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REGULATING THE ENVIRONMENTAL RELEASE OF GENETICALLY ENGINEERED ORGANISMS: *FOUNDATION ON ECONOMIC TRENDS V. HECKLER**

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I. INTRODUCTION

Recombinant DNA technology, commonly referred to as genetic engineering,[1] has revolutionized scientific thinking.[2] Scientists now have the ability to remove a fragment of the genetic material from one organism and "splice" it into an unrelated organism. By "recombining" the genetic material of two different species, scientists can create new life forms in the laboratory which would never occur in nature. This technology has been successfully employed in industry to genetically reprogram micro-organisms to "ferment" scarce complex organic molecules such as human insulin or interferons.[3] Scientists are also developing ways to correct genetic defects in humans by "splicing in" functional genes to take the place of defective genes.[4] "Genetic surgery" differs from conventional treatment of genetic defects in that the genetic cure is inheritable.

This revolutionary technology challenges traditional social, political, and religious concepts. Basic constitutional principles, such as individual autonomy, equal rights, separation of church and state, even the meaning of being human and of family lineage, are being challenged. Religious groups have reacted strongly, questioning the propriety of developing techniques which may lead to an attempt to "enhance" and "perfect" human beings. Scientists are accused of "playing God," opening a Pandora's box of mischief and harm.[5]

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* The author gratefully acknowledges the contributions of Dr. Stanley Barban, Administrative Scientist, National Institutes of Health, and Mr. Edward Lee Rogers, Attorney, Washington, D.C.

1. Genetic engineering refers to the manipulation of hereditary characteristics through direct interaction with the genetic material, deoxyribonucleic acid (DNA), rather than through natural selection or breeding.

2. Abelson, *A Revolution in Biology*, 209 SCIENCE 1319 (1980).

3. Heitzman, Leung, Perry, Kohr, Levine & Goeddel, *Secretion of Human Interferons by Yeast*, 219 SCIENCE 620 (1983); Johnson, *Human Insulin from Recombinant DNA Technology*, 219 SCIENCE 632, 633 (1980); Pestka, *The Purification and Manufacture of Human Interferons*, SCI. AM., Sept. 1981, at 37.

4. Kolata, *Gene Therapy Method Shows Promise*, 223 SCIENCE 1376 (1984).

5. PRESIDENT'S COMMISSION FOR THE STUDY OF ETHICAL PROBLEMS IN MEDICINE AND BEHAVIORAL RESEARCH, SPLICING LIFE: THE SOCIAL AND ETHICAL ISSUES OF GENETIC ENGINEERING WITH HUMAN BEINGS (Nov. 1982) (cover letter from Chairman) [hereinafter cited as SPLICING LIFE].

Until now, all work involving recombinant DNA has been performed in laboratory or industrial containment facilities.[6] Scientists, attracted by the commercial potential of finding cheaper and more efficient ways to manage environmental resources, are beginning to use recombinant DNA techniques to develop organisms for deliberate release into the environment. Naturally occurring organisms have evolved specific characteristics to serve their own purposes: survival and reproduction. Scientists have begun applying recombinant DNA techniques to "reprogram" these organisms to serve man. These new organisms can perform specific commercially useful tasks upon release into the environment.

On May 16, 1984, Judge John Sirica of the United States District Court for the District of Columbia stunned the administration of the National Institutes of Health and the scientific community at large. He ordered an injunction halting what was to have been the first-ever intentional environmental release of organisms genetically engineered through recombinant DNA techniques.[7] The halted experiment would have released genetically engineered bacteria onto a field of potato plants in California in an attempt to biologically control frost damage in frost sensitive plants. The agricultural industry suffers from $1-3 billion in frost damage to frost sensitive crops annually.[8]

The success of this experiment could have been a boon to Florida citrus growers who suffered from severe freezes in 1977, 1981, 1982, 1983, and 1985.[9] The Christmas freeze of 1983 alone caused $1.1 billion in frost damage.[10] Florida Commissioner of Agriculture Doyle Conner wrote after hearing of the Sirica injunction: "While we all recognize the need to be aware of environmental hazards, this frost-protection program could be quite important to farmers everywhere and we would not want legal maneuvers to unnecessarily hamper biotechnological development."[11] Conner thought the creation of the bacterium was one of the promising developments

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6. Interview with Dr. Stanley Barban, Administrative Scientist, of the Office of Recombinant DNA Activities, National Institutes of Health, in Washington, D.C. (Aug. 20, 1984). *See* David, *Suit filed against NIH*, 305 NATURE 262 (1983).

7. Norman, *Judge Halts Gene-Splicing Experiment*, 224 SCIENCE 962 (1984). *See infra text* accompanying note 122.

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

9. White, *Frozen Out: Cold Weather and Imports Killed the Citrus King*, FLA. TREND, Sept. 1984, at 79.

10. Washington Post, July 3, 1984, at E6, col. 4.

11. Conner, *Farm Front*, FLA. MARKET BULL., July 1, 1984, at 1, col. 1.

of genetic engineering and called those who opposed it "Luddites" who were challenging the "wave of the future."[12]

We are about to enter an era in which our ability to manage environmental resources will be greatly enhanced through the use of genetically engineered organisms. Such organisms will, for example, increase the energy efficiency and thoroughness of oil and mineral recovery.[13] A bacterium has been patented which can "eat" oil spills[14] and others are being developed to eat other pollutants such as dioxin.[15] A bacterium has been developed to fixate nitrogen, eliminating the need for nitrogen fertilization of agricultural plants. This bacterium could provide an inexpensive method for increasing the crop yield of underdeveloped countries.[16]

"New technologies, especially those as powerful as biotechnology, raise completely new questions. Some of the questions are so unique that they don't come under the rubric of existing laws."[17] There is a lack of consensus among Congress, the executive branch, scientists, local governments, environmentalists, and commercial biotechnology companies on how, if at all, environmental releases should be regulated.[18] This comment will examine the technology, evaluate the need for federal oversight, and assess the adequacy of current regulatory mechanisms.

II. RECOMBINANT DNA TECHNOLOGY

"Biotechnology is nothing new, except for lawyers." Dr. Davies, of the Swiss biotechnology firm BioGen, began a university lecture by expressing the perception of biotechnology companies of an information lag in the legal community.[19] Recombinant DNA tech-

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12. *Id.* "The Luddites were the workers who, in the early 19th Century, stood in the way of sweeping industrialization of the textile industry by the introduction of labor-saving machines." *Id.*

13. STAFF OF HOUSE COMM. ON SCIENCE AND TECHNOLOGY, SUBCOMM. ON INVESTIGATIONS AND OVERSIGHT, 98TH CONG., 2D SESS., REPORT ON ENVIRONMENTAL IMPLICATIONS OF GENETIC ENGINEERING 15 (Comm. Print 1984) [hereinafter cited as STAFF REPORT].

14. Diamond, Comm'r of Patents & Trademarks v. Chakrabarty, 447 U.S. 303 (1980).

15. STAFF REPORT, *supra* note 13, at 15.

16. *Id.* at 14; *see also* Valentine, *Genetic Engineering in Agriculture with Emphasis on Biological Nitrogen Fixation*, in RESEARCH WITH RECOMBINANT DNA 224-31 (1977).

17. Flaherty, *A Brave New World for Biotech Lawyers*, NAT'L L.J., Oct. 8, 1984, at 1, col. 3 (quoting Robert B. Nicholas, Chief Counsel and Staff Director of a subcommittee of the House of Representatives Committee on Science and Technology).

18. Perpich, *Federal Policies on Environmental Release of Recombinant DNA Containing Organisms*, GENETIC ENGINEERING NEWS, July-Aug. 1984, at 5, col. 5.

19. Lecture by Professor Davies, European Molecular Biology Organization, at University of Bielfeld (Sept. 10, 1983), *reprinted in* Kircher, *Biotechnologie*, 18 DIE UMSCHAU 536

nology is bringing about a revolution in industrial processes, agriculture, and health care. The scientific novelty of modifying life forms is raising complex and equally novel legal problems. In order to comprehend the profound effect recombinant DNA technology will have on the future of man and to discuss the issue of regulation in its proper context, it will be useful for the reader to first develop a basic understanding of the technology.[20]

The broad implications of the technology are due to the amazing uniformity among all life forms on the macromolecular level. All organisms are composed of a relatively small fraction of the total possible organic compounds. All organisms use the macromolecule deoxyribonucleic acid (DNA) as the template for the production of these organic compounds and as the carrier of information from one generation to the next.[21]

The DNA molecule can be visualized as a very long ladder. Each rung represents one of four possible chemical base pairs. Imagine a language in which there are only four letters, and in which all words have exactly three letters. There would be sixty-four possible words, some of which would make sense, while others would be unintelligible. The "language" of DNA is structured on sets of three contiguous chemical base pairs. A triplet of base pairs which codes for an amino acid is known as a codon.[22] There are twenty possible amino acids and each recognizes its own codon. This correspondence of codons to amino acids is the same in all organisms, giving rise to the concept of the "universal genetic language."[23]

A protein is a linear sequence of amino acids. The sequence of amino acids for a particular protein is encoded in a corresponding sequence of codons in a strand of DNA. A sequence of codons which encodes a protein is called a gene. The magic of the genetic language occurs when a gene directs a cell's machinery to assemble some hundreds of amino acids into a linear sequence which in turn folds upon itself to become a functional protein. The sequence of amino acids in the protein determines that protein's properties,

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(1984).

