNA is inserted into a virus and the virus is then injected into a patient, this genetically unique virus might be considered a biological "drug" subject to FDA regulation.⁵³

While there is little doubt that gene therapy produces "new drugs," one possible limitation on FDA power to regulate new drugs and pharmaceutical testing is found in the FDA's enabling statute—the requirement that the drugs or testing products move in interstate commerce.⁵⁴

50. 475 F. Supp. 52 (S.D.N.Y. 1979), *rev'd and remanded* 629 F.2d 795 (2d Cir. 1980) (The Second Circuit affirmed the trial court's interpretation that a drug may be considered a new drug under 21 U.S.C. § 321(p)(1)

even if the active ingredient is considered safe and effective).

51. 460 U.S. 453, 454 (1983).

52. Statement of Policy for Regulating Biotechnology Products, 49 Fed. Reg. 50,878, 50,880 (1984). These "points to consider" are designed to guide manufacturers in their efforts to obtain marketing approval.

53. FDA Biological Products, 21 C.F.R. §§ 600.3-600.22 (1985). The problem is not that the regulations are *per se* ambiguous. Rather, the FDA presently has no separate and distinct regulations for products created with gene-splicing techniques. It must therefore rely on a case by case approach to ascertain whether a particular bioengineered drug will fall within the scope of a particular regulation. Although the production of biological drugs is more strictly regulated than the production of other drugs, the rules pertaining to "investigational experiments" are the same for both kinds of products. McGarity & Shapiro, *supra* note 45, at 195.

54. *See, e.g.*, 21 U.S.C. § 331(a)-(c) (1982 & Supp. II 1984) (prohibiting certain "acts of interstate commerce involving drugs"). Several other sections of the Federal Food, Drug and Cosmetic Act limit the FDA's jurisdiction. For example:

The alteration, mutilation, destruction, obliteration, or removal of the whole or any part of the labeling . . . if such act is done while such article is held for sale (whether or not the first sale) after shipment in interstate commerce and results in such articles being adulterated or misbranded [is prohibited].

21 U.S.C. § 331(k) (1982 & Supp. II 1984).

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

21 U.S.C. § 355(a) (1982 & Supp. II 1984).

Under recent case law, the FDA is effectively powerless if drug distribution by manufacturers or physicians does not fall within these statutory provisions. For example, in *United States v. Evers*, 643 F.2d 1043 (5th Cir. 1981), a physician had been

If genetically engineered materials are not shipped in interstate commerce, the FDA arguably lacks jurisdiction to regulate the manufacture and distribution of such substances. However, the argument can be made that the revolutionary aspect of successful gene therapy (that the inserted DNA segment will remain with the patient and continue to provide its therapeutic effects for the remainder of a subject's lifetime) encourages patients to cross state lines to obtain a supply of a drug from a gene therapist to take back to his home state. This kind of behavior was held sufficient to satisfy the interstate commerce requirement in *United States v. Sanders*.⁵⁵

However, if the patient resided and continued to reside in the gene therapist's home state, then the interstate commerce requirement would have to be established along more "conventional" lines. In this regard, the FDA has argued that physicians cannot offer for sale any unapproved drugs in a promotional context.⁵⁶ That is, the physician cannot represent that the use of an unapproved drug is safe or effective or "otherwise promote or commercialize the article."⁵⁷ If the FDA successfully expands its jurisdiction over purely intrastate activity in this manner, local recombinant DNA gene therapists will be significantly affected.⁵⁸ For example, FDA regulations would govern how recombinant DNA

prescribing a drug for a use which was unapproved by the FDA, although the drug was available to his patients in the local pharmacy. The court agreed with the government that the promotion of any drug which had previously moved in interstate commerce satisfied the jurisdictional requirements of the Federal Food, Drug, and Cosmetic Act. However, the court noted that there must be distribution of the drugs to other physicians in order to have the requisite commercial quality. Because distribution of drugs to patients involved only the practice of medicine and not commerce, the court found no violation of § 331(k). *Id.* at 1054.

55. 196 F.2d 895, 898 (10th Cir.), *cert. denied*, 344 U.S. 829 (1952) (to be guilty of "violating the Act it was not necessary that appellee be engaged in interstate commerce with respect to a misbranded drug."). *See also* McGarity & Shapiro, *supra* note 45, at 196-97, 203.

56. *See* *United States v. Evers*, 643 F.2d 1043, 1047 (5th Cir. 1981) (holding that the government must establish that a drug is held for sale after shipment in interstate commerce in order to find a violation of 21 U.S.C. § 331(k) (1982)).

57. Notice of Proposed Rulemaking, Qualifications of Clinical Investigators or Regulated Articles, 43 Fed. Reg. 35,210, 35,226 (1978).

58. *See* *United States v. Evers*, 643 F.2d 1043. In this case, the court determined that, although the defendant-doctor had received his drugs from a local pharmacy in a purely intrastate transaction, theoretically he could still be prosecuted for misbranding a drug that was "held for sale . . . after shipment in interstate commerce." Nevertheless, the 5th Circuit concluded that there had been no violation of the interstate commerce requirement in this case because the misbranding could occur only if the defendant-doctor was holding the drug for sale with inadequate directions to other physicians. Therefore, even if the drug had previously moved in interstate commerce somewhere up the distribution chain, the doctor had not violated the statute because he had only recommended the drugs to his *patients*.

research may proceed and would mandate that the therapist comply with informed consent requirements.

In regulating intrastate research, the FDA can also rely on the Supreme Court's decision in *Weinberger v. Bentex Pharmaceuticals, Inc.*,⁵⁹ which interprets the FDA's authorizing statute (the Federal Food, Drug and Cosmetic Act) broadly. The Court in *Bentex* indicated that the FDA has the broad power to effectuate its regulatory scheme with "administrative finality."⁶⁰ It appears that after *Bentex*, any person, including a conventional manufacturer or physician who undertakes clinical research intended to gain approval for a drug, can assume the role of a "drug promoter" and thus may be regulated by the FDA.⁶¹

Although the FDA has the power to regulate health related uses of recombinant DNA, commentators have questioned whether the FDA can require compliance with the NIH Guidelines when recombinant DNA research is conducted specifically for developing products subject to FDA approval. "Although NEPA [the National Environmental Policy Act] requires that federal agencies take environmental considerations into account in their planning and decision-making processes, such authority does not necessarily give the FDA the power to require compliance with the Guidelines."⁶² Congress limited the FDA's regulatory authority under the Federal Food, Drug, and Cosmetic Act "to adopting those regulations that can reasonably be expected to improve the purity or quality of food and drugs."⁶³ The NIH Guidelines address only the methodology of conducting safe research, which does not necessarily correlate with improving the purity or quality of products. While the fact that each bioengineered product is made with a NIH approved host-vector system may ensure safety and efficiency, it does not necessarily mean that a product is of a high quality. Therefore, FDA regulation of the production of many bioengineered drugs should not require mandatory compliance with the NIH Guidelines since such regulation would fall outside the FDA's statutory objectives.⁶⁴

59. 412 U.S. 645 (1973).

60. *Id.* at 653.

61. See McGarity & Shapiro, *supra* note 45, at 201.

62. Korwek, *Recombinant DNA and the Law: Review of Some General Legal Considerations*, 15 GENE 1, 3 (1981). NEPA requires that drug manufacturers provide evidence of no adverse environmental effects.

63. *Id.*

64. See Korwek, *supra* note 36, at 633. Dr. Korwek makes a persuasive argument that the FDA has no authority whatsoever to compel adherence to the provisions of the NIH Guidelines. *Id.* at 635. Dr. Korwek also maintains that although the argument can be made that regulations passed pursuant to these statutory sections provide authority to force compliance with the Guidelines, the better view is that the purpose of the NIH Guidelines is much too different from that of the Federal Food, Drug, and Cosmetic Act to fall within even the broad scope of the FDA's function. *Id.* at 642-43. He also makes

C. Environmental Protection Agency

The Environmental Protection Agency has broad statutory authority to regulate genetic engineering activities under the Toxic Substance Control Act ("TSCA"),⁶⁵ the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"),⁶⁶ and other federal environmental statutes.⁶⁷ As discussed below, the definition of a "chemical substance" in TSCA appears to give the EPA regulatory jurisdiction over *all* recombinant DNA material. However, the statute explicitly excludes a number of materials regulated by the EPA under the authority of other statutes as well as materials regulated by the FDA.⁶⁸

The EPA's regulation of a "chemical substance" under TSCA is dependent upon a showing that the substance may present "an unreasonable risk of injury to health or the environment."⁶⁹ The Toxic Substance Control Act states that it is unlawful for any person to manufacture or process a substance covered by the Act without notifying the EPA Administrator at least 90 days in advance of such manufacture or processing.⁷⁰ The statute broadly defines a chemical substance as "any organic or inorganic substance of a particular molecular identity."⁷¹ The EPA has interpreted the term "chemical substance" to include nucleic acids and genetically engineered organisms, and has subjected these products to TSCA premanufacture notification requirements.⁷²

The Toxic Substance Control Act requires that the EPA perform a premanufacture review of all new chemical substances, and also authorizes the EPA to regulate new and existing toxic materials. The EPA thus

a similar argument concerning the relevant provisions of the Public Health Service Act. *Id.* at 647 (citing 42 U.S.C. § 264 (1982)).

