Regulation for the Deliberate Release of Biotechnology Products[1]

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ABSTRACT. The use of living organisms to make or modify products is ancient. The 1980s brought widespread use of novel genetic engineering techniques for modifying the hereditary characteristics of living organisms. In response, rulemakers formed a federal biotechnology policy.

Articulated federal policy for biotechnology holds that existing laws, as currently implemented, address regulatory needs adequately. The agencies that administer federal laws have found several significant laws to be adequate. These are: The Federal Food, Drug, and Cosmetic Act (FDCA), the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Toxic Substances Control Act (TSCA), the Federal Plant Pest Act (FPPA), the Plant Quarantine Act (PQA), and the Virus-Serum-Toxin Act (VST). The National Institutes of Health's "Guidelines for Research Involving Recombinant DNA Molecules" have also set standards for experimental containment and release.

Lawsuits brought by the Foundation on Economic Trends against federal agencies have sought to prevent deliberate release experiments. These lawsuits have alleged violations of the National Environmental Policy Act (NEPA). This act is a Federal procedural statute that all agencies must comply with unless their actions are found to be functionally equivalent to the NEPA requirements.

This survey paper reviews federal agency publications, reported cases, newspaper articles, federal statutes, federal regulations, and telephone conversations with key participants. The review covers only deliberate release of genetically engineered products into the environment. It excludes product licensing by the Food and Drug Administration. The following discussion first addresses federal regulations and policy to control deliberate release experiments, and then reviews litigation initiated to prevent deliberate release experiments.

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INTRODUCTION

In 1975, leading scientists gathered at Pacific Grove, California to discuss the safety of genetic engineering. The first effective restriction enzymes had become available in 1970, through the work of H. Smith at Johns Hopkins University. In 1973, Boyer and Cohen had announced the first universally effective method for making recombinant DNA (Watson 1986). The Conference at Pacific Grove reflected public concern that new, genetically engineered life forms might threaten public health or cause undesirable social changes.

The following year the National Institutes of Health (NIH), through the Recombinant DNA Advisory Committee (RAC), began reviewing research protocols for recombinant DNA (rDNA) experiments. The NIH published safety standards in 1976 under the title "Guidelines for Research Involving Recombinant DNA Molecules" (NIH 1976). For roughly a decade, RAC approval under the Guidelines functioned as the only review process that specifically addressed risks unique to genetic engineering.

By the mid-1980s, federal regulation of biotechnology activities had blossomed. In 1986, federal rulemakers announced a revised comprehensive, interagency regulatory scheme for organisms and products created through biotechnology. Articulated federal biotechnology policy holds that existing laws, as currently implemented, address regulatory needs adequately.

During the 1970s and 1980s, lawsuits to prevent deliberate release experiments also flourished. These suits alleged violations of the National Environmental Policy Act (NEPA). NEPA is a federal procedural statute which requires federal agencies to assess the effects of their proposed actions on the human environment and human health.

DISCUSSION

FEDERAL REGULATIONS AND POLICY TO CONTROL DELIBERATE RELEASE EXPERIMENTS. The National Institutes of Health (NIH) has traditionally provided financial support for basic biomedical research. Oversight of biotechnology research is relatively new. The Re-

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combinant DNA Advisory Committee's legal jurisdiction has always been limited to recombinant DNA research at institutions that receive any support for rDNA research from NIH. The NIH can penalize failure to comply by withholding funds. It has never had regulatory authority over projects conducted by most commercial biotechnology firms, nor has it reviewed bioengineering techniques other than research involving rDNA molecules. Despite the introduction into Congress of bills that would have imposed the NIH Guidelines on private industry, no such Federal statute was enacted (Gore 1986).