20. The material in this section is derived largely from two reference publications. The first, the entire September 1981 *Scientific American* issue, provides the nonscientist with a basic understanding of the mechanics and uses of recombinant DNA technology. The other, entitled *Research with Recombinant DNA*, is a transcript of a scientific forum convened in 1977.

21. Abelson, *Introduction to Recombinant DNA Research*, in RESEARCH WITH RECOMBINANT DNA, *supra* note 16, at 4-13.

22. *Id.* at 7-8.

23. *Id.* at 8.

and the set of genes possessed by an organism determines that organism's characteristics.[24]

The cell's DNA thus determines what products will be constructed by the cell's "machinery." Certain naturally occurring single cell organisms, while converting raw materials into substances essential for their own growth and maintenance, happen to produce substances, such as penicillin, or by-products, such as ethyl alcohol, which are useful to man. Although man has been taking advantage of these processes for at least eight thousand years, it has only been since the turn of the century that geneticists began applying scientific methods to improve the industrial qualities of these organisms.[25] Improvements were made in one of two ways: by carefully screening cultures of the organism for random mutants which may have beneficial characteristics, or by selective breeding of the most productive organisms over many generations to "evolve" a commercial grade of organism.[26]

In 1973 scientists discovered biochemical techniques for removing a segment of DNA from one organism and inserting it into the DNA complex of an unrelated organism. These techniques, known as recombinant DNA techniques, revolutionized classical genetics. It became possible to directly intervene in the genetic constitution of an organism rather than to rely on natural selection or domestic breeding. And because the genetic code is universal it became possible, in theory at least, to cause the genes from a tomato to be expressed in a fish.[27] Since such changes are not *surgical,* but *genetic,* this new organism has the ability to reproduce and to pass its newly acquired characteristics on to subsequent generations.

When recombinant DNA techniques were first reported, scientists thought that the barriers of evolution would tumble and that man could create any desired organism at will. In the past decade, however, scientists have learned that genes are not as fungible as first predicted. Generally, evolutionary barriers inhibiting DNA expression in foreign species have been found to be much stronger than originally suspected.

Recombinant DNA techniques involve the use of special enzymes, known as restriction endonucleases, which cleave the DNA at specific sites. Some of these endonucleases produce fragments

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24. Hopwood, *The Genetic Programming of Industrial Microorganisms,* SCI. AM., Sept. 1981, at 91, 92.

25. Kircher, *supra* note 19.

26. *Id.*

27. Abelson, *supra* note 21, at 8.

with "sticky ends." Each endonuclease recognizes and cleaves DNA only at a particular sequence of base pairs specific to that endonuclease. This sequence of base pairs occurs at random along a DNA molecule and is more likely than not present in the DNA of many different organisms. When the DNA of two unrelated organisms is fractionated with the same endonuclease, the sticky ends of the fragments will be identical. When the fragments of these two organisms are mixed, they will join at the sticky ends. Nicks remaining in the new strand of DNA are sealed with another enzyme called a ligase.[28] The resulting DNA molecule contains a peculiar set of genes which cannot be found in any one naturally occurring organism.[29]

Scientific euphoria over the discovery of these techniques diminished slightly as scientists discovered that is is not sufficient for a segment of foreign DNA merely to be incorporated into a host organism's DNA for the introduced DNA to become expressed. Intracellular regulation of protein synthesis is very complex. A cell must be able to synthesize the correct amount of a product, such as an enzyme, and only when needed. Structural genes, which code for proteins, are preceded by a promotor segment of DNA and followed by terminator sequences. Transcription, where a secondary template ribonucleic acid (RNA) is made from the primary template DNA, will not occur if the foreign gene is not situated inside the proper regulatory sequences.[30]

Once the DNA is transcribed into RNA it must be "translated" into amino acid sequences by a ribosome. Even if the foreign DNA is successfully transcribed, it will not be translated unless the ribosomal binding site on the foreign RNA is sufficiently recognizable by the host to permit host ribosomes to attach and begin translation.[31]

Genes in higher organisms (eukaryotes) are often split by noncoding intervening sequences called "introns." Introns lie within the structural genes and make it impossible to directly translate the primary RNA transcript into a protein. Introns are transcribed from the DNA along with coding sequences (exons) and must first be excised in a splicing process which brings the gene's exons together to form a "mature" RNA molecule. Only this mature RNA molecule can be translated into amino acids for the

28. Hopwood, *supra* note 24, at 98-99.
29. Abelson, *supra* note 21, at 10.
30. Hopwood, *supra* note 24, at 101.
31. *Id.*

formation of a protein.[32] Bacteria lack the enzymes to splice the introns out of a primary RNA transcript. This prevents most naturally occurring eukaryotic genes from being expressed in bacteria.[33]

Bacteria have been modified for commercial purposes to "ferment" human interferons, human insulin, and human growth hormones. The genetic material spliced into the bacteria to induce manufacture of these complex organic molecules cannot be in the form of intron-containing human DNA. Instead, artificial DNA sequences must first be laboriously constructed without introns.[34] Even when a bacterium has been successfully induced to manufacture a foreign protein, there is a further problem in that bacteria often digest any foreign protein in their cells. The industrial bacteria may have to be genetically modified to shut down its protein digesting mechanism.[35]

Today laboratory recombinant DNA techniques are generally regarded as safe. The strong evolutionary barriers preventing expression of foreign genes provide a natural safety mechanism. Another natural safety mechanism is the fact that each of an organism's characteristics usually requires tens or hundreds of genes to be fully expressed. Continuous field monitoring of a novel organism for newly acquired mild traits will indicate the development of a few undesired genes and will permit discontinuation of the use of that organism before it evolves all the genes necessary to become fully potent.[36]

These natural safety mechanisms, taken together with laboratory containment procedures, have minimized the risk of conducting recombinant DNA experiments in the laboratory. Today recombinant DNA techniques are seen as powerful but safe scientific tools.

III. The National Institutes of Health Guidelines

Scientists today prefer to overlook the incident which initiated the chain of events leading to the creation of the National Institutes of Health (NIH) Guidelines. Stanford researcher and pioneer of recombinant DNA technology Dr. Paul Berg developed a prototype recombinant method in 1971. One experiment he was plan-

32. *Id.* at 92.
33. *Id.* at 99.
34. *Id.*
35. *Id.* at 101.
36. Bundesminister fur Forschung und Technologie, Chancen und Gefahren der Genforschung (1980) [hereinafter cited as Chancen und Gefahren].

ning to conduct involved the transfer of DNA from an animal tumor virus to a virus which can infect *Escherichia Coli,* the common human intestinal bacteria. When cancer researcher Robert Polack heard about the proposed experiment he "had a fit" and advised Berg that if the new virus were to escape from the laboratory it might survive in the human intestinal bacteria. This would expose humans to a tumor-causing DNA which might even result in an "epidemic of cancer" in humans. After months of soul searching, Berg decided to defer his experiment.[37]

Concern in the scientific and public communities mounted over the conjectured health and safety risks of recombinant DNA research. In 1973 Dr. Berg chaired a committee of prominent scientists who wrote an open letter to the scientists of the world. The "Berg letter" was published in the National Academy of Sciences journal, *Science,*[38] and the English journal, *Nature.*[39] The letter appealed to scientists of the world to voluntarily defer recombinant DNA research involving toxic or highly infectious organisms until containment guidelines could be established. The letter also called on the NIH to establish an oversight and advisory committee for interfacing the technology with governmental and public interests.