It should also be noted that FDA approval of a new drug application is required before that drug can be marketed. "[S]trategies have been developed for the evaluation of various 'biotechnological' or 'genetically engineered' products, as well as for other products." As already noted, these strategies are product-specific rather than technology-specific. The agency's explanation for this approach is that "although scientific considerations may dictate areas of generic concerns for certain techniques, the use of a given biotechnological technique does not require a different administrative process." Statement of Policy for Regulating Biotechnology Products, 49 Fed. Reg. 50,878, 50,879-80 (1984).

65. 15 U.S.C. §§ 2601-2929 (1982).

66. 7 U.S.C. §§ 136-136y (1982).

67. *See, e.g.*, Federal Water Pollution Control Act, 33 U.S.C. §§1251-1376 (1982); Clean Air Act, 42 U.S.C. §§ 7401-7476 (1982); Resource Conservation and Recovery Act, 42 U.S.C. §§ 6901-6987 (1982).

68. 15 U.S.C. § 2608 (1982).

69. 15 U.S.C. § 2603(a)(1)(A)(i) (1982).

70. 15 U.S.C. §§ 2604-2614 (1982).

71. 15 U.S.C. § 2602(2)(A) (1982).

72. *See* Proposed Policy Regarding Certain Microbial Products, 49 Fed. Reg. 50,880, 50,887 (1984).

has extremely broad power to regulate recombinant DNA manufacturing and research, whether performed by private industry, government agencies, or institutions receiving government funding. In addition, the National Environmental Policy Act ("NEPA") requires that all agencies prepare an environmental impact statement on "major Federal actions significantly affecting the environment."⁷³

The EPA regulates genetically engineered pesticides under FIFRA.⁷⁴ The EPA has received several applications for experimental use permits for genetically engineered microbial pesticides ("GEMPS") and has granted permits to two applicants.⁷⁵ The disclosure requirements for product registration generally focus upon three elements: product analysis, toxicology (impacts on human health), and ecological effects.⁷⁶

Concern with GEMPS is sparked by previous instances where entry of organisms into a new environment resulted in adverse effects to the surrounding ecology.⁷⁷ For example, the American chestnut became nearly extinct in the early twentieth century after a parasitic fungus was brought to the United States on nursery plants from Asia. Imported insect species have also been especially damaging. Previous experiments and studies done with materials regulated under TSCA may provide useful information on the effects of biologically engineered pesticides. In situations where few detailed studies of a genetically engineered pesticide exists, information from previous experiments done with similar, but non-biologically engineered chemical substances will be all that is available to provide clues to the possible toxicity of a particular compound or organism containing recombinant DNA.⁷⁸ Of course, the EPA has the

73. 42 U.S.C. § 4332(2) (1982).

74. See Proposed Policy Regarding Certain Microbial Products, 49 Fed. Reg. 50,880, 50,880 (1984).

75. Applications were received from the University of California, 51 Fed. Reg. 10,114 (1986), the Monsanto Company, 51 Fed. Reg. 6,035 (1986), and Advanced Genetic Sciences, Inc. ("AGS"), 50 Fed. Reg. 49,760 (1985). The first experimental use permit was granted to AGS. 50 Fed. Reg. 49,760 (1985). The EPA subsequently suspended the permit pending an investigation of AGS testing procedures. See Schneider, *Field Testing Permit for Genetic Concern Lifted for False Data*, N.Y. Times, Mar. 25, 1986 at 1, col. 1. The second experimental use permit was granted to the University of California, to test frost-fighting microbes on a California potato patch. Pasztor, *EPA Clears Field Test on Potato Seeds And Young Plants of Altered Bacteria*, Wall St. J., May 14, 1986, at 10, col. 2.

76. See Betz, Levin & Rogul, *Safety Aspects of Genetically Engineered Microbial Pesticides*, 6 RECOMBINANT DNA TECH. BULL. 135, 137 (1983). In support of its application, Monsanto submitted 800 pages of research data. See Schmeck, *Gene-Altered Pesticide Readied for Field Test*, N.Y. Times, Jan. 8, 1985, at C7, col. 1.

77. See Betz, Levin & Rogul, *supra* note 76, at 135; Sharples, *Spread of Organisms with Novel Genotypes; Thoughts from an Ecological Perspective*, 6 RECOMBINANT DNA TECH. BULL. 43 (1983).

78. Interview with Dr. Stanley Abramson, Environmental Protection Agency (May 27, 1985).

authority under TSCA to prohibit or restrict the use of chemicals in situations where the data is insufficient to evaluate the chemical effects.⁷⁹

Presently, notification is required as an interim procedure for all small-scale field studies involving the direct release of nonindigenous and genetically engineered microbial pesticides into the environment.⁸⁰ As under TSCA, the EPA has 90 days to review potential effects of a release on human health and the environment.⁸¹ Regulations under FIFRA indicate that the development and use of genetically modified microbial pesticides by the EPA will be determined on a case-by-case basis.⁸²

D. The United States Department of Agriculture

The United States Department of Agriculture currently has no special regulations governing organisms containing recombinant DNA. However, USDA regulations do prohibit the circulation of certain pathogens,⁸³ and it is USDA policy to limit the distribution of certain potentially unsafe organisms and to make such materials available only to qualified researchers on a case-by-case basis.⁸⁴ USDA also has a reviewing process and licensing policy under which licensing applications for biological products are evaluated to insure purity, potency, safety, and efficacy.⁸⁵ USDA interest in recombinant DNA experiments peaked in 1984 when the Agricultural Research Service began to promote recom-

79. 15 U.S.C. § 2603 (1982).

80. Microbial Pesticides; Interim Policy on Small Scale Field Testing, 49 Fed. Reg. 40,659 (1984).

81. *Id.* at 40,661. If the agency determines that the testing of a genetically engineered pesticide involves significant environmental or health hazards, then the applicant could be required to obtain an experimental permit before it proceeds with the tests. *Id.* at 40,659.

82. 40 C.F.R. § 158.65 (1985).

83. For example, the Federal Plant Pest Act of 1957 prohibits importation and movement of plant pests across state lines unless authorized by the USDA. 7 U.S.C. § 150 (1982). The Act defines a "plant pest" as any living organism that is injurious to plants, such as insects, mites, nematodes, fungi, bacteria, viruses, and viroids. 7 U.S.C. § 150aa (1982). The USDA also has the authority to regulate cultures or collections of organisms which may transmit any contagious or infectious disease to animals and poultry. Tolin, *The Role of USDA Quarantine Regulations and Culture Collections in Recombinant DNA Research*, 4 RECOMBINANT DNA TECH. BULL. 156, 158-59 (1981). Experiments with certain organisms are restricted by the USDA, including experiments with the viruses that cause foot-and-mouth disease, African horse sickness, lumpy skin disease, pseudofarcy and rinderpest. *Id.* at 159 (Table 1 and text).

84. See Tolin, *supra* note 83, at 159.

85. Office of Science and Technology Policy: Proposal for a Coordinated Framework for Regulation of Biotechnology, 49 Fed. Reg. 50,860 (1984).

binant DNA research by establishing the Competitive Research Grants Program to award \$28.5 million to biotechnology projects.⁸⁶

The USDA also began conducting its own experiments involving a gene which produces a growth hormone in human beings. Working with investigators at the University of Pennsylvania, government scientists introduced this gene into domestic animals to make them grow larger.⁸⁷ The implantation of human genes into animals has been a very controversial undertaking. In 1984, the Foundation on Economic Trends filed a suit against the Department of Agriculture to halt the permanent implantation of new genetic information into pigs and sheep.⁸⁸ The Foundation asserted that the Department of Agriculture did not adequately prepare an environmental impact statement or environmental assessment of the animal research program. Plaintiffs also argued that because no serious attention was paid to the potential repercussions of developing and operating these animal breeding research programs, the defendants thus failed to "utilize a systematic, interdisciplinary approach which will insure the integrated use of the natural and social sciences . . . in planning and in decision making which may have an impact on man's environment," as required by the National Environmental Policy

86. Keller, *Key Farm Laboratory Plans "Overdue" Move to Genetics*, N.Y. Times, May 29, 1984, at 1, col. 3. On September 13, 1985, the Department of Agriculture solicited applications for competitive research grants for fiscal year 1986. Such grants cover work in biotechnology in which any agriculturally important organism(s) is used to accomplish the objectives of this program area. In particular, a subprogram area will emphasize identification, isolation, and characterization of:

- (1) genes and gene products;
- (2) regulatory mechanisms of gene expression;
- (3) interactions between nuclear and organelle genes;
- (4) mechanisms of gene recombination and transposition;
- (5) molecular bases of chromosomal replication; and
- (6) mechanisms of interaction with beneficial or deleterious microorganisms.