Notwithstanding RAC's limited jurisdiction, it is widely believed that from 1976 to the present most institutions performing rDNA research complied voluntarily with the guidelines. By the mid-1980s, biotechnology had emerged as a commercial force. Novel techniques for modifying the genetics of living organisms, such as cell fusion, hybridoma technology, and somatic cell culture came into widespread use, often for purposes that were ultimately commercial (Jaworski 1986). Public research institutions and private firms developed products intended for deliberate release into the environment. This raised questions about the appropriate regulation.

By 1983, the RAC and NIH had approved three government-sponsored applications for the deliberate release of rDNA products. One application submitted by Drs. N. Panapoulos and S. Lindow at the University of California proposed to test a gene-deleted, frost-inhibiting bacterium. Dr. R. Davis of Stanford University requested approval to test corn plants with added genes; Dr. J. Sanford of Cornell University wanted to field-test tomato and tobacco plants transformed with bacteria and yeast DNA. Litigation brought by the Foundation on Economic Trends halted the field tests. Congressional concern resulted in a hearing on 22 June 1983 by a Congressional Subcommittee on Investigations and Oversight. Albert Gore, Jr. chaired the hearing. A resulting staff report was released in February, 1984 (Subcommittee 1983).

The Subcommittee found that federal agencies lacked the expertise and experience to evaluate deliberate releases of live, genetically engineered organisms. While recognizing the leadership of the RAC, the staff report urged greater involvement by the Environmental Protection Agency (EPA). It suggested a General Accounting Office (GAO) investigation of whether the Department of Agriculture (USDA) should assume greater regulatory responsibility. The RAC was urged to stop reviewing, under its voluntary compliance policy, projects not getting NIH funds. The subcommittee also recommended an interagency panel to facilitate cooperation among federal agencies. It recommended the inclusion of experts specifically trained in ecology and environmental science on review committees within the NIH and USDA (Subcommittee 1984). The USDA's review committee had not then assumed regulatory duties.

In 1984, the Cabinet Council on Natural Resources and the Environment formed an interagency working group. On 31 December 1984, the working group published in the Federal Register a 51-page proposal, with contributions from four federal agencies. The U.S. Department of Agriculture (USDA), the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA), and the Office of Science and Technology Policy (OSTP) published policy statements. A 28-page matrix addressed statutory jurisdiction among the agencies for every imaginable product at every commercial stage, from the research laboratory to final distribution and disposal. This occurred at a time when not one product of the new bioengineering was ready for licensing. The voluminous interagency document formed the basic structure for emerging biotechnology regulation (OSTP 1984).

On 14 November 1985, the Office of Science and Technology Policy published a revised "Coordinated Framework for Regulation of Biotechnology." This document responded to public comment in accordance with the notice and comment provisions of the Administrative Procedure Act. It also established the Biotechnology Science Coordinating Committee (BSCC). This interagency committee included senior representatives from agencies involved in biotechnology regulation. The BSCC does not conduct any second-level review of applications under consideration by the federal agencies. Instead its charter stresses interagency coordination and information sharing (OSTP 1985).

In the spring of 1986, the GAO published results of its requested investigation of USDA review procedures. It characterized the USDA's review procedure as confused and disorganized. The GAO found that the rDNA review committee for agriculture had almost no authority, met infrequently, had no budget, and could express no clear mission (Hilts 1986).

The Office of Science and Technology Policy published a third, revised "Coordinated Framework for Regulation of Biotechnology" in June, 1986. Within this document some agencies modified policy positions. The publication reflected efforts of the newly formed, interagency Biotechnology Science Coordinating Committee (BSCC) to clarify statutory definitions and achieve uniform levels of review among agencies. Most important, the publication endorsed previously articulated federal biotechnology policy: that existing laws, as currently implemented, address regulatory needs adequately. The regulatory scheme, as previously announced, assigned responsibility among the traditional, existing agencies according to product use (OSTP 1986).

The Food and Drug Administration (FDA) would license new drugs and biologics for human use, new animal drugs, and new medical devices created through biotechnology. Should new products of biotechnology be marketed as food, the FDA would maintain its traditional regulatory duties (FDA 1986). The agency would apply established regulations promulgated under the Federal Food, Drug, and Cosmetic Act. These regulations require proof of safety and efficacy (FDA 1986).