In 1975 the National Academy of Sciences sponsored an international conference for genetic scientists at the Asilomar Conference Center in Pacific Grove, California.[40] The scientists who met were by this time more familiar with recombinant DNA techniques and worked together to produce guidelines for physical and biological containment to prevent accidental release of recombinant organisms into the environment.[41]

The day after the Asilomar conference ended, the National Institutes of Health Recombinant DNA Advisory Committee (RAC) met for the first time. The committee recommended adoption of the Asilomar guidelines by the NIH. A year later the NIH Guidelines for Research Involving Recombinant DNA Molecules were published (NIH Guidelines).[42] The NIH Guidelines are applicable only to research involving recombinant DNA molecules. Recombi-

37. Swazey, Sorenson & Wong, *Risks and Benefits, Rights and Responsibilities: A History of the Recombinant DNA Research Controversy,* 51 S. CAL. L. REV. 1019, 1021 (1978).

38. Letter from Paul Berg, et al. to the Editor, 185 SCIENCE 303 (1974).

39. Letter from Paul Berg, et al. to the Editor, 250 NATURE 175 (1974).

40. Swazey, Sorenson & Wong, *supra* note 37, at 1030.

41. *Id.* at 1035.

42. 41 Fed. Reg. 27,902 (1976) [hereinafter cited as NIH Guidelines].

nant DNA molecules are defined in the Guidelines as "molecules which are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell."[43] Other genetic engineering techniques, such as protoplast fusion, radiation, or hybridoma techniques are intracellular and are not covered.

The Guidelines establish a Recombinant DNA Advisory Committee. Committee members are chosen to provide, collectively, expertise in scientific, legal, and ethical fields relevant to recombinant DNA technology.[44] The Guidelines also establish the Federal Interagency Advisory Committee on Recombinant DNA Research. Seventeen federal departments and agencies are currently represented on the committee. The purpose of the committee is to provide for communication and exchange of information necessary to maintain coordination of federal programs and activities relating to recombinant DNA research.[45]

The NIH is tasked with overseeing federally funded research in curing diseases and promoting public health. The NIH is heavily involved in sponsoring research in fundamental concepts of molecular genetics of microorganisms and higher organisms and is the major federal sponsor of research involving recombinant DNA. This revolutionary technology is seen as a means of understanding the genetics of cancer and disease-causing microorganisms. Understanding the genetic mechanics of carcinogenic and virulent pathogenic diseases is the first step towards devising a cure.

The NIH realized that these experiments could be dangerous. By altering the genetic constitution of highly infectious microorganisms, new organisms would be created possessing novel infectuous capabilities. The NIH was concerned that newly created highly infectious microorganisms might escape from the laboratory and infect employees or the general public.[46] Regulations provided in the Guidelines are therefore containment oriented; they were created to insure that recombinant DNA experiments funded by the NIH would not accidentally contaminate the environment.[47]

The Guidelines attempt to quantify the biological hazard of experiments by classifying organisms involved in the experiments on the basis of their hazard to health. The Guidelines assign physical

43. NIH Guidelines, 48 Fed. Reg. 24,555, 24,557 (1983).
44. *Id.* at 24,562.
45. *Id.* at 24,577.
46. STAFF REPORT, *supra* note 13, at 3.
47. *Id.* at 28.

and biological containment procedures commensurate with the risk involved. There are four levels of physical containment, designated P-1 through P-4. Special laboratory installations, procedures, and equipment are prescribed to provide physical barriers to accidental release of experimental organisms.[48] The facilities required to furnish the most stringent level of physical containment, P-4, are so elaborate[49] that only a few P-4 facilities exist in the United States, and only one exists in Europe.[50]

Biological containment procedures are designed to minimize the possibility of an experimental organism being carried out of the laboratory on a friendly host and to minimize the survivability of an organism once outside the laboratory.[51] Strains of experimental organisms have been produced, for example, which require special nutritional supplements to survive. These supplements are not available outside the laboratory, virtually eliminating the chances of environmental contamination.

The NIH Guidelines apply to all recombinant DNA research conducted at or sponsored by an institution that receives support for any recombinant DNA research from the NIH.[52] Noncompliance with the Guidelines would result in withholding of NIH funds for the conduct of recombinant DNA research from that institution.

Compliance with the NIH Guidelines by institutions which do not receive funds from the NIH, such as commercial biotechnology companies, is purely voluntary.[53] Commercial industrial institutions have thus far been complying with the Guidelines for two reasons. First, compliance with the only regulatory standards in existence would tend to mitigate tort liability. Second, the appearance of industrial compliance with federal guidelines would dissuade local governments from enacting independent, perhaps stricter, ordinances regulating recombinant DNA research.[54] There is currently, however, no federal legal prohibition on any privately

48. NIH Guidelines, 48 Fed. Reg. 24,555, 24,557 (1983).

49. *Id.* at 24,571 (app. G-II-D).

50. CHANCEN UND GEFAHREN, *supra* note 36, at 29-30 (quoting Sir John Kendrew, Director-General of the European Molecular Biology Laboratory, Heidelberg, Germany).

51. NIH Guidelines, § II, 48 Fed. Reg. 24,555, 24,557 (1983).

52. *Id.* § I-C.

53. STAFF REPORT, *supra* note 13, at 27, commented, however, that "[g]iven the highly competitive nature of the biotechnology industry, it is not unlikely that some companies may decide not to request RAC approval out of concern that the approval process could cause costly delays in testing and marketing their products."

54. *See infra* notes 69-72 and accompanying text.

funded recombinant DNA experiment, even deliberate release experiments.

The Guidelines as originally published in 1976[55] contained six strict prohibitions. One of these was a prohibition on deliberate release into the environment of recombinant DNA-containing organisms.[56] The Guidelines were first revised and relaxed in 1978[57] to reflect a growing familiarity with the technology.[58] When scientists became interested in using recombinant techniques to genetically engineer organisms to perform commercially useful tasks upon deliberate release into the environment, a concept not contemplated under the original Guidelines, the NIH moved to legitimize RAC review over this new area by "relaxing" the original strict prohibition on deliberate release. The 1978 revision of the Guidelines permitted the Director of NIH to make "exceptions"[59] to the prohibitions contained in the original Guidelines.[60] This revision is the subject of *Foundation on Economic Trends v. Heckler*.[61] In 1983 the NIH further relaxed the Guidelines by establishing conditions under which certain plants containing recombinant DNA may qualify for RAC authorization for environmental release.[62]

By 1983 the Director of NIH had exercised his power and approved three applications for waivers of the prohibition on NIH-funded direct release experiments.[63] The first experiment involved field testing of corn plants modified by recombinant DNA tech-

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55. NIH Guidelines, 41 Fed. Reg. 27,902 (1976).

56. *Id.* § III-A-iv, 41 Fed. Reg. at 27,914-15.

57. NIH Guidelines, 43 Fed. Reg. 33,042 (1978); 43 Fed. Reg. 60,083 (1978).

58. The Secretary of Health, Education and Welfare explained the purpose of the first revisions as follows:

> The original Guidelines are being updated in light of NIH's experience operating under them and in light of our increasing knowledge about the potential risks and benefits of this research technique. As experience accumulates, we should review and evaluate the evidence to assure that the restrictions imposed are appropriate to potential risks—strengthening restrictions where needed, relaxing regulation where justified.

NIH Guidelines, 43 Fed. Reg. 33,042 (1978).

59. *Id.* at 33,110.

60. The 1978 amendments retained the prohibition, *id.* § I-D-4, 43 Fed. Reg. at 33,070, but included a waiver provision. The NIH further relaxed the Guidelines in 1982 and 1983, but only the 1978 changes had any substantive effect on the ability of the Director of NIH to authorize direct releases. NIH Guidelines, §§ III-A-2, IV-E-1-b-(1)-(3), 47 Fed. Reg. 17,180, 17,186-87, 17,191 (1982).

61. No. 83-2714 (D.D.C. filed Sept. 14, 1983).

62. NIH Guidelines, 48 Fed. Reg. 24,548, 24,549 (1983).

63. Milewski & Talbot, *supra* note 8, at 143.

niques to induce synthesis of additional amino acids. This new corn is nutritionally complete and able to provide the entire complement of amino acids essential to humans.[64] The second experiment proposed to demonstrate that pollen modified by recombinant techniques could confer disease resistance on tomato and tobacco plants.[65]

The third experiment (the Lindow experiment) was proposed by Doctors Lindow and Panopoulos of the University of California, Berkley.[66] The intent of the experiment was to investigate the possibility of biologically controlling frost damage in frost sensitive plants.