Department of Agriculture, Competitive Research Grants Program for Fiscal Year 1986, Solicitation of Applications for Competitive Research Grants Program, 50 Fed. Reg. 37,478, 37,479-80 (1985).

87. *Livestock Given Human Gene for First Time*, N.Y. Times, June 27, 1985, at A17, col. 1. Recently, USDA-supported researchers at the University of Pennsylvania and the University of Washington inserted a functioning human growth gene into rabbits, pigs and sheep for the first time. This research could lead to larger, more feed-efficient and more disease-resistant livestock. The researchers worked with the gene that orders production of the growth hormone in human beings. This human gene was first joined to a portion of a mouse gene which can activate the human gene segment. This combination of genetic material was introduced into the bodies of laboratory mice, and "expressed itself" in these mice. Schmeck, *In the Gene Lab, Scientists Manipulate Codes of Life*, N.Y. Times, Jan. 21, 1986, at C1, col. 4. See generally, Jones, *Genetic Engineering in Domestic Food Animals: Legal and Regulatory Considerations*, 38 FOOD DRUG COSM. L.J. 273 (1983).

88. *Foundation on Economic Trends v. Block*, No. 80-3045 (D.D.C. filed Oct. 1, 1984).

Act.⁸⁹ Plaintiffs further alleged that the Department of Agriculture failed to adequately assess the extent to which the fundamental genetic nature of the species of animals used in these experiments would be altered by genetic engineering.⁹⁰ Although this suit is still pending, the outcome promises to provide some indication of the type and extent of environmental research required before permanent genetic implantation may take place.⁹¹

89. *Id.* at 32-33 (citing National Environmental Policy Act, 42 U.S.C. § 4332(2)(A)(1982)). The plaintiffs also alleged that the Department's failure to develop, or at least articulate, alternatives to their research program constituted arbitrary agency action in violation of the Federal Administrative Procedure Act. *Id.* at 33-34.

90. Complaint for Declaratory and Injunctive Relief, *Foundation on Economic Trends v. Block*, No. 84-3045 (D.D.C. filed Oct. 1, 1984); *See also* Plaintiff's First Amended Complaint, *Foundation on Economic Trends v. Block*, No. 84-3045 (filed Feb. 8, 1985) (elaborating the claims arising under a proposed federal common law of nuisance, the National Environmental Policy Act, and the Administrative Procedure Act). The defendants argued in a motion for summary judgment that the Department of Agriculture's broad policy objectives in conducting the experiments were not subject to judicial review because, among other reasons, no significant major federal action occurred which significantly affected the environment. Memorandum in Support of and Motion for Summary Judgment at 16-17, *Foundation on Economic Trends v. Block*, No. 84-3045 (D.D.C. served Apr. 17, 1985). There is no violation of NEPA because the experimental results are not sufficiently ripe for NEPA review. *Id.* at 19.

91. The defendants also contended that there were no APA violations because no arbitrary and capricious action took place. Furthermore, there is sufficient statutory authority to allow the Department of Agriculture to proceed with a broad variety of research programs. Memorandum in Support of and Motion for Summary Judgment at 26-29, *Foundation on Economic Trends v. Block*, No. 84-3045 (D.D.C. served Apr. 17, 1985). In addition, defendants argued that the availability of the federal common law of nuisance should be narrowly construed, and that the plaintiffs did not have standing to allege a cause of action on this ground. *Id.* at 30-37.

In *Foundation on Economic Trends v. Weinberger*, No. 84-3542 (D.D.C. filed Nov. 21, 1984), although the complaint did not specifically address the proper use of genetic engineering, plaintiff articulated a concern with respect to the proper procedure for the United States Army's biological research at the Dugway Proving Ground in Utah. Plaintiff alleged that the Army prepared neither an environmental impact statement, nor an environmental assessment of any of its proposals to construct a new materials testing facility and a new aerosol testing laboratory. These assessments, plaintiff alleged, were required by NEPA. Complaint For Declaratory and Injunctive Relief, *Foundation on Economic Trends v. Weinberger*, No. 84-3542, at 9-10 (D.D.C. filed Nov. 21, 1984).

On May 31, 1985, the federal district court issued a permanent injunction forbidding the Army from building these facilities. Judge Green concluded that because of the deadly nature of the tested material, consideration of the larger interests of society militates heavily in favor of enjoining construction. Judge Green also stated that the environmental assessment prepared by the Army last year was "clearly inadequate" and therefore constituted a substantive violation of the National Environmental Policy Act. Biddle, *Judge Forbids Army to Build Germ War Facility*, *N.Y. Times*, June 1, 1985, at 24, col. 1.

III. INADEQUACY OF THE CURRENT REGULATORY STRUCTURE

The preceding discussion illustrates the two central problems of the current regulatory structure. First, the dispersal of expertise and power among many regulatory agencies causes inconsistent regulatory decision making. Second, the existence of overlapping jurisdictional authority by different agencies under different statutes creates the potential for serious inter-agency conflicts.

At the present time, the Recombinant DNA Advisory Committee of the National Institutes of Health remains the principle federal authority regulating genetic engineering. However, the EPA has begun to regulate recombinant DNA research under TSCA and FIFRA, the Department of Agriculture now sponsors and regulates genetic engineering research, and the FDA has become active in regulating the manufacturing and distribution of biological drugs. The National Science Foundation is yet another federal agency funding recombinant DNA research.⁹² Separate agencies with separate mandates will evaluate the risks and benefits of recombinant DNA research in different ways, and will thus produce inconsistent and conflicting regulations. In addition, recombinant DNA experiments may have effects that fall within the jurisdiction of several different agencies, thus producing inter-agency conflicts. The combination of overlapping jurisdiction and inconsistent regulations creates a great degree of confusion by baffling researchers to the point that they do not know how to comply with the complex interrelationship of agency regulations. It also generates a high risk that potentially hazardous experiments or areas of recombinant DNA research will fail to be regulated.

A. Biotechnology Science Coordinating Committee

The pressing problem of uncoordinated regulation of biotechnology research has already begun to be addressed. In November, 1985, the White House Office of Science and Technology Policy created the Biotechnology and Science Coordinating Committee ("BSCC").⁹³ The Committee is composed of senior representatives from NIH, EPA, USDA, FDA and NSF. The Committee provides federal officials from different agencies with a forum for discussing scientific questions raised by regulatory and research applications. The purpose of the BSCC is to

92. *NAS's Frank Press: New Shapes for Science Policy*, CHEMICAL & ENGINEERING NEWS, Mar. 3, 1986, at 98.

93. See *Coordinated Framework for Regulation of Biotechnology; Establishment of the Biotechnology Science Coordinating Committee*, 50 Fed. Reg. 47,174 (1984) [hereinafter cited as *Coordinated Framework for Regulation*].

promote a greater understanding of emerging biotechnology issues among the regulatory agencies and to foster consistency in agency decisions. The BSCC will analyze broad scientific issues which extend beyond the concern of any one agency, and will develop generic scientific recommendations that can assist agency officials in evaluating new applications.⁹⁴ The committee will also address issues of public concern raised by agencies, and may hold meetings open to the public.⁹⁵ Because the BSCC will not conduct a second level review of agency applications, it will not delay agency decisionmaking.

The Biotechnology and Science Coordinating Committee will help to coordinate the actions of the various regulatory agencies and will help promote the interdisciplinary expertise necessary to adequately address recombinant DNA research concerns. However, the limited powers of BSCC reduce its ability to administer the kind of centralized regulatory scheme needed to deal with the potential risks of recombinant DNA technology. The BSCC has been criticized as having "no authority" to "resolve disputes or come up with common policies" relating to biotechnology.⁹⁶ Robert Rabin, Assistant Director of the White House Office of Science and Technology Policy, acknowledged that the committee "has no authority to insist or impose mandates" on any agency, but he indicated that the group has shown "every indication" of wanting to "work together."⁹⁷ He noted that one of the "first and probably most important" tasks of the BSCC will be to examine the review procedures of each of the agencies. The group will also work to clarify "jurisdictional" authority among the agencies.⁹⁸

However, because federal regulatory authority over genetic engineering still resides in separate agencies, the possibility remains prevalent that these agencies will create inconsistent regulations. For example, because of the overlapping jurisdictional authority created by different statutes, the FDA and NIH could create inconsistent standards in the areas of clinical human trials and drug testing.⁹⁹ Indeed, while in

94. *Id.*

95. The committee has the following specific purposes: (1) to serve as a coordinating forum for addressing scientific problems and sharing information among regulatory agencies; (2) to promote consistency in the development of the review procedures and assessments of federal agencies; (3) to facilitate continuing cooperation among federal agencies in emerging scientific issues; and (4) to identify gaps in scientific knowledge concerning biotechnology. *Id.*

96. BLUE SHEET, Nov. 20, 1985, at 2 (quoting Senator A. Gore (D.-Tenn.)).

97. *Id.*

98. *Id.* at 3.