The Environmental Protection Agency (EPA) would regulate live microbial products used as pesticides, under authority granted by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The EPA would regulate genetically engineered microorganisms used for commercial purposes under the Toxic Substances Control Act (TSCA). Under authority granted by these and other acts, the EPA would monitor all stages of product development from field tests through final disposal.

Excepted from EPA control were non-pesticidal, live microbial products intended only for agricultural use.

These would fall under USDA jurisdiction. The USDA and EPA would share information on releases of a few kinds of microorganisms that fall within the statutory mandate of both agencies (EPA 1986).

The USDA, through its Animal and Plant Health Inspection Service (APHIS), would regulate the introduction of any genetically engineered organism or product that is or may reasonably be a plant pest. Authority would spring from the Federal Plant Pest Act (FPPA) and the Plant Quarantine Act (PQA). New regulations became effective in July, 1987. These are the first final regulations exclusively addressing biotechnology. The USDA would also continue to license genetically engineered veterinary biologics such as the pseudorabies vaccine under the Virus-Serum-Toxin Act (USDA 1986).

The NIH would fund and approve biomedical experiments which come under its Guidelines. Authority would be limited to institutions receiving NIH support for rDNA research. The NIH would also continue to review proposals submitted voluntarily by private firms, but would address only those proposals that fall outside the authority of any federal agency (NIH 1986).

The NIH review procedures have provided a model for other agencies. With the June, 1986 policy statement, the USDA Cooperative State Research Service published a "Notice of Intent to Propose Research Guidelines." The first draft emulated the NIH Guidelines but covered other genetic engineering techniques in addition to rDNA research. It applied to federally funded agricultural research not supported and regulated by another federal agency (USDA 1986b).

Subsequently, regulators from several agencies initiated an effort to have only one set of federal research guidelines. As a result, the upcoming revised NIH Guidelines should contain some provisions for whole plants and animals. The USDA may then publish a "Part II" for agricultural research, which would deal with bioengineering research other than rDNA experiments and would cover the entire spectrum of living organisms. According to Dr. D. Jones (pers. comm.) at USDA/OAB, this unified approach would minimize conflicts created from applying two similar, but different, sets of guidelines. Access to a unified set of guidelines is important for institutions funded by both the NIH and the USDA.

The evolution of the NIH guidelines reflects growing experience with rDNA regulation. The original guidelines, published in 1976, outlined laboratory containment procedures only (NIH 1976). Deliberate release of organisms containing rDNA was not permitted. Currently, the Guidelines classify experiments according to biosafety level. Deliberate release of an organism containing rDNA is a Class III-A experiment, requiring RAC review, specific NIH approval, and publication in the Federal Register. The Guidelines also include, however, Class III-D experiments. These are exempt even from approval by Institutional Biosafety Committees (IBC) at the research institution level (NIH 1986). Many rDNA plant applications now fall into this category, but may require APHIS approval if they are deemed regulated articles and are introduced under terms of the regulation.

Today's guidelines require each research institution to support or affiliate with a committee of experts that will review projects at the institution's level. Every Institutional Biosafety Committee (IBC) must include experts in rDNA technology, containment, and biological safety. Each IBC must consult with persons who know about institutional commitments and policies, applicable law, professional standards, community attitudes, and the environment. At least one member must be from a laboratory technical staff. For experiments other than Class III-A, the IBC can provide the only review. The NIH encourages public IBC meetings and open communication with local communities. The public can obtain minutes of IBC meetings upon request (NIH 1986).

THE FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA). The Environmental Protection Agency assumed regulation of genetically engineered microbial releases in 1984 (EPA 1984). The EPA's authority rested on a federal statute that granted authority to regulate products used as pesticides. This was the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended in 1972. This act broadly defined the term "pesticide" as "any substance or mixture . . . intended for preventing, destroying, repelling, or mitigating any pest, and . . . intended for use as a plant regulant, defoliant, or dessicant" (FIFRA 1972). Regulators started treating frost-inhibiting bacteria and similar products as microbial pesticides.