Lindow proposed to displace the naturally occurring frost inducing bacteria from the surfaces of plants by spraying the area with a mutant of the bacteria from which he had deleted, through recombinant techniques, the gene for the production of the ice nucleating protein. Lindow's was the first direct release experiment that was ready to proceed, and thus became the subject of the lawsuit in *Foundation on Economic Trends v. Heckler.*

Scientists today feel that recombinant DNA technology is safer than many other types of research and that the only reason the NIH Guidelines exist is because the public still mistrusts the technology.[67] The RAC, in fact, had proposed a revision of the Guidelines to make them wholly voluntary in 1981,[68] but received strong feedback from scientists who wanted the mandatory nature retained for public policy reasons.

The following are selected comments received by the RAC: "The public is not yet ready for voluntary Guidelines."[69] "[I]n an era when science is suspect in the (public) community, evidence of institutional review is most important."[70] "Scientists could no longer argue that they were following a policy of self regulation."[71] "[I]t might lead to more stringent regulation at the local level."[72]

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64. 46 Fed. Reg. 40,331 (1981). This experiment, though not subject to the injunction which halted the Lindow experiment, has been voluntarily postponed at least until the summer of 1985. Budiansky, *Rifkin strikes at corn this time,* 310 NATURE 3 (1984).

65. 48 Fed. Reg. 16,459 (1983).

66. *Id.* at 24,549.

67. *See* SPLICING LIFE, *supra* note 5, at 2, 14-16 (discussion on the "Frankenstein factor").

68. 46 Fed. Reg. 59,734 (1981).

69. 47 Fed. Reg. 17,166, 17,168 (1982) (statement of Dr. Mason).

70. *Id.* at 17,175.

71. *Id.* at 17,168 (statement of Mr. Mitchell).

72. *Id.* at 17,167 (statement of Dr. Baltimore).

Concern was also expressed specifically over deregulation of deliberate release. The RAC accepted the recommendations of the scientists and retained the mandatory provision of the Guidelines.[73] Today, however, ninety percent of recombinant DNA experiments have either been exempted from the NIH Guidelines or require only local (Institutional Biosafety Committee) review.[74]

IV. THE LINDOW EXPERIMENT

The experiment proposed by Doctors Lindow and Panopoulos is simple in theory and profound in application. Lindow and associates observed that frost sensitive plants grown in bacteria free laboratory chambers were able to tolerate mildly freezing temperatures without actually freezing. The same plants when later sprayed with a solution containing certain common bacteria and again exposed to mildly freezing temperatures froze and exhibited frost damage upon thawing. Lindow deduced that the bacteria, which normally inhabit the superstructures of plants, are the promoters of frost damage in frost sensitive plants.[75]

Tropical plants such as Florida's citrus trees, which have not developed mechanisms for tolerating internal ice formation, are classified as frost sensitive plants. Frost sensitive plants can tolerate short periods of mild subfreezing temperatures by supercooling.[76]

Even at freezing temperatures water molecules will not spontaneously fall into the symmetrical alignment necessary to initiate ice crystal formation. Small volumes of pure water can be supercooled to minus-forty degrees celsius before ice crystals begin to form spontaneously. For ice crystals to begin forming at warmer temperatures, certain catalysts, called ice nucleation centers, are necessary.[77] Lindow and associates discovered that three common species of bacteria produce a protein which is perhaps the strong-

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73. *Id.* at 17,170.

74. STAFF REPORT, *supra* note 13, at 26. Certain microbes which have been routinely used in laboratory experiments and are known to be safe are listed as categorically exempted under app. A of the Guidelines. Certain nonweed, harmless plants have been categorically exempted from prior RAC review under app. L of the Guidelines. 48 Fed. Reg. 24,555, 24,564, 24,580 (1983).

75. Lindow, Arny, Upper & Barcher, *The Role of Bacterial Ice Nuclei in Frost Injury to Sensitive Plants*, in PLANT COLD HARDINESS AND FREEZING STRESS (A. Sakai & P. Li ed. 1978).

76. I. TING, PLANT PHYSIOLOGY 186 (1982).

77. Lindow, *Methods of Preventing Frost Injury Caused by Epiphytic Ice-Nucleation-Active Bacteria*, 67 PLANT DISEASE 327, 327 (1983).

est naturally occurring ice nucleus.[78] This protein can cause ice crystal formation at temperatures as warm as minus-one degree celsius.[79] The protein does this by exhibiting a crystaline surface very similar to an ice crystal. At freezing temperatures the protein chemically induces water molecules to align themselves on its surface. Once a "seed" of ice has been formed, it becomes easy for an ice crystal to grow.

Lindow used these observations to construct a series of experiments. He first sprayed a field of crops with a bactericide to reduce the bacteria population. He found that this reduced crop damage, but that even dead bacteria remaining on the plants contained the ice nucleation protein and could still cause frost damage.[80]

Lindow next used classical mutagenic techniques to create a point mutated bacterium lacking the ability to produce the ice nucleation protein. He refers to this mutant bacteria, which was similar to the naturally occurring (INA+) bacteria in all other respects, as "ice-nucleation active minus" (INA-) bacteria. Lindow attempted to biologically control frost damage in plants by using the INA- bacteria as a "biological bactericide." Since the INA- bacteria inhabit the same environmental space and compete for the same nutrients as the INA+ bacteria, Lindow was able to displace the naturally occurring INA+ bacteria by saturating a field with these INA- mutants before the seasonal population of natural INA+ bacteria could take hold. By suppressing the natural population of ice inducing bacteria, Lindow was able to effectively reduce the frost damage.[81]

Lindow next created an INA- mutant using recombinant techniques. The recombinant mutant had two commercial advantages over the classically mutated bacteria. First, recombinant mutations extend over thousands of base pairs and are permanent, while classical mutagenic techniques produce point mutations of single base pairs which tend to revert in nature. Second, recombinant induced DNA mutations are well defined, while classical techniques produce random "spot" mutations which are not well defined and

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78. *Id.* at 328.

79. *Id.*

80. Lindow & Connell, *Reduction of Frost Injury to Almond by Control of Ice Nucleation Active Bacteria*, 109 J. AM. SOC'Y HORTICULTURAL SCI. 48 (1984).

81. Lindow, *Population Dynamics of Epiphytic Ice Nucleation Positive Bacteria on Frost Sensitive Plants and Frost Control by Means of Antagonistic Bacteria*, in PLANT COLD HARDINESS AND FREEZING STRESS, *supra* note 75.

may produce latent defects in organisms modified this way.[82]

Lindow intended to repeat the format of his earlier experiment substituting the recombinant INA- bacteria for the classical INA- bacteria. Lindow first had to petition the NIH for a waiver of the deliberate release prohibition.[83] His petition was discussed during an open Recombinant DNA Advisory Committee meeting. Questions over the environmental impact of the experiment were raised and authorization was deferred.[84] Lindow's second petition was modified to conform to the concerns raised during the earlier RAC meeting.[85] The second petition was unanimously recommended for approval by the RAC and approved by the Director of NIH.[86] Before the experiment could proceed it was halted by the federal court injunction.[87]

V. Environmental Concerns of Opponents of the Lindow Experiment

Opponents of the Lindow experiment find support in Lindow's own scientific papers on the ecological role of the INA+ bacteria. Lindow wrote that INA+ bacteria may cause frost damage not only to frost sensitive plants but also to frost sensitive insects. The opponents rely on this proposition to argue that eliminating an environmental control on frost sensitive insects could result in the undesired proliferation of insect pests.[88]

Lindow thinks that the INA+ bacteria may play a role in atmospheric precipitation.[89] The bacteria can be found in the atmo-

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82. Letter from Advanced Genetics Sciences, Inc. to Dr. William Gartland, NIH (Mar. 22, 1984) (request for approval of field trials).

83. *See supra* note 52 and accompanying text. "Lindow is required to seek RAC approval, even though NIH is not funding the work, because the university receives support from the NIH." Norman, *supra* note 7, at 963. *See* 48 Fed. Reg. 24,563 (1983).

84. 48 Fed. Reg. 1,156, 1,158 (1983).

85. 48 Fed. Reg. 9,436, 9,441 (1983); Milewski & Talbot, *supra* note 8, at 142.

86. 48 Fed. Reg. 24,548, 24,549 (1983).

87. Order Granting Preliminary Injunction at 13, 28, Foundation on Economic Trends v. Heckler, No. 83-2714 (D.D.C. May 16, 1984).

88. Many insects can supercool to very low temperatures . . . . However, since most of these species must supercool to survive, factors that decrease the supercooling capacity of these insects would reduce their survival. . . . Analogous to plant frost survival, the presence of these [ice nucleation-active] bacteria would be detrimental to survival of frost sensitive insects and possibly beneficial to frost tolerant insect species.