99. RAC will continue to oversee gene therapy research, while the FDA will currently review research proposals for drugs to be tested in human subjects. In such cases, both the FDA and NIH will exercise jurisdiction, thus continuing the possibility that conflicting regulations will be established. BLUE SHEET, Oct. 16, 1985, at 7.

the past the FDA has often stayed at "arm's length" from NIH funded experiments involving clinical research on only a few patients, it now appears that the FDA will assert its own authority over human gene therapy. A top FDA official has publicly criticized the composition of NIH working groups for being overstaffed with nonscientists, while deficient in scientists and clinicians. He suggested that physicians who are planning to begin human gene therapy should file an investigational new drug application with the FDA instead of going through NIH channels.¹⁰⁰

In making regulatory decisions concerning biotechnology, each agency acts on the basis of its own perception of the best balance of the risks and benefits involved. Because each agency was created to serve different interests, this separate balancing of values tends to produce uncoordinated results. This incoherent matrix of regulation, coupled with the absence of any ultimate authority to resolve inter-agency disputes, creates confusing and contradictory regulatory requirements, especially in areas where the jurisdictions of different agencies overlap. These problems will ultimately have to be resolved in the courts, at great cost to the public. There is a growing need to coordinate agency efforts in order to promote safe and consistent regulation and to prevent jurisdictional squabbles.

B. Litigation Under the Current Regulatory Structure

An examination of recent court cases illustrates the kind of problems that arise under the current disorganized regulatory structure. In both *Mack v. Califano*¹⁰¹ and *Foundation on Economic Trends v. Heckler*,¹⁰² plaintiffs alleged that NIH failed to comply with overlapping federal laws in the administration of its Guidelines. In both actions, NIH was alleged to have violated the National Environmental Policy Act of 1969 by inadequately assessing the environmental effects of genetic engineering experiments.

In *Mack*, the plaintiff sought a preliminary injunction to prevent the testing of certain biological properties of DNA recombinants which had been cloned in bacterial cells at the Frederick Cancer Research Center in Fort Detrick, Maryland.¹⁰³ The plaintiff, a private citizen residing in the

100. Culliton, *New Biotech Review Board Planned*, 229 SCIENCE 736, 737 (1985).

101. 447 F. Supp. 668 (D.D.C. 1978).

102. 587 F. Supp. 753 (D.D.C. 1984), *aff'd in part and vacated in part*, 756 F.2d 143 (D.C. Cir. 1985).

103. The experiment in *Mack* was an investigation of the biological properties of polyoma DNA, which was being cloned in bacterial cells. 447 F. Supp. at 668. The research was restricted to implanting new genes into enfeebled strains of *E. coli*, a human intestinal bacterium. The scientists in *Mack* claimed that this bacterium had been previously modified to make it as completely safe as the new DNA's laboratory host.

vicinity of the laboratories, contended that the environmental impact statement ("EIS") submitted to NIH before the experiments were conducted did not comply with the requirements of NEPA.¹⁰⁴

The district court in *Mack* denied the injunction, finding that NIH had carefully considered the potential risks of the experiments under the Guidelines and had taken the necessary precautions.¹⁰⁵ The court found that none of the plaintiff's affidavits established that the experiment was likely to cause harm to human health or the environment.¹⁰⁶ In fact, the court found that the defendants had succeeded in demonstrating that the risk of harm was minimal. The defendants stressed that the research was restricted, in accordance with NIH Guidelines, to implanting genes into enfeebled *E. coli* bacteria. Because such bacteria are unable to colonize within human or other mammalian intestinal tracts, there was little risk of causing or spreading disease. The defendants also emphasized that the researchers would conduct the experiments under physical containment conditions in special laboratories which could safely contain microbes presenting a known hazard to man or the environment.¹⁰⁷

Although the plaintiff's motion for injunction in *Mack* was denied, another group of plaintiffs recently prevailed in part in an analogous suit in the D.C. Circuit Court of Appeals. In *Foundation on Economic Trends v. Heckler*,¹⁰⁸ the plaintiffs sought two injunctions: first, they sought to enjoin scientists at the University of California from releasing genetically

Id. at 669. The research itself involved dividing and then rejoining the heredity-carrying material of the various organisms, in order to create recombinant hybrids which carried some of the traits of the two previously unrelated forms. It was contended by the defendants that this work was necessary for the production of new medicines, vaccines, industrial chemicals, and crops. *Id.* at 670.

104. Under NEPA, for every major government action affecting the environment, the appropriate government agency must conduct a study culminating in a report called an environmental impact statement. This report should demonstrate that the agency has considered the possible adverse consequences of the proposed action to the environment and that no harm will result. 42 U.S.C. § 4332(2) (1982).

105. The experiments involved risk-assessment of polyoma virus and *E. coli* K-12 host vector systems. The research was conducted by Drs. Malcolm Martin and Wallace Rowe. Because these experiments were funded by the intramural research program of NIH's National Institute of Allergy and Infectious Diseases, compliance with the NIH Guidelines was mandatory. Letter from Elizabeth Milewski to Adrienne B. Naumann (written on behalf of William J. Garland, Jr., Ph.D., Director, Office of Recombinant DNA Activities, National Institute of Allergy and Infectious Diseases) (Jan. 6, 1986).

106. 447 F. Supp. at 670.

107. The laboratory at Fort Detrick was a P4 facility, and the experiment was to be conducted under P4 physical containment requirements. 447 F. Supp. at 671. P4 is the most restrictive level of physical containment. See 1976 Guidelines *supra* note 18, at 27,912-14.

108. 587 F. Supp. 753 (D.D.C. 1984), *aff'd in part and vacated in part*, 756 F.2d 143 (D.C. Cir. 1985).

modified ice-nucleating bacteria into the Northern California environment; and, second, they sought to enjoin NIH from authorizing any similar experiments in the future.¹⁰⁹

Scientists at the University of California at Berkeley ("UC") had been conducting experiments with ice-nucleating bacteria. They discovered that bacteria living on certain plants promote ice crystal formation by acting as nuclei. If the bacteria are removed, the plants can withstand temperatures ten to twelve degrees cooler than normal without forming ice crystals, thereby helping to reduce frost damage. Instead of isolating the bacteria found in the natural environment, the scientists, using recombinant DNA techniques, developed a modified bacterium with all the characteristics of the natural bacteria except that it did not act as a nucleus and thus did not assist ice formation.¹¹⁰ The scientists proposed an experiment involving the deliberate release of this modified bacteria into the open environment. They planned to plant potatoes sprayed with the bacteria *Pseudomonas syringae* pv. *syringae* and

109. *Id.* at 756. During the two year pendency of *Foundation on Economic Trends v. Heckler*, NIH approved several outdoor tests of genetically altered organisms. "Two weeks after [Judge John] Sirica halted Dr. Steven Lindow's planned field trial of recombinant ice-nucleating bacteria, the Recombinant DNA advisory committee of NIH approved a virtually identical proposal from Advanced Genetic Science, Inc. at its meeting on June 1." Budansky, *Bacterial Field Trial to Go Ahead*, 309 NATURE 483 (1984). "Sirica's decision specifically exempted commercial [non-NIH grantee] proposals." *Id.* RAC also conditionally endorsed a plan by the Cetus Madison Corporation of Madison, Wisconsin, to conduct a field test of genetically engineered plants which had shown resistance to disease in greenhouse and growth chambers. See *Recombinant DNA Research; Actions under the Guidelines*, 50 Fed. Reg. 46,834 (1985). In addition, an advisory committee to NIH tentatively endorsed the first outdoor field test of a genetically engineered organism by an industrial concern. Boffrey, *Plan Gains for First Test of Genetically Altered Plant Life*, N.Y. Times, Sept. 23, 1983, at C7, col. 3. See also Schmeck, *Growth of Bacterial Toxin Endorsed*, N.Y. Times, Feb. 7, 1984, at C1, col. 3; *Recombinant DNA Research; Availability of Environmental Assessment for Public Comment; Request for Comments on Need for a Programmatic Environmental Impact Statement*, 50 Fed. Reg. 14,794, 14,795 (1985) [hereinafter cited as *Request for Comments on Environmental Impact Statement*]; *Comment, supra* note 39, at 901-02. The EPA recently suspended the experimental use permit for a genetically engineered microbial pesticide pending an investigation of the user's testing procedures. See Schneider, *Field Testing Permit for Genetic Concern Lifted for False Data*, N.Y. Times, Mar. 25, 1986 at 1, col. 1.