The Federal government registered the first microbial pesticide, *Bacillus popilliae,* in 1948. It was not until 1984 that the EPA promulgated regulations on microbial pesticides (CFRb). The agency has applied them to genetically engineered microorganisms used as pesticides, as well as to non-engineered ones (EPA 1986).

The Federal Insecticide, Fungicide, and Rodenticide Act gives the EPA authority over the distribution, sale, and use of pesticide products. It also operates as a registration statute. No one can market a pesticide commercially until it is registered with the EPA under FIFRA. The Environmental Protection Agency supervises preregistration activities through an Experimental Use Permit (EUP) system. The producer of a live microbial pesticide submits data to the Agency. After reviewing the data the Agency may issue an Experimental Use Permit. At the Agency's discretion, the application for an EUP or the application for final registration can result in public notice. This occurs by publication in the Federal Register (CFRc).

Traditionally, many small-scale field tests were exempted from obtaining EUPs. A small-scale test involves environmental application on 10 acres or less of land or 1 surface acre or less of water. In 1985, the EPA announced an Interim Policy that imposed higher preregistration scrutiny for small-scale field tests of microbial pesticides. The Agency clarified this policy in 1986. Currently, even small-scale field tests of deliberately created intergeneric microorganisms require EPA notification and review. The same is true for deliberately created intrageneric ones with pathogenic source organisms. Intergeneric refers to those products containing genetic material from source and recipient organisms of different genera. All non-indigenous microorganisms, as well, will face the new data submission requirements.

The EPA contends that these types of microorganisms may behave unpredictably in the environment. It will revise EUP regulations accordingly. Excepted from the Interim Policy are intergeneric microorganisms created

from different genera, where only well-characterized, non-coding regulatory regions are transferred (EPA 1986).

To date, several tests of microbial pesticides in the field have occurred under FIFRA. The Monsanto Company asked to test in the field a genetically engineered bacterium that would, it was hoped, repel rootworms. The Agency requested further tests which the company has not submitted. The EPA granted Advanced Genetic Science's application to test frost-inhibiting bacteria in the field, and then revoked permission when officials discovered that scientists had tested the bacteria under tree bark on a roof top. After paying a fine, the company again gained EPA approval and conducted field tests. Dr. S. Lindow's much delayed field test of frost-inhibiting bacteria took place in the spring of 1987.

THE TOXIC SUBSTANCES CONTROL ACT (TSCA). Clearly, many genetically altered microbes and the like can never fall under FIFRA's qualifier "used as a pesticide". Recognizing this, the EPA now regulates many microorganisms as new chemicals under Section 5 of the Toxic Substances Control Act (TSCA). These include microorganisms that will be used to degrade toxic pollutants, leach minerals, enhance oil recovery, and produce industrial chemicals (EPA 1986). Congress enacted TSCA in 1976 to correct the then uneven and piecemeal regulation of chemicals believed to be toxic (Congressional Advice and News 1976). The statute covers those chemicals that are unreasonably risky to human health or the environment.

Substances and mixtures intended for commercial use are regulated by TSCA. The EPA has interpreted the terms "substances and mixtures" to include organic substances. This brings DNA molecules, other nucleic acids, and constituents of cells into the agency's jurisdiction under TSCA (EPA 1984). The statute specifically exempts all pesticides, tobacco products, nuclear materials, feeds, food additives, drugs and cosmetics (TSCA 1976).

The Toxic Substances Control Act operates through a published chemical substances inventory. The initial inventory of all chemicals manufactured or processed in the United States consisted of some 43,000 substances (EPA 1979). Detailed testing of the now over 60,000 listed chemicals would be impossible. However, TSCA requires the EPA to set test rules for those chemicals that may present an unreasonable risk to human health and the environment. A priority list, revised every 6 months, contains 50 or fewer selected chemical substances. Within 12 months of the listing of a chemical on the priority list, the Agency must start writing a test rule or explain publicly why it has not done so.