S. Lindow, Phytopathogenic Prokaryotes, vol. I, § III, ch. 8, at 24 (Dept. of Plant Pathology, Univ. of Cal. 1983) (citation omitted). Removing ice inducing bacteria would result in a proliferation of frost sensitive insects.

89. Lindow, *supra* note 77, at 332.

sphere and are active inducers of ice crystal formation. It follows that the bacteria may play a role in inducing rain. The opponents argue that large scale displacement of INA+ bacteria by the introduction of INA- bacteria may interfere with global weather patterns.[90]

Lindow believes that INA+ bacteria help frost hardy plants survive. When ice crystals form inside plant cells they cause damage by mechanically piercing cell walls, and also by absorbing intercellular water which "feeds" the ice crystals as they grow, causing dehydration.[91] Plants which evolved in areas of freezing weather have developed mechanisms for tolerating the internal ice.[92] Lindow theorizes that the INA+ bacteria cause ice crystals to begin forming at warmer subfreezing temperatures, which cause the crystals to grow more slowly. This permits the frost tolerant plants to accommodate more gradually than if the ice crystals began forming at very cold temperatures and grew rapidly. Frost sensitive plants, however, which cannot tolerate internal ice and which supercool to survive mildly subfreezing temperatures, may be helped by the displacement of the INA+ bacteria. Thus, the opponents argue, the benefits to frost sensitive agricultural plants might be offset by the potential harm to frost tolerant plants.[93]

Lindow preferred to use recombinant INA- mutants for their greater stability. Classical mutants tend to revert in nature, while recombinant mutations are permanent. The opponents argue that if the recombinant mutants are more stable, then the magnitude of ecological risk would also be greater.[94]

The arguments advanced by the opponents rely on the premise that the INA- bacteria could, ultimately, outcompete the naturally occurring bacteria and displace it in nature. The NIH and the Regents of the University of California contend that the "proliferation argument" is not plausible for two reasons. First, it would be contrary to the accepted principles of evolution. A species is closely integrated into its environment through natural selection and competition with other species. If the INA+ characteristic were not

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90. David, *supra* note 6.

91. I. TING, *supra* note 76, at 184-85.

92. *Id.*; S. LINDOW, *supra* note 88, at 23.

93. S. LINDOW, *supra* note 88, at 21-22. "Ice nucleating bacteria which may play a significant role in frost survival of frost tolerant plants conversely are detrimental to frost sensitive agricultural plants." *Id.* at 23.

94. Interview with E. Lee Rodgers, counsel for the Foundation on Economic Trends, in Washington, D.C. (July 2, 1984).

beneficial to the survival of the species, it would have been discarded long ago. Second, Lindow actually observed in laboratory environmental simulation chambers that his recombinant mutants were not able to outcompete the naturally occurring bacteria.[95]

Although the Lindow experiment is, in all probability, rather harmless in its experimental stage, its commercial impact could be significant. Lindow's mutant may not be able to ecologically out compete its natural counterpart, but if the mutant is commercially successful it will be propagated indirectly by farmers. Employment of the organism over an entire agricultural belt may have the same effect as though the organism were able to outcompete its natural counterpart.

Future direct release experiments might not be as safe as the Lindow experiment. If direct release experiments can be analogized to the introduction into the environment of exotic organisms such as the kudzu weed, the gypsy moth, or the mediterranean fruit fly, then history prescribes caution.[96]

VI. *Foundation on Economic Trends v. Heckler*

On September 14, 1983, the Foundation on Economic Trends brought suit against the National Institutes of Health. Jeremy Rifkin, President of the Foundation, is a prolific author,[97] citizen-advocate, and a leading speaker on the genetic engineering controversy. Rifkin advocates halting all genetic engineering because he believes that progress in the technology will result in desanctification of human life and a collapse of social values.[98]

Rifkin sees the development of biotechnology initiating a revolution, much as the introduction of petrochemicals brought about the industrial revolution. "Pointing to the negative externalities in the petrochemical-based economy—acid rain, economic dislocation due to market pressures and the destruction of environments in the search for fuel and feedstock—he asks that society choose to reject still another disruptive, possibly destructive technical revolution."[99]

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95. Letter from Advanced Genetics Sciences, Inc., *supra* note 82, at 9.

96. David, *supra* note 6. The oriental kudzu plant was introduced into southern states by railroad companies as a cover for embankments. The plant has outcompeted natural flora and is now known as kudzu weed. STAFF REPORT, *supra* note 13, at 19.

97. T. HOWARD & J. RIFKIN, WHO SHOULD PLAY GOD? (1977); J. RIFKIN, ALGENY (1983).

98. Interview with Jeremy Rifkin, President of the Foundation on Economic Trends, in Washington, D.C. (July 2, 1984).

99. *Jeremy Rifkin and the Courts: Last Line of Containment for Recombinant DNA,*

Margaret Heckler was being sued in her official capacity as Secretary of Health and Human Services. In this capacity she is ultimately responsible for the administration of all activities of the NIH. The NIH has been the de facto regulator of all research involving recombinant DNA technology[100] and has assumed the role of regulator of all deliberate release experiments.

The NIH Recombinant DNA Advisory Committee is the only federal body with expertise and experience in recombinant DNA technology regulation.[101] The committee feels that if it did not expand its role to cover deliberate release experiments, the pressures of commercial competition would push biotechnology companies into proceeding with deliberate release without the benefit of any regulatory oversight.[102]

The suit is an attack on the regulatory authority of the Director of the NIH and the RAC for permitting deliberate release into the environment of organisms genetically modified through recombinant DNA techniques.[103] The Foundation on Economic Trends raised procedural challenges to the manner in which the Director of NIH permitted the authorizations of the deliberate release experiments to occur. The Foundation argued that revising the NIH Guidelines to permit authorization of deliberate release experiments and authorizing three such experiments constituted a "major federal action."[104] It felt that failure to precede a major federal action with a documented "hard look" at the environmental implications of that action constituted a violation of the National Environmental Policy Act of 1969.

The National Environmental Policy Act of 1969[105] was enacted by Congress to insure that the federal government would not undertake any major programs or actions without first considering the potential environmental consequences. The Act places an affirmative obligation on a federal agency to address potential environmental hazards in a forum open to the public before it embarks

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GENETIC ENGINEERING NEWS, July 6, 1984, at 6, col. 1; *see also* Davis, *Science, Fanaticism, and the Law*, GENETIC ENGINEERING NEWS, July 6, 1984, at 4, col. 1; Marshall, *The Prophet Jeremy*, NEW REPUBLIC, Dec. 20, 1984, at 20.

100. STAFF REPORT, *supra* note 13, at 25.

101. *Id.*

102. Interview with Dr. Stanley Barban, Administrative Scientist of the Office of Recombinant DNA Activities, in Washington, D.C. (July 3, 1984).

103. Interview with E. Lee Rogers, *supra* note 94.

104. Plaintiff's First Amended Complaint, Foundation on Economic Trends v. Heckler, No. 83-2714 (D.D.C. Sept. 18, 1983).

105. 42 U.S.C. §§ 4321-4370 (1982).

on any particular course of conduct significantly affecting the environment. The Act requires that an agency compile an environmental impact statement prior to final approval of all "major Federal actions significantly affecting the quality of the human environment" or an Environmental Assessment showing a finding of no major potential environmental hazard.[106]

When the NIH Guidelines were originally published in 1976 they contained a strict prohibition on deliberate release of recombinant DNA molecule containing organisms into the environment.[107] The NIH drafted an environmental impact statement in September 1976[108] and adopted a final environmental impact statement for the NIH Guidelines in October of 1977.[109] Because the original Guidelines strictly prohibited the release of recombinant DNA containing organisms into the environment, the 1977 environmental impact statement did not address deliberate release experiments.

When proposing the revisions to the Guidelines, the Director stated that in the revised Guidelines "the prohibition of deliberate release into the environment of recombinant DNA containing organisms can be waived only if all the requirements . . . of the National Environmental Policy Act . . . are met."[110] The revised NIH Guidelines of 1978 list the authorizing of individual waivers by the Director of NIH as a "major action."[111] The Environmental Assessment accompanying the 1978 revision of the Guidelines also characterized the modification permitting waiver of the prohibition of deliberate release experiments by the Director of NIH as a "major" revision.[112]

The National Environmental Policy Act requires that an agency evaluate its action at the point of commitment.[113] The Director of NIH argued that although it was impossible to assess with certainty the impact of a deliberate release experiment prior to its initiation, the review he had given the experiment indicated that it

106. *Id.* § 4332(2)(c).

107. NIH Guidelines, § III-A-iv, 41 Fed. Reg. 27,902, 27,914-15 (1976).

108. 41 Fed. Reg. 38,425 (1976).