110. Thompson, *Zeroing in on Icy Bacterium*, Chicago Tribune, Apr. 8, 1984, § 6, at 1, col. 2. Through random chemical mutation, the scientists had successfully developed and released bacteria into the environment which did not cause ice formation. Because this bacteria was not created using recombinant DNA techniques, it could be tested in the field without review by NIH. However, recombinant-DNA-produced bacteria hold several advantages over random chemically induced mutations because the bacteria cannot spontaneously revert to its previous form and because the scientists know exactly what alterations have been made to the bacteria. When scientists at the University of California at Berkeley began using recombinant DNA techniques, they were required to seek NIH approval, which they eventually obtained. *Id.*

Erwinia herbicola, in which all or part of the genes involved in ice nucleation had been deleted, in a small field in an isolated part of Northern California.¹¹¹

The Recombinant DNA Advisory Committee initially reviewed the UC proposal in October, 1982.¹¹² Although RAC recommended approval of the proposed experiments, NIH withheld its approval because of concerns about possible environmental consequences and questions about the necessity of releasing the bacteria at six different sites. In March, 1983, RAC received UC's revised proposal which responded to previous concerns by limiting the release to one site. RAC unanimously recommended approval of the revised proposal and NIH accepted it on June, 1983, thereby granting permission to the UC scientists to conduct their deliberate release experiments.¹¹³

The Foundation on Economic Trends subsequently filed suit to enjoin the deliberate release experiments, advancing two theories in support of their claim for injunctive relief.¹¹⁴ First, plaintiffs emphasized that the original NIH Guidelines prohibited the release or propagation of recombinant DNA molecules outside of the laboratory, and that NIH had prepared an environmental impact statement in support of this policy at the time it drafted the Guidelines. Although the Guidelines were subsequently modified to permit the release of recombinant DNA into the natural environment, no new EIS was prepared to justify this change in policy. Instead, the revisions to the Guidelines were accompanied by a mere environmental assessment in which NIH concluded that there was no need to prepare an EIS since the direct release of many forms of recombinant DNA outside the laboratory have no significant effect on the environment. Plaintiffs challenged the substantive conclusions of the environmental assessment and argued both that it did not comply with the requirements of NEPA¹¹⁵ and that a full EIS was required.¹¹⁶

111. Milewski & Talbot, *Proposals Involving Field Testing of Recombinant DNA Containing Organisms*, 6 RECOMBINANT DNA TECH BULL. 141, 143 (1983).

112. Initially, RAC was established only to review NIH-funded biomedical research. However, its activities were expanded to include voluntary review of industrial research and field tests such as the Berkeley experiment. In March, 1984, the RAC added Dr. Frances Sharples, an ecologist from Oak Ridge National Laboratory, to its committee to broaden RAC's environmental expertise. Thompson, *DNA Crop Test Creates a Storm of Controversy*, Chicago Tribune, Apr. 8, 1984, § 6, at 1, col. 1.

113. Milewski & Talbot, *supra* note 111, at 145. The NIH Guidelines were modified to indicate NIH's permission for this type of experiment. 1983 Guidelines, *supra* note 22, at 24,567.

114. Plaintiffs also alleged a violation of the Administrative Procedure Act and asserted a federal common law claim of nuisance. Plaintiffs' Complaint at 19, *Foundation on Economic Trends v. Heckler*, 587 F. Supp. 753 (D.D.C. 1984), *aff'd in part and vacated in part*, 756 F.2d 143 (D.C. Cir. 1985) [hereinafter cited as Plaintiffs' Complaint].

115. *Id.* at 17-18.

116. *Id.* at 13-15.

Second, the plaintiffs alleged that RAC lacked the requisite interdisciplinary expertise to evaluate deliberate release experiments. Specifically, plaintiffs claimed that among the members of RAC, there were no ecologists, botanists, plant pathologists, population geneticists, or anyone else with expertise about non-commercial species of plants and animals.¹¹⁷ Plaintiffs argued that this lack of expertise violated the NEPA requirement that all federal agencies "utilize a systematic, interdisciplinary approach which will insure the integrated use of the natural . . . sciences . . . in decisionmaking which may have an impact on man's environment."¹¹⁸

In May, 1984, Judge Sirica granted the plaintiffs' request for a preliminary injunction, holding that they were likely to prevail at trial on the claim that NIH failed to prepare a programmatic EIS in making its decision to permit deliberate release experimentation,¹¹⁹ thus violating the requirements of NEPA. The judge indicated that NIH had failed to take a "hard look"¹²⁰ at the environmental consequences of what was certainly a "major" federal action.¹²¹ Judge Sirica concluded that there would be no significant injury if the UC experiment was delayed,¹²² and he stressed that maintaining the status quo, at least until a programmatic EIS on deliberate release experimentation was completed, would be in the best interests of the public.¹²³

The defendants appealed the injunction. NIH had several objections to the district court's finding that a programmatic EIS was required before NIH could authorize any deliberate release experiments. First, the defendants argued that the plaintiffs had failed to demonstrate that NIH had a "program" of deliberate release experimentation which would require the agency to file a programmatic EIS under NEPA.¹²⁴ Second, the defendants argued that "even if there were a 'program', [the plaintiffs] had failed to establish that NIH was arbitrary or capricious in

117. *Id.* at 16; see also Thompson, *supra* note 112.

118. Plaintiffs' Complaint, *supra* note 114, at 18 (citing 42 U.S.C. § 4332 (1982)). Plaintiffs also argued that the defendants' failure to develop protocols for risk assessment violated NEPA requirements. *Id.*

119. 587 F. Supp. at 768.

120. *Id.* at 769.

121. *Id.* at 761.

122. *Id.* at 768.

123. *Id.* Judge Sirica claimed to have no opinion on the scientific merits of the controversy. He thoroughly addressed all of the statutory requirements of NEPA and discussed the traditional prerequisites for injunctive relief, as well as the standard of judicial review for government agency actions. *Id.* at 756-57, 761-64. As he noted: "This Court's sole task is to review whether the federal defendants should have issued an environmental impact statement under the circumstances of this case." *Id.* at 755.

124. Reply Brief for the Federal Appellants at 2, *Foundation on Economic Trends v. Heckler*, 758 F.2d 143 (D.C. Cir. 1985).

not preparing a programmatic EIS" in making the Guideline revisions.¹²⁵ NIH pointed out that there had only been three proposals for deliberate release experiments submitted to them, and emphasized that these experiments had such different characteristics that no generalizations about potential environmental effects could be deduced from them. Thus, NIH contended that the district court's injunction was much too broad because it unreasonably required an appraisal of an ill-defined class of experiments and because it halted all recombinant DNA research, thereby destroying the very process for predicting the harms that NIH was required to assess in order to comply with the injunction.¹²⁶

The Circuit Court of Appeals for the District of Columbia held that the district court's action enjoining the UC experiments was proper.¹²⁷ The circuit court found that NIH did not adequately assess the impact on the environment when it approved the University of California's plan for deliberate release. It stressed that "NIH should give greater consideration to the broad environmental issues on deliberate release of organisms containing recombinant DNA, and its own responsibility for approving these deliberate release experiments."¹²⁸ In so ruling, the court noted that "NIH has not yet displayed the rigorous attention to environmental concerns demanded by the law"¹²⁹ and that "there was a violation of NEPA when the record revealed only scattered, conclusory statements of 'no impact.'"¹³⁰ The release of microbes outside of the UC laboratory was thus barred until "an appropriate environmental assessment is completed."¹³¹

However, the circuit court reversed the district court's institutional injunction, holding that NIH had the institutional capability to approve requests for the outdoor release of genetically altered organisms and also that a programmatic EIS was not required under NEPA.¹³² The court admonished, however, that "if NIH fails to give appropriate environmental consideration to any other experiment, as it has failed to do with the

125. *Id.*

126. *Id.* Significantly, the American Council on Education and the National Association of State Universities and Land Grant Colleges, in an amicus brief, argued that irreparable harm to university research might occur if private industry were not subjected to the same equitable sanctions as university recipients of NIH funds. Brief of Amici Curiae at 6, *Foundation on Economic Trends v. Heckler*, 756 F.2d 143 (D.C. Cir. 1985).

127. 756 F.2d at 146.

128. *Id.*

129. *Id.*

130. *Id.* at 154. An agency's failure to meet statutory requirements is a violation of a nondiscretionary duty. *Id.* at 151.

131. *Id.* at 146.

132. *Id.* at 160; see also *Court Upholds Delay of Microbe Testing*, N.Y. Times, Feb. 28, 1985, at A14, col. 5.