All new chemicals and all new uses of old (listed) chemicals undergo EPA scrutiny under TSCA before manufacture or importation commences. At least 90 days before importing or commencing manufacture of a new chemical, its manufacturer or distributor must file a Premanufacture Notification (PMN). Section 5 of TSCA establishes this statutory requirement. The PMN must include data sufficient for the EPA to decide whether the substance presents an unreasonable risk of injury to human health or the environment (TSCA 1976).

Naturally occurring chemicals have traditionally enjoyed exemption from the PMN requirements, even though they are unlisted on the inventory. The reporting rules have always distinguished new from naturally occurring chemicals according to the level of human intervention (CFRd). One of the most criticized aspects of the EPA's December, 1984 policy statement was its application of this principle to live microorganisms. The agency articulated a "process" approach, justified by the lack of distinct taxonomic categories for microorganisms (EPA 1984).

The EPA attempted to list processes that would mandate full agency review. These included *in vitro* synthesis, rDNA, rRNA, and cell fusion. The agency took no position regarding transformation, transduction, transfection, promotion of plasmid transfer and conjugation, and undirected mutagenesis (EPA 1984). Distinguishing new from naturally occurring microorganisms according to the process by which they were developed produced inconsistent results. The manufacture of a chemical substance through modern biotechnology triggered heightened review, even where the identical microorganism existed in nature.

In its June, 1986 policy statement, the EPA deemphasized the degree of human intervention as a test for newness of a chemical. The agency now considers the following to be new chemical substances: microorganisms deliberately formed to contain genetic material from different genera, except where only well-characterized, non-coding, regulatory regions are transferred. Intrageneric and non-engineered microbes will be considered naturally occurring (EPA 1986).

The EPA acknowledged a category of living organisms which, although not new, should also receive a high level of scrutiny. These are genetically engineered, intergeneric or even intra-generic microorganisms that are pathogenic or contain genetic material from pathogens. Any release of these chemical substances into the environment will be considered a significant new use, subject to full review under TSCA. The notification requirements are similar to those for new chemicals.

It is widely believed that no genetically engineered products that fall under TSCA have progressed beyond research and development. Under the statute, chemical substances manufactured in small quantities solely for research and development have traditionally enjoyed an exemption from Premanufacture Notification. In 1986, the EPA expressed an intention to narrow this exemption. It published a statement that limited exposure and limited risk should not be assumed for any field-tests of living organisms. Amended regulations will probably specify that, for the research and development exemption, many field-tests of microorganisms should fall outside the statutory definition of small quantities (EPA 1986).

Until new regulations are published, commercial researchers intending to release new, living organisms must report prior to commencing activities. The same is true for commercial researchers planning to release many genetically engineered pathogens. Purely noncommercial research and development would retain its exemption from Premanufacture Notification.

To date the EPA has permitted no open release of live microorganisms treated as chemicals subject to TSCA. However, the agency is currently in the process of reviewing a nitrogen-fixing product developed by Biotechnica. This is *Rhizobium meliloti,* a nitrogen-fixing

microorganism to be tested on alfalfa. Scientists have added another gene from the *R. meliloti* itself, making this an intrageneric organism under the EPA definitions.

It is inescapably true that many non-engineered commercial chemicals that are quite dangerous escape regulation by the EPA. Currently, the chemical substances inventory, which lists chemicals already in production, includes over 60,000 chemicals. The agency lacks the resources to even select those chemicals that should undergo testing. As of January, 1985, it had taken action to regulate existing chemicals on only six occasions since TSCA was enacted (Florio 1985).