109. *See* National Institutes of Health Environmental Impact Statement on NIH Guidelines for Research Involving Recombinant DNA Molecules of June 23, 1976 (pts. 1 & 2) (Oct. 1977).

110. NIH Guidelines, 43 Fed. Reg. 33,042, 33,110 (1978).

111. *Id.* at 60,126-27.

112. *Id.* at 33,096-107.

113. 42 U.S.C. § 4332(2)(C) (1982); 40 C.F.R. § 1500.1(b) (1984).

posed no risk to the environment.[114] Therefore, in his opinion, no environmental impact statement was necessary at this time. The plaintiffs argued that the NIH had embarked on a "program" of deliberate release experiments and that an environmental impact statement should have been prepared, if not at the point of the 1978 revision of the Guidelines introducing the waiver provision, then at least prior to the 1983 authorizations of the three direct release experiments.[115]

The 1978 revisions were, in fact, accompanied by two documents entitled Environmental Assessments: one for the revisions as proposed[116] and one for the revisions as adopted.[117] The second document concluded that the revisions to the NIH Guidelines presented "no adverse impact upon the environment." Although Judge Sirica admitted the court lacked the competence to rule on technical questions or on the effect of the recombinant organisms on the environment,[118] he stated that "the dispute would revolve around the Director's conclusion that the change had no significant impact on the environment."[119]

Judge Sirica stated that he could find nothing in the record to show that the Director of NIH had evaluated any specific deliberate release experiments or any generic environmental issues which could be common to all recombinant DNA experiments. Judge Sirica felt that the Director, who only two years before had strictly prohibited direct release experiments for fear of endangering the environment, was not now in a position to declare that deliberate release experiments would pose "no significant impact on the environment."

"[U]nless the court were to assume that all such experimentation would have no significant environmental impact, the administrative record strongly indicates that plaintiffs will succeed in demonstrating"[120] that the Director "approved a major Federal action

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114. Order Granting Preliminary Injunction, *supra* note 87, at 13, 28.

115. *Id.* at 7.

116. 43 Fed. Reg. 33,096 (1978).

117. *Id.* at 60,101.

118. Order Granting Preliminary Injunction, *supra* note 87, at 2, 21; *see also* Diamond, Comm'r of Patents & Trademarks v. Chakrabarty, 447 U.S. 303 (1980). The Supreme Court has had no exposure to biotechnology cases since *Diamond*, and has no biotechnology cases pending. Conversation with Justice John Paul Stevens of the United States Supreme Court, Tallahassee, Florida (Jan. 25, 1985). For a discussion of the possible utility of a court composed of scientist-judges, see Martin, *The Proposed "Science Court,"* 75 MICH. L. REV. 1058 (1977).

119. Order Granting Preliminary Injunction, *supra* note 87, at 18.

120. *Id.*

without benefit of a specific or general investigation into the environmental hazards of deliberate release experimentation."[121]

Sirica found the plaintiffs had a substantial chance of success on the narrow legal issue of whether the Director of NIH should have prepared an environmental impact statement. Further, finding the prerequisites for a preliminary injunction to be satisfied, Judge Sirica granted the injunction requested by the plaintiffs. He enjoined the NIH from "[a]pproving or continuing to approve experimentation involving the deliberate release of recombinant DNA . . . until such time as the Court enters final judgment on the merits" and further enjoined the Regents of the University of California "from proceeding with the deliberate release experiment approved by NIH."[122]

Judge Sirica also found that, as the NIH has no regulatory authority over non-NIH-funded deliberate release experiments, he could not order the NIH to cease reviewing those experiments.[123] There is currently no legal prohibition against any kind of recombinant DNA experiments conducted by the private sector. Following the legal entanglement of the Lindow experiment in the federal courts, Advanced Genetics Sciences, Inc., petitioned the RAC for approval to conduct experiments similar to Lindow's.[124] Advanced Genetics Sciences is the commercial sponsor of Lindow's research on biological control of frost damage. The experiments proposed by Advanced Genetics Sciences would involve the deliberate release of the very organism created by Lindow. The proposed experiments differed only in the types of plants which were to be exposed.[125] The RAC reviewed the petition and recommended approval to the Director of NIH. The Director usually accepts the recommendation of the committee, but has not yet had time to act on this recommendation.[126]

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121. *Id.*

122. *Id.* at 38.

123. *Id.* at 31.

124. Letter from Advanced Genetics Sciences, Inc., *supra* note 82; *see also* 49 Fed. Reg. 17,672, 17,674-75 (1984).

125. Letter from Advanced Genetics Sciences, Inc., *supra* note 82.

126. Three non-NIH-funded corporations, BioTechnica International, Inc., Cetus Madison Corp., and Advanced Genetics Sciences, Inc., have voluntarily petitioned the NIH for approval to conduct deliberate release experiments. Interview with Dr. Stanley Barban, *supra* note 6. Biotechnology companies, impatient with the delays, are considering conducting tests out of the country or bypassing NIH and asking the EPA for permission to conduct deliberate release experiments. Sun, *Biotechnology's Regulatory Tangle*, 225 SCIENCE 697, 698 (1984). Monsanto plans to ask the EPA for permission to conduct field trials in 1986 of a newly developed bacteria soil pesticide. Monsanto scientists transplanted the

VII. FEDERAL OVERSIGHT: THE NIH, THE EPA, OR . . . ?

The NIH Recombinant DNA Advisory Committee was established in 1976 to oversee and insure the safety of NIH-funded research where recombinant techniques are used. As the NIH was tasked with finding cures for diseases, much of the recombinant work being funded at the time involved infectious pathogens. The RAC was initially composed of geneticists and physicians to provide expertise in the health safety aspects of these experiments. As the recombinant DNA technology grew in pace, breadth, and complexity, the RAC displayed an amazing ability to modify or augment its membership to provide expertise in each new area. The RAC currently has members and consultants from a wide variety of sciences and governmental agencies,[127] reflecting the universal applicability of recombinant DNA technology.

The extremely rapid transition from laboratory techniques to applied commercial technology has attested to the efficient interface by the RAC between the scientists and the government. The long safety record with recombinant DNA technology demonstrates the responsible representation of the public interest.[128] Despite the commendable record of public service the RAC has acquired, the RAC has been receiving increasing criticism for their move to expand their role to oversee direct release experiments.[129]

The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research recommended the creation of a new RAC "broadly based and not dominated by geneticists or other scientists." "It would also be desirable for this 'next generation' RAC to be independent of Federal funding bodies such as the NIH, which is the major Federal sponsor of gene splicing research, to avoid any real or perceived conflict of interest."[130] Dr. Elena Nightingale, while a member of the RAC, "suggested the NIH might not be the best location for an oversight

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toxin producing gene from an airborne microbial pesticide into a common soil bacteria and hope to use it to protect seeds against pests in the soil. Ellis & Rhein, *A Test for One of Biotech's New Watchdogs*, BUS. WK., Jan. 14, 1985, at 69.

127. Office of Recombinant DNA Activities, NIH, Interoffice RAC Membership List of June 1984. Responding to environmental concerns, the RAC has recently appointed two ecologists—Dr. Sharples and Dr. Parone. Letter from Dr. Stanley Barban, Administrative Scientist of the Office of Recombinant DNA Activities, to author (Nov. 15, 1984).

128. Johnson, *Role of the Recombinant Advisory Committee*, 224 SCIENCE 243 (1984).

129. Budia, *Rifkin wins interim injunction*, 309 NATURE 296 (1984); David, *supra* note 6; Fox, *Despite Doubts RAC Moving To Widen Role*, 223 SCIENCE 798 (1984); Norman, *supra* note 7; Sun, *Biotechnology's Regulatory Tangle*, 225 SCIENCE 697 (1984).