University of California experiment, injunctive relief would clearly be proper."¹³³

As a result of this litigation, NIH took steps to comply with the court's directive regarding NEPA compliance. For example, the agency made available to the public a comprehensive environmental assessment of the effects of the University of California deliberate release experiment.¹³⁴ The environmental assessment addressed many of the specific environmental concerns of the plaintiff, such as the effects of the direct release on local insect populations and commercial crops.¹³⁵ Based on

133. 756 F.2d at 146.

134. Request for Comments on Environmental Impact Statement, *supra* note 109, at 14,794.

135. National Institutes of Health, Environmental Assessment and Finding of No Significant Impact (Jan. 21, 1985) (environmental assessment and finding of no significant impact concerning Drs. Steven Lindow and Nickolas Panopoulos' application to field test ice-nucleation-minus bacteria prepared by recombinant DNA techniques for purposes of biological control of frost damage to plants; available on request at NIH office). This 60 page document contains the following topics:

1. a description of the proposed action and alternatives
2. environmental effects:
 - a. physical environment
 - b. proposed test organisms
 - (1) characteristics of the *P. syringae* and *E. herbicola* strains
 - (2) construction of INA deletion mutants
 - (3) previous tiled tests with Ic NA minus bacterial
3. effects of the proposed field test
 - a. risk assessment
 - b. test plot
 - c. crops and non-commercial plant species
 - d. local epiphytic bacterial populations
 - e. insect populations
 - f. animal populations
 - g. atmosphere and climate
 - h. scientific and agricultural benefits
 - i. worst case analysis
4. effects of alternatives
 - a. approval of original proposal without restriction
 - b. approval of modified proposal without restriction
 - c. approval of proposal as approved by NIH on June 1, 1983, with changes proposed by the investigators
 - d. withhold approval
5. consultation
6. references
7. appendices

The environmental assessment explicitly found that the INA bacteria prepared by recombinant DNA techniques will not express any foreign proteins. Furthermore, neither the original nor the altered bacteria are pathogenic to insects, animals, birds, or man. Finally, the original and altered bacteria to be used in the experiment were shown to be non-pathogenic to any of the major crops growing in the area. *Id.* at 2; see Request For Comments on Environmental Impact Statement, *supra* note 109, 50 Fed. Reg. 14,794 (1985).

this environmental assesment, NIH reaffirmed its approval of the UC experiment.

Recent action by the Reagan administration has resolved the conflict between NIH and the EPA with regard to deliberate release experiments by removing RAC's jurisdiction over such experiments. RAC will not review basic research proposals involving deliberate environmental release, but rather such applications will be evaluated by the National Science Foundation ("NSF"), and field testing of genetically altered microorganisms will require EPA approval.¹³⁶

The experience of NIH with regard to the UC experiments illustrates the kinds of problems that arise when regulatory power is dispersed among several uncoordinated bodies. In *Foundation on Economic Trends v. Heckler*, it is clear that NIH failed to demonstrate an adequate appreciation of the importance of fully evaluating the potential environmental effects of recombinant DNA experiments. This institutional shortcoming would have been minimized if decisionmaking had been subjected to appeal and review before an interdisciplinary body.

IV. CONGRESSIONAL INACTION

There is no comprehensive federal legislation regulating biotechnology. The Reagan administration, however, has recently expressed its belief that existing environmental and health laws provide adequate protection from the dangers of genetically engineered products.¹³⁷ Nevertheless, officials representing federal agencies have stressed the need for more thorough and timely review of technologies using genetic engineering techniques in order to assure their safety. Members of the White House Office of Science and Technology Policy recently concluded that the existing process for reviewing the safety of recombinant DNA technologies "is not adequate to accommodate the needs of all the Federal agencies now involved."¹³⁸ In November, 1985, the Office of Science and Technology Policy created the BSCC, a coordinating committee to oversee future DNA research. Unfortunately, this committee will serve only as an information clearinghouse and will be unable to perform a centralized management function since it lacks the authority to enforce agency compliance with its recommendations.

The first attempt to establish federal legislation to regulate recombinant DNA research involved a proposal to make the nation's entire

136. BLUE SHEET, Oct. 16, 1985, at 7 (reporting on upcoming federal notices).

137. See Hanson, *Biotech Regulatory Policy Issues Aired*, CHEMICAL & ENGINEERING NEWS, Mar. 3, 1986, at 29.

138. Shabecoff, *U.S. Studies Rules on Gene Products*, N.Y. Times, Dec. 12, 1984, at A26, col. 1.

research community comply with the NIH Guidelines. In February, 1976, FDA General Counsel Peter Hult suggested converting the Guidelines into regulations applicable to all researchers in the United States, whether or not they were funded by the government.¹³⁹ To evaluate the feasibility of this proposal, President Ford created the Federal Interagency Committee on Recombinant DNA Research to consult with public and private organizations about the merits of Hult's recommendations.¹⁴⁰ A subcommittee of the Interagency Committee was also created to determine whether then existing laws and regulations could be used to adequately regulate recombinant DNA technology. After reviewing the Occupational Safety and Health Act of 1970, the Toxic Substance Control Act, the Hazardous Materials Transportation Act, and section 361 of the Public Health Service Act, the subcommittee concluded that no single legal authority or combination of authorities existed which could oversee all possible uses of recombinant DNA technology.¹⁴¹

The Interagency Committee submitted its recommendations to Department of Health, Education, and Welfare ("HEW") Secretary Joseph Califano, who drafted legislation which President Carter submitted to Congress in March, 1976.¹⁴² The bill established primary responsibility for the regulation of recombinant DNA research with NIH. The regulatory power of NIH would have been expanded so that all recombinant DNA activities were under the control of a centralized regulatory authority. The administration's proposal did not alter existing laws governing DNA research, proprietary information or patent rights because these laws were deemed satisfactory.¹⁴³ It is interesting to note that both the House and Senate versions of the bill contained provisions that required disclosure by biotechnology researchers of any data necessary to protect health or the environment.¹⁴⁴ This requirement reflected the concern of many legislators about the risks associated with recombinant DNA research.¹⁴⁵

However, no legislation regulating genetic engineering was enacted. Congress' failure to pass comprehensive legislation regulating recombinant DNA technology was caused by the emergence of new scientific research which demonstrated the safety of most recombinant DNA

139. Perpich, *Industrial Involvement in the Development of NIH Recombinant DNA Research Guidelines and Related Federal Policies*, 5 RECOMBINANT DNA TECH. BULL. 59, 61 (1982).

140. *Id.* at 62.

141. *Id.* at 63.

142. *Id.* at 64.

143. *Id.*

144. *Id.* at 65.

145. *Id.*

experiments. The fact that a major revision of the Guidelines was under way during the time the legislation was being considered also influenced legislators not to pursue the matter.¹⁴⁶ Since that time, Congressional interest in coordinating the regulation of biotechnology has waned considerably. For example, while sixteen bills were introduced and twenty-six hearings were held dealing with the regulation of recombinant DNA technology in the first session of the 95th Congress (1977), no bills were introduced and no hearings were held on the subject in the 97th Congress.¹⁴⁷

Congress has been shortsighted in failing over the last ten years to enact a comprehensive statute regulating recombinant DNA technology. Despite the information supporting the safety of recombinant DNA research, Congress should have erred on the side of caution and passed comprehensive legislation. It is true that federal agencies have taken significant steps in coordinating their efforts so that genetic engineering projects do not fall into regulatory gaps. However, given the risks of recombinant DNA research, stop-gap measures developed by uncoordinated agency action are inadequate. The present regulatory structure is so complex and inconsistent that the potential for error is extremely high, raising the prospect that many unsafe activities may go unregulated. The present "interagency" regulatory approach also engenders discord between existing agencies because the numerous existing statutes authorizing agency regulation confer conflicting jurisdiction.¹⁴⁸ No clear hierarchy of authority exists in the event of a jurisdictional dispute.

V. TIME FOR CHANGE: PROPOSED ALTERNATIVES TO THE PRESENT REGULATORY STRUCTURE

As recombinant DNA technology matures, more and more biological materials are created that have the potential for commercial exploitation.¹⁴⁹ As experiments move out of laboratory containment into field testing, and eventually to commercial distribution, the need for coherent regulation increases. The optimal solution would be for Congress to pass comprehensive legislation to coordinate the actions of the various agencies by creating a modified "super-agency" in charge of regulating genetic engineering. The new agency should possess both the necessary

146. *Id.*

147. *Id.*

148. Proposal for a Coordinated Framework for Regulation of Biotechnology, 49 Fed. Reg. 50,856 (1984).

149. See, e.g., *Biotechnology Research Hearing Airs Flaws in Bacteria Test*, CHEMICAL & ENGINEERING NEWS, Mar. 10, 1986, at 4 (discussing an experiment with the bacterium "Frostban").

pooling of interagency expertise and an enforcement mechanism sufficient to command compliance to its regulatory actions.