Notwithstanding the existing toxic chemicals problem, public concern has caused the agency to focus on new biotechnology products. The policy will be to scrutinize microorganisms used in the environment which may be pathogenic or which may contain new combinations of traits. The EPA is currently replacing its scientific advisory panels with a formal Scientific Advisory Committee for Biotechnology. This group will consist of members of the lay public and independent scientists, and will review scientific proposals submitted under all EPA statutes. It will also oversee biotechnology regulations.

THE FEDERAL PLANT PEST ACT AND PLANT QUARANTINE ACT (FPPA). The USDA's Animal and Plant Health Inspection Service (APHIS) has promulgated the first final rule that exclusively governs biotechnology products. The new regulations, which control genetically engineered organisms and products that are plant pests, became effective on 16 June 1987. The final regulations also control genetically engineered organisms and products which administrators have reason to believe are plant pests. The regulations apply only to the introduction of these organisms. Introduction, as used within the final rule, refers to importation, interstate movement, or environmental release (CFRe).

The Federal Plant Pest Act (FPPA) defines plant pest as any of a variety of listed life forms "which can directly or indirectly injure or cause disease or damage in any plants or parts thereof, or any processed, manufactured or other products of plants" (FPPA 1957). Federal regulations delegate actual regulation under the Act to the Deputy Administrator of the Plant Protection and Quarantine Program, Animal and Plant Health Inspection Service (USDA 1987).

The Federal Plant Pest Act does not expressly authorize regulation of environmental releases. Its terms cover only importation and interstate movement (USDA 1987). Nevertheless, the new final regulations contain provisions requiring a permit prior to release into the environment of certain genetically engineered organisms, or of products containing such organisms (CFRe). USDA attorneys maintain that the new deliberate release provisions constitute a reasonable construction of the USDA's statutory responsibilities. This position is strengthened by the broad grants of authority contained in the Plant Quarantine Act (USDA 1987).

The new final rule for biotechnology applies only to those genetically engineered organisms that are deemed "regulated articles." It defines regulated articles with reference to a list of all genera or taxa that may contain plant pests. Determination of whether a genetically engineered product is a regulated article is a two-step process. The first test is whether the donor organism, recipient organism, vector, or vector agent belongs to any listed genus or taxon. Second, within any listed genus or taxon, only those organisms that meet the regulatory definition of plant pest are regulated articles.

Where the first test is met, unclassified organisms and those for which classification is unknown can also trigger regulated article status. The same is true for products containing plant pests, and for any other organisms or products which the Deputy Administrator determines or has reason to believe are plant pests. Excluded from the definition of regulated articles are recipient microorganisms that are not plant pests and that have resulted from the addition of genetic material from a donor organism, where the material is well characterized and contains only non-coding, regulatory regions (CFRe).

Interstate movement or importation of a regulated article requires a limited permit, obtained in advance. Generally the regulations require the USDA to complete its review 60 days after receiving the completed application. For interstate movement only, the responsible person can apply for a limited permit valid for the movement of multiple articles, and can also apply for a limited permit valid for multiple destinations. These permits are good for 1 year.

Applications for release into the environment involve a 120-day maximum review period. This reflects the necessity to conduct an environmental assessment prior to the issuance of such a permit. The application itself requires submission of data on the identity of the donor organism, recipient organism, and vector or vector agent. Additionally, the application requires a description of how the genetically altered material in the regulated article differs from that in the non-modified, parent organism. The responsible person must describe purpose, quantity, location and procedural safeguards for the planned field test. The USDA estimates the in-house cost for each application for release at $5,000 (CFRe).

For all permit applications, state notification is an integral part of the review process. Standard permit conditions can be supplemented by APHIS, where appropriate. The Biological Assessment Support Staff (Biotech Unit) of APHIS is now in place and has begun taking permit applications under the final regulations.

THE VIRUS-SERUM-TOXIN ACT (VST). The USDA's Animal and Plant Health Inspection Service (APHIS) regulates, among other things, the field testing and licensing of animal biological products. Authority springs from the Virus