130. SPLICING LIFE, *supra* note 5, at 4.

committee; the NIH funds and advocates scientific research."[131]

The RAC recently screened two ecologists for consideration as members: Martin Alexander of Cornell University and Frances Sharples of Oak Ridge National Laboratory. Neither ecologist is satisfied with the RAC as regulatory authority for direct release experiments. Alexander feels that in areas affecting the ecology, other agencies with "more competence, interest, and regulatory clout"[132] should replace the NIH. Sharples agrees, but adds that the "EPA is not prepared to take on the task at the moment."[133]

In February of 1984, the House Committee on Science and Technology (Don Fuqua, Florida, Chairman) released a congressional report entitled *The Environmental Implications of Genetic Engineering*.[134] The report found that the damage that could occur as a result of release into the environment of genetically engineered organisms is great.[135] The report further found that predicting the environmental effects of any novel organism prior to its release into the environment would be "extremely difficult, if not impossible, at the present time."[136] The report concluded that "[t]he current regulatory framework does not guarantee that adequate consideration will be given to potential environmental effects of a deliberate release."[137]

The report recommended, inter alia, that:

> The EPA should proceed with its stated intention to extend its authority to include all deliberately released organisms not specifically identified as part of the legal obligation of another agency. . . .
>
> Until such time as EPA's regulations are promulgated, an interagency task force should be established to review all proposals for deliberate releases. . . .
>
> . . . .
>
> The NIH should cease its practice of evaluating and approving proposals for deliberate releases from commercial biotechnology companies.[138]

The committee found that no single governmental body cur-

131. Recombinant DNA Advisory Committee, Minutes of Meeting 8 (Apr. 11, 1983).
132. Fox, *supra* note 129. *But see supra* note 127.
133. Fox, *supra* note 129.
134. STAFF REPORT, *supra* note 13.
135. *Id.* at 9.
136. *Id.* at 10.
137. *Id.*
138. *Id.* at 11-12.

rently possesses the interdisciplinary expertise necessary for evaluation and regulation of deliberate release experiments.[139] The report recommends that all organisms genetically engineered for deliberate release, not just products of recombinant techniques, be regulated under an interagency committee. Regulatory authority of this agency should extend over all experiments, private and industrial as well as federal. Such an agency had, in fact, been established under President Ford in 1976. However, as a commentator recently pointed out: "The Committee has been dormant for the past two years because federal oversight has been accomplished by the Recombinant Advisory Committee with federal agency representatives serving as *ex officio* members of the RAC."[140]

A cabinet level working group, headed by the White House Office of Science and Technology, is currently working on analyzing existing law in terms of health and environmental protection, and evaluating jurisdictional problems. The working group is debating a larger role for the RAC. While a "super-RAC" may carry with it the credibility and technical expertise of the RAC, a bureaucratic expansion of the small and efficient current RAC may be tampering with a good thing.[141] The working group is looking favorably upon a draft proposal, which is being worked on by the EPA, by which the EPA will assume control over some aspects of direct release experiments.[142]

The EPA has, in fact, announced its intention to regulate environmental releases under the authority of the Toxic Substances Control Act (TSCA).[143] The TSCA regulates testing, manufacture, and use of certain "chemical substances" that pose potential risks to health or environment. Jurisdiction to regulate genetically engineered life forms under TSCA hinges on the issue of whether life forms can be classified as chemical substances under TSCA.[144] The EPA advances arguments that life forms fit under the statutory language of TSCA because "the term 'chemical substance' means

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139. NEPA demands an "interdisciplinary" inquiry. *See* 42 U.S.C. § 4332(2)(A) (1982); 40 C.F.R. § 1502.6 (1983).

140. Perpich, *supra* note 18, at 5, col. 3.

141. Sun, *supra* note 129, at 698.

142. Budiansky, *Prospect of new US regulation*, 310 NATURE 613 (1984).

143. 15 U.S.C. §§ 2601-2629 (1982). *See* Sun, *EPA Revs Up To Regulate Biotechnology*, 222 SCIENCE 823 (1983); Sun, *supra* note 129.

144. STAFF REPORT, *supra* note 13, at 31-33. *See also* OFFICE OF PESTICIDES AND TOXIC SUBSTANCES, ENVIRONMENTAL PROTECTION AGENCY, REGULATION OF GENETICALLY ENGINEERED SUBSTANCES UNDER TSCA (1983 draft), *reprinted in* STAFF REPORT, *supra* note 13, app. B, at 109-42.

any organic or inorganic substance . . . , including—(i) any combination of such substances occurring in whole or in part as a result of a chemical reaction or occurring in nature . . . ."[145] The EPA admits that this interpretation might be subject to legal challenge.[146]

There are conceptual problems with the attempt to subjugate genetically engineered life forms to the regulatory framework of TSCA. The traditional "chemical substances" which TSCA was designed to regulate cause problems only when human use concentrates the substances to levels of toxicity. While inert chemical substances either stagnate or decompose in nature, genetically engineered microbes are prolific breeders in favorable environmental conditions. Inert toxins may be controlled by regulating human use, but microbes are almost impossible to contain once released. While inert toxins may be policed and cleaned up, microbes are ubiquitous and no method has yet been devised to insure extermination of every last existing targeted undesired microbe. Chemicals have easily quantifiable chemical properties, while living organisms have complex behavorial properties. While a chemical is an end product to be regulated under TSCA, living organisms may only be "raw materials" whose effects and by-products are not felt until they are permitted to fully interact with the ecosystem and assume an environmental role or niche.

The EPA is also considering regulating genetically engineered microbial pesticides (GEMP's) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).[147]

> When a living organism is intended for use as a biological control agent to prevent, repel, or destroy or mitigate a pest, or it is intended for use as a plant growth regulator, defoliant or desiccant, it is considered a pesticide under FIFRA, section 2(u), and is therefore regulated under that Act.[148]

FIFRA is limited in scope; it covers only pesticides and categorically exempts field trials on land of less than ten acres.[149] While a

145. 15 U.S.C. § 2602(2)(A) (1982).
146. Sun, *supra* note 129, at 698.
147. 7 U.S.C. §§ 136-136(y) (1982).
148. 40 C.F.R. § 162 (1984).
149. *Id.* § 172.3(a) (Experimental Use Permits) states:

> A substance or mixture of substances being put through . . . field trials . . . is not considered a pesticide within the meaning of the Act and no experimental use permit will be required. This purpose will be presumed for the following types of

ten-acre exemption may be reasonable with respect to regulating experiments involving inert chemicals, such an exemption would eclipse the regulation when applied to living organisms which tend, once released, to "go forth and multiply." EPA also exempts many organisms on the grounds that they are already "adequately regulated" by other federal agencies.[150] The Administrator of the EPA may register a pesticide under FIFRA if he determines that:

> It will perform its intended function without unreasonable adverse effect on the environment; and . . . [w]hen used in accordance with *widespread* and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment. . . . To permit this determination, the applicant for registration of a pesticide must provide data . . . so the Agency can evaluate the potential hazards posed by its intended use(s).[151]

FIFRA requires the EPA to assess potential hazards of GEMP's from data supplied by the applicant. The test protocol for data submission establishes that certain representative animals and plants be exposed to the GEMP's for a period of time after which an assessment of GEMP survivability will be conducted. If the GEMP's do not proliferate, no further risk assessments need be undertaken.[152] This risk assessment procedure is inadequate in that it not only invites biased data, but does not provide for detection of the spectrum of ecological effects which may be associated with environmental release. The bacteria causing Dutch Elm Disease, for example, only cause damage in mature elm trees and would have been assessed as environmentally safe under the existing procedure.

Neither the TSCA nor the FIFRA provides the EPA with a sufficiently encompassing jurisdictional base upon which to establish a regulatory framework for the oversight of direct release of genetically engineered organisms. Similar shortcomings plague the remaining existing federal acts: the Plant Quarantine Act gives control over only the importation or interstate movement of disease-

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tests.

(1) Land use. Tests conducted on a cumulative of not more than 10 acres . . . .

150. 47 Fed. Reg. 23,928 (1982); 40 C.F.R. § 162.5(c) (1982).

151. 47 Fed. Reg. 53,192, 53,200 (1982) (Pesticide Registration; Proposed Data Requirements—Part 158) (emphasis added).

152. Betz, Levin & Rogul, *Safety Aspects of Genetically-Engineered Microbial Pesticides*, 6 RECOMBINANT DNA TECHNICAL BULL. 135, 139 (1983).

carrying plants,[153] the Plant Variety Protection Act does not grant the USDA any power to prevent a release,[154] and the Federal Noxious Weed Act and the Federal Plant Pest Act do not apply to the production of the plants and micro-organisms they otherwise regulate.[155]

A comparison of potential regulation of direct release under NIH Guidelines with EPA's regulatory reach under FIFRA demonstrates their respective strengths and weaknesses. Direct release is perhaps more an environmental concern than a recombinant DNA issue, and the EPA has more experience than NIH in predicting environmental impact. While the regulatory authority of the NIH under the Guidelines is limited to NIH-funded recombinant DNA experiments, the EPA under FIFRA could regulate all GEMP's regardless of mutagenic technique or funding source.

These differences are directly applicable to the Lindow experiment which was enjoined in *Heckler*. The injunction was possible because Lindow desired to use recombinant DNA techniques for production of a more commercially suitable mutant, and because his research happened to have been conducted at a university which received support from the NIH. Had Lindow decided to commercialize the INA mutant he had created through classical mutagenic techniques there would have been no RAC review, no court case, and no legal prohibition. As it was, the recombinant DNA containing bacteria whose use was enjoined by Judge Sirica was removed from the jurisdiction of the court and the NIH as a result of Advanced Genetics Systems' decision to fund the deliberate release experiment itself. While Advanced Genetics Systems is not subject to NIH oversight, it is subject to regulation by the EPA. However, current data submission requirements under FIFRA might not have provided sufficient basis for the EPA to assess the bacteria as harmful to the environment.

The congressional report recommends that "[n]o deliberate release should be permitted by EPA, NIH, USDA, or any other federal agency until the potential environmental effects of the particular release have been considered by the [proposed] interagency review panel."[156] The report also points out a technical problem: "[P]redicting the specific type, magnitude, or probability of envi-

153. 7 U.S.C. §§ 151-167 (1982); STAFF REPORT, *supra* note 13, at 35-36.

154. 7 U.S.C. §§ 2321-2583 (1982); STAFF REPORT, *supra* note 13, at 36-37.

155. 7 U.S.C. §§ 2801-2813 (1982); *id.* §§ 150(aa)-(jj); STAFF REPORT, *supra* note 13, at 37-41.

156. STAFF REPORT, *supra* note 13, at 11.

ronmental effects associated with the deliberate release of genetically engineered organisms will be extremely difficult, if not impossible, at the present time."[157] It will be necessary to devise a system for recognition of characteristics of novel organisms which are indicators of potential environmental impact before it will become possible to responsibly regulate deliberate release.[158] The EPA is building on the experience acquired by regulating nongenetically engineered microbial pesticides and is developing standard data requirements and hazard assessment procedures.[159]

In regulating deliberate releases of genetically engineered organisms many conflicting interests must be addressed. Environmentalists would have all direct release experiments made public under the Freedom of Information Act to permit public participation in the decision-making process prior to any experiment. Biotechnology companies rely on the Trade Secrets Act to protect commercially valuable proprietary information from mandatory public disclosure. The Toxic Substances Control Act, for example, prohibits the EPA from disclosing trade secrets otherwise exempt from the disclosure under section 52(b)(4) of the Freedom of Information Act. The government has an interest in keeping the edge in biotechnology development, and the revenues from international patent licensing royalties in the United States.[160] Congress must reconcile these diverse interests and act to establish and empower a competent and unencumbered regulatory authority.

VIII. SUMMARY

The NIH is currently the de facto regulator of all work involving recombinant DNA. The Guidelines under which the NIH regulates the technology were originally established to insure that dangerous organisms created during NIH-funded recombinant DNA experiments would not be accidentally released into the environment. As scientists discovered the inherent safety of recombinant techniques the NIH relaxed the Guidelines to the point where today ninety percent of proposed recombinant DNA experiments are categorically exempt from prior RAC review.

Recombinant DNA techniques are the primary methods employed in the engineering of new commercially valuable organisms

157. *Id.* at 10.
158. Sun, *supra* note 129, at 698.
159. Betz, Levin & Rogul, *supra* note 152, at 141.
160. Sun, *supra* note 129, at 697.

intended for release into the environment.[161] The NIH has taken the initiative to establish itself as the regulatory authority for experiments involving deliberate environmental release of these organisms. The obvious reason for this development is that the NIH is the only federal regulatory authority familiar with recombinant DNA technology, and, in the absence of NIH's assumption of federal oversight, this emerging field would simply go unregulated. A less obvious reason may be that scientists and biotechnology companies, who prefer the liberal voluntary review standards of the NIH to the stricter mandatory standards of the EPA under TSCA or FIFRA, may have been exerting political pressure to keep the NIH as the decision-making body for deliberate release experiments.

Compliance with the NIH Guidelines is voluntary for non-NIH-funded recombinant DNA experiments, and the Guidelines cover only those organisms modified by recombinant DNA techniques. Under FIFRA, the EPA has a broader legal basis for asserting control over deliberate release: all genetically engineered microbial pesticides would be covered regardless of mutagenic technique or funding source used in their production. The EPA, however, is not yet ready to regulate deliberate release experiments. It does not have a method of risk assessment for predicting the effects of an exotic new organism on the ecosystem, and the FIFRA under which the EPA intends to regulate GEMP's currently categorically exempts all environmental releases covering less than ten acres.

The NIH Recombinant DNA Advisory Committee is receiving criticism for having assumed the role of regulator of direct release experiments under guidelines which are oriented towards prevention of accidental release and not towards oversight of deliberate release. In *Heckler,* Judge Sirica ordered the NIH to cease reviewing NIH-funded deliberate release experiments until the NIH complied with the National Environmental Policy Act but permitted the NIH to continue reviewing non-NIH-funded experiments. A congressional report on the environmental implications of genetic engineering found that the RAC did not possess the interdisciplinary expertise or jurisdiction to regulate deliberate release experiments. The report recommended that the NIH regulate only NIH-funded experiments, which is exactly what the injunction issued by Judge Sirica prevents it from doing.

The congressional staff report recommended that the EPA ex-

161. STAFF REPORT, *supra* note 13, at 30 n.44.

pand its base of expertise to regulate deliberate release experiments. A look at Lindow's experiment demonstrates that the environmental aspects of his experiment eclipse the recombinant DNA aspects. The RAC, by its own admission, considers recombinant DNA techniques inherently safe and ready for deregulation. Because the primary danger of deliberate release experiments is the potential unintended ecological harm, it is only appropriate that the agency with the most experience in forecasting ecological impact be tasked with their oversight.

The final decision of the federal district court in *Heckler* may have significant policy impact, but it will have little actual impact on deliberate release of genetically engineered organisms. If the court follows the recommendation of the congressional staff report and permits the NIH to continue to review NIH-funded deliberate release experiments, there will be little pressure to correct the regulatory deficiencies. The court has, however, strongly indicated that it will find for the plaintiff on the narrow legal question of whether the NIH should be required to prepare an environmental impact statement in accordance with the National Environmental Policy Act before it may authorize deliberate release experiments. Under this ruling the RAC may again review NIH-funded research when the Director of NIH completes an environmental impact statement. The Director expects an environmental impact statement to be completed by late 1985. In the meantime all deliberate release experiments will simply be funded by the corporate sponsors of the academic researchers and thereby be exempt from the injunction.

The congressional staff report stated: "In view of EPA's stated conclusion that the Toxic Substances Control Act (TSCA) does provide it with authority to oversee deliberate releases . . . , no additional legislation or clarifying amendments are needed at this time."[162] A close look at the legal bases upon which the EPA premised its assertion, however, reveals significant inadequacies in regulatory jurisdiction.

IX. CONCLUSION

Progress involves risk. Federal regulatory agencies provide risk assessment and enforce risk management policies to insure that the benefits of scientific advances are not outweighed by the dan-

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162. *Id.* at 43.

gers of blind commercialization. As the Lindow experiment wends its way through the courts, it tests for the first time the adequacy of federal regulatory mechanisms in the field of genetic engineering. Powerful scientific breakthroughs are raising such novel and complex questions that prescriptive regulation is all but impossible within the existing regulatory framework.

The Reagan Administration is reluctant to impose any new regulations which may risk compromising the United States' lead in this promising new technology.[163] Federal regulatory agencies, attempting to establish control over the new technology through inapplicable and inadequate existing laws, are creating a patchwork of conflicting regulatory policies.[164]

While federal regulatory mechanisms are currently deficient, it would be premature to call for comprehensive regulation at this time. As the Lindow experiment demonstrates, the environmental risks associated with direct release experiments are due not to the fact that the experimental organisms are genetically engineered, but rather to the fact that the organisms are exotic to the environment. Scientists do not yet have the ability to predict how a novel organism will interact with a given ecosystem. It is therefore impossible to regulate environmental releases within the constraints of current scientific understanding.

To permit development of risk assessment protocols, it is necessary at this time to proceed with carefully selected and closely monitored deliberate release experiments. Data from these experiments can be used to develop uniform guidelines for the review of proposals for future direct release experiments. While it may never be possible to predict with complete certainty the risk of ecological harm harbored within each new genetically engineered organism, it is the function of federal oversight to insure that the risks associated with scientific progress are minimized.

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163. Rhein, *Splicing Together a Regulatory Body for Biotechnology*, Bus. Wk., Jan. 14, 1985, at 69.

164. For TSCA to apply, life forms must fit the definition of "chemicals." FIFRA exempts environmental releases of less than ten acres. Compliance with the NIH Guidelines is voluntary for industry.