Regulatory power over recombinant DNA experimentation must be vested in a body competent to evaluate the risks and benefits of this new technology. Competence includes not only the technical expertise to evaluate the risks, but also the appreciation of social values necessary to make responsible choices. Even if the probability of the occurrence of any adverse effect is low, the social cost associated with a recombinant DNA disaster is tragically high. This high cost indicates that after-the-fact remedial legislation will be inadequate. Rather, the high risk of a biological disaster mandates the exercise of a high degree of foresight. Congress should act now.

A. Biotechnology Science Coordinating Committee

In November, 1985, the Biotechnology Science Coordinating Committee was established.¹⁵⁰ BSCC is a loose federation of government agencies involved in the funding and regulation of recombinant DNA technology and research. It is composed of senior representatives from NIH, USDA, EPA, FDA, and NSF, and is co-chaired by the director of NIH and the director of the NSF. The purpose of the committee is to coordinate the actions of the various federal agencies regulating recombinant DNA. It will provide a forum for the sharing of information related to scientific questions, and may recommend authorization for research and grant applications which are submitted to federal research and regulatory agencies for approval.¹⁵¹ BSCC will also address issues of public concern which are brought before the committee by the member agencies. The Federal Coordinating Council for Science, Engineering, and Technology ("FCCSET"), under the auspices of the White House Office of Science and Technology Policy, was deemed an appropriate organizational location in which to house this new coordinating committee.¹⁵²

The most crucial aspect of BSCC, however, is that it will *not* have the power to conduct a second level of review of research applications submitted to regulatory agencies, and thus it will have no power to second guess or trump regulatory decisions. This follows from the fact that the committee was placed within FCCSET.¹⁵³ FCCSET is

150. Culliton, *Another Biotech Board Proposal*, 230 SCIENCE 46, 46 (1985).

151. *Id.*

152. See Office of Science and Technology Policy, *Coordinated Framework for Regulation of Biotechnology; Establishment of the Biotechnology Coordinating Committee*, 50 Fed. Reg. 47,176 (1985).

153. *Id.*

empowered to create informational committees and does not have the power to create boards or commissions with powers of enforcement.¹⁵⁴

The limited power of BSCC should find favor among regulatory agencies who would like to avoid losing any of their current authority to a super-agency committee. It should also be supported by interested parties who fear that the current status and authority of RAC would be undermined by a super-agency committee.¹⁵⁵ However, BSCC's lack of enforcement power fails to resolve the problem of ultimate authority when a dispute between agencies arises. A coordinating committee without enforcement or compliance power will only work until a heated "turf battle" develops, over which there is no effective referee except the judicial system. Constantly resorting to litigation in the federal courts to resolve such issues is costly to the taxpayer and to the agencies involved. More important, it drastically delays and retards recombinant DNA research and development.

A coordinating committee with no enforcement mechanism will not be sufficient to solve the problems associated with the current uncoordinated regulatory structure. Because BSCC does not possess the power to perform a second level of review of applications submitted to existing regulatory agencies, regulation of recombinant DNA technology will continue to consist of a jumble of differing agency rules and standards. What is needed is a centralization of regulatory authority over genetic engineering technology.

B. Creation of a "Super-Agency"

A proposed alternative to coordinate the efforts of the federal agencies presently regulating recombinant DNA technology¹⁵⁶ is to place NIH, USDA, EPA, FDA and NSF under the supervision of an independent Biotechnology Review Board created within the Department of Health and Human Services ("HHS"), and headed by an Assistant Secretary of HHS.¹⁵⁷

This new agency would have the legal authority to resolve inter-agency disputes and to set a coherent government policy. In the present system, inter-agency conflict exists between the EPA, the FDA and NIH. NIH attempted to deal with this problem unilaterally by installing a provision in the Guidelines which allows other agencies to have final say in the review of certain research applications where it is determined that

154. 42 U.S.C. § 6651 (1982).

155. *Id.*

156. Culliton, *supra* note 100, at 737.

157. *Id.* at 736.

NIH review would be duplicative.¹⁵⁸ However, this provision still does not resolve the problem of who has the final say in a turf battle where the prestige and scope of a particular regulatory issue is extremely high, and neither agency wishes to compromise. Such an example occurs in the areas of clinical human trials and new drug testing, where the FDA and NIH have concurrent jurisdiction.¹⁵⁹ As a result, there exists a growing and crucial challenge to coordinate agency efforts to prevent or resolve jurisdictional disputes. To resolve these inter-agency disputes, the proposed Board would have the power to enforce agency compliance with its rules and regulations. A Board with such superseding authority would need Congress to pass an enabling statute delegating rule-making and adjudicating authority to the new body.¹⁶⁰

One consequence of creating this super-agency would be to subordinate the role of RAC to a new panel of experts. RAC would become a scientific advisory body for the NIH alone, losing its present *de facto* status as the final arbitrator of many recombinant DNA issues. The major difference between the proposed super-agency Board and the present structure of RAC is that the new Board would possess legal authority to govern the actions of all of the federal agencies involved in regulating recombinant DNA technology, thus enabling it to establish a clear and coherent government policy. As previously emphasized, NIH and RAC have no legal authority to regulate genetic engineering where it is undertaken without NIH funding or where no specific contract license agreements exist with NIH grantees. The current members of RAC and its staff would be prime candidates for the new super-agency Board because of their expertise in the biotechnology field.¹⁶¹

158. A new sentence at the end of Section III-A of the NIH Guidelines now reads as follows:

If experiments in this category are submitted for review to another Federal agency, the submitter shall notify ORDA [Office of recombinant DNA Activities]; ORDA may then determine that such review serves the same purpose, and based on that determination, notify the submitter that no RAC review will take place, no NIH approval is necessary, and the experiment may proceed upon approval from the other Federal agency.

Notice of Actions under NIH Guidelines for Research Involving recombinant DNA Molecules, 50 Fed. Reg. 48,344, 48,349 (1985).

159. Under the newly established BSCC, RAC will continue its oversight of gene therapy research with the FDA concurrently reviewing research proposals where "something is going to be put back in a human subject," such as a pill or injection. The FDA will require an investigational new drug application in such cases. BLUE SHEET, Oct. 16, 1985, at 7.

160. An agency only has that authority which has been delegated to it by its enabling statute. See K. DAVIS, ADMINISTRATIVE LAW TEXT 27-45 (3d ed. 1972).

161. RAC already draws on top experts in biology, medicine, and law to "resolve" complex scientific and legal issues.

Critics of this super-agency proposal have argued that placing the agency in the Department of Health and Human Services might bias regulatory decisions in favor of regulatory bodies, such as NIH, which are under the auspices of HHS.¹⁶² They also argue that the super-agency's review process would unreasonably burden applicants by creating a second tier of bureaucratic review, thus taking even more time to process research or grant applications and stalling needed research.¹⁶³ It is further contended that the proposed Board would lack the necessary prestige to operate effectively because it would lack the requisite expertise to make complex scientific decisions superseding the authority of other regulatory bodies.

C. Creation of a Commission

A more appropriate alternative for solving the dual problems of uncoordinated regulation and overlapping jurisdictional authority is to create a commission in the form of a "super-agency." Such a commission would possess three key features of a super-agency. First, it would have authority to review and trump agency decisions. Such review would be available upon the appeal of a regulatory agency or an interested party. Second, the commission would settle jurisdictional disputes between agencies. In the event of conflicting agency decisions, any interested party, as well as either agency, could appeal to the commission. The commission would then make a final determination as to which agency or party should prevail. For example, suppose both NIH and the FDA claimed jurisdiction over a particular biomedical application in human gene experiments. The commission could do the following: (1) adjudicate jurisdictional disputes between agencies; (2) adjudicate appeals by private parties, such as a private drug manufacturer, of any application denied by either agency; (3) prospectively adjudicate any jurisdictional issues for this specific type of gene experiment; and (4) promulgate binding rules to resolve such jurisdictional issues in advance.

Finally, in addition to reviewing agency decisions and settling jurisdictional disputes, the commission would possess the authority to engage in independent rulemaking in important biotechnology areas not regulated by other agencies. The commission would need independent statutory authority from Congress both to enforce its own regulations and to adjudicate individual disputes.¹⁶⁴ Congress would have to pass a statute creating the commission and authorizing it to promulgate regula-

162. See Coordinated Framework for Regulation, *supra* note 93, at 47,176.

163. *Id.* at 47,175 (1985); see also Rhein, *Splicing Together a Regulatory Body for Biotechnology*, *Bus. Wk.*, Jan. 14, 1985, at 69.

164. See, e.g., 42 U.S.C. § 5841 (1982). See generally K. DAVIS, *supra* note 160, at 129.

tions binding other government agencies. Under the Administrative Procedure Act, such regulations would have the force and effect of laws passed directly by Congress, although they could not exceed the scope of the authorizing statute.¹⁶⁵

Such a commission would avoid the bias which would occur if a coordinating body was located within an existing regulatory agency, such as the EPA. The proposed commission could be located within the Office of Science and Technology, just as the existing Biotechnology and Science Coordinating Committee, and could operate under the direction of FCCSET.¹⁶⁶

Further, although the commission would have the power to conduct a second tier of review of agency applications, the additional review procedure would not be unduly burdensome to private parties. Unless there is an appeal or dispute brought before the commission, existing agencies would continue to handle routine applications for research or funding approval within their own jurisdictions. When a dispute arises, a coordinated system would exist to quickly and efficiently resolve the controversy by making binding decisions on the agencies and individual parties involved. If the subordinate agencies or other aggrieved parties are dissatisfied with this centralized review process, then such parties could seek review of agency action in the federal courts.¹⁶⁷ However, the courts may not choose to apply a high standard of review to commission decisions given the "super-agency's" independence and expertise.

Staffing problems are also manageable. To ensure adequately informed decision-making, the new commission would require a support staff with members of appropriate scientific and technological expertise. However, such a support staff need not be prohibitively large, despite the multiplicity of possible recombinant DNA uses and applications. The commission could rely on panels of experts to handle each problem as it arises.¹⁶⁸ The experts should be independent, impartial, and not affiliated with any agency involved in the dispute.¹⁶⁹ These panels would be able to review the findings, conclusions, and data collected by the regulatory agencies involved in the dispute. However, these

165. 5 U.S.C. § 706(2)(c) (1982).

166. Coordinated Framework for Regulation, *supra* note 93, at 47,176.

167. See generally K. DAVIS, *supra* note 160, at 508-24 (discussing unreviewable administrative actions).

168. Regulatory agencies currently utilize outside experts. For example, the EPA plans to use an "extensive peer process," using a subpanel of external experts drawn from the EPA's advisory apparatus, to evaluate approval of biotechnology proposals. BLUE SHEET, Dec. 11, 1985, at 2.

169. K. DAVIS, *supra* note 160, at 232-39.

materials need not control the panels' recommendations to the commissioners. In addition, experts from existing regulatory agencies could testify before the panels and contribute their knowledge to the commission.

The problem of lack of prestige in the early phases of the agency can also be overcome. The recruitment of experienced RAC members to the new commission, at least in its early stages, would transplant the prestige and "track record" of the RAC to the new agency. Although such a step could be construed as raiding the RAC of its most knowledgeable members,¹⁷⁰ it would, at least partially, erase any "power" gap between the two bodies.

The creation of a "super-agency" commission would be the most effective solution to alleviate the pressing problems confronting the present pluralistic regulatory system. The superseding pre-emptive regulatory authority of the commission would effectively resolve problems of conflicting jurisdiction. The centralized management role of the commission would permit it to coordinate the regulation of recombinant DNA technology. Retaining a body of diverse experts, who would rely upon their own technical staffs as well as select liaisons from various agencies, would give the commission the necessary expertise to effectively and swiftly resolve complex biotechnology disputes.

CONCLUSION

Because BSCC lacks the authority to force agency compliance with its decisions, it is an inadequate solution to present regulatory problems. The future of recombinant DNA research will not mesh with the apparently neat categories of current government regulation. Instead, it will be driven by pressing human needs and unforeseen scientific breakthroughs. The rapid and unpredictable progress of recombinant DNA technology will soon stress the present structure of federal regulation to its breaking point. The most serious unresolved turf battle may lie in the area of human genetics, which presently falls within the expertise of several regulatory agencies.

There is no doubt that recombinant DNA technology has vast human potential. Consider recent advances in clinical medicine where recombinant DNA technology has led to the development of novel approaches for diagnosis and treatment of human disease, especially in the area of genetic disorders. For example, with the advent of recombinant DNA technology, alterations in gene expression¹⁷¹ in early stages of

170. See Coordinated Framework for Regulation, *supra* note 93, at 47,175.

171. Davies, *The Application of DNA Recombinant Technology to the Analysis of the Human Genome and Genetic Diseases*, 58 HUMAN GENETICS 351, 355-56 (1983); See also B. DAVIS, MICROBIOLOGY 170, 223, 292 (2d ed. 1973) (discussing and defining the biology of gene expression).

cancer can now be analyzed by comparison with normal chromosomal configurations¹⁷² to determine whether the disease caused an alteration in the genetic material, or vice versa. The recombinant DNA technique has also been applied to the diagnosis and understanding of neuro-genetic disorders, especially ones which are inherited, such as Huntington's disease.¹⁷³ In fact, the techniques are so precise that even the few fetal cells available in a small sample of amniotic fluid contain sufficient DNA to define the genotype of the fetus with respect to the gene of risk.¹⁷⁴

Gene transplantation from one mammalian species to another also has tremendous positive potential, particularly in the treatment of severe hereditary defects of the immune defenses. In addition, RAC has recently endorsed a United States Army research proposal in which genetic material is used to produce an important bacterial toxin. The research is aimed at developing cheap and effective vaccines against major worldwide causes of dysentery, including cholera.¹⁷⁵

Recombinant DNA techniques also have a bright future in the field of commercial drug manufacturing.¹⁷⁶ At least one commentator predicted that recombinant DNA technology would enable production of

172. Investigators have suggested that viral genes, known as oncogenes, were integrated into the hereditary material of some organisms millions of years ago, and later evolved, presumably in embryogenesis, to provide for the normal functioning of these organisms. Stimulation of this oncogene later in the organism's life might be responsible for seemingly spontaneous cancers. B. DAVIS, *MICROBIOLOGY* 1436 (2d ed. 1973).

173. Altman, *Researchers Report Genetic Test Detects Huntington Disease*, N.Y. Times, Nov. 9, 1983, at B8, col. 1.

174. L. HOUSMAN & S. GUSELLA, *APPLICATION OF RECOMBINANT DNA TECHNIQUES TO NEUROGENETIC DISORDERS* 167-72 (Association for Research in Nervous and Mental Disease Research Publications No. 60) (1983). The recombinant DNA technique makes an unequivocal diagnosis much easier, especially with respect to globin gene disorders such as sickle cell disease and thalassemia. This technique differs radically from the previous approach where there was always doubt whether a particular patient was outside the "normal" range. Harley, *Genetic Engineering and the Clinician*, 42 *ANNALS OF RHEUMATIC DISEASES* 234, 235 (1983); see also Altman, *supra* note 173, at A1, col. 1.

175. Schmeck, *Gene-Splicing Panel Endorses Plan to Create Toxin-Producing Bacteria*, N.Y. Times, Feb. 7, 1984, at C1, col. 3; see also Sagandanes-Bennol & Matthews, *The Selection of Antigens for the Diagnosis, Prognosis, and the Evaluative Study of Parasite Diseases*, 14 *VETERINARY PARASITOLOGY* 173, 185-91 (1984). The hypothesis is set forth that schizodeme (DNA) typing of *Trypanosona* and possibly other parasites may be used to treat clinical disease. In particular, *T. Cruzi* clones may turn out to be useful in disease diagnosis, production of species (generic) vaccines and the study of auto immunity.

176. Miller, *Designer Genes for Producing Drugs: Will They Wash?*, 1 *DNA* 102 (1982). For example, the Cetus Corporation was granted a patent on a new genetically engineered drug that scientists say may eventually offer treatment for various cancers. The drug, named Interleukin-2, is one of a group of natural proteins called lymphokines, that regulate the body's disease fighting immune system. *Cancer Drug Made by Gene Splicing is Patented*, N.Y. Times, May 22, 1985, at B4, col. 1.

human insulin, human growth hormones, human calcitonin, vaccines for hepatitis B, interferons, and other protein hormones. The FDA has recently approved the production of human insulin and growth hormones by recombinant DNA techniques.¹⁷⁷

Because of the tremendous human potential which recombinant DNA technology holds, the government should continue to strongly encourage its research and development. In the meantime, reassessment of the current structure of federal regulation of genetic engineering is essential. The dual problems of uncoordination and overlapping jurisdiction continue to plague the present system, creating a tremendous risk that the safety of biotechnological research will be sacrificed or disregarded.

Unfortunately, the perennial unlearned lesson from science is that adequate safeguards are never provided until an injury has already occurred. The creation of a commission empowered with independent statutory authority to engage in independent rulemaking and to be the final arbiter of jurisdictional disputes between agencies would be the most effective way for Congress to fulfill its obligations. Congress has the legal and moral responsibility to act with foresight to ensure that effective regulation promotes the safe development of recombinant DNA technology. It is time for a change.

177. Statement of Policy for Regulating Biotechnology Products, 49 Fed. Reg. 50,878, 50,880 (1984); see also Hamilton, *Genentech Gets a Shot at the Big Time*, BUS. WK., Oct. 28, 1985, at 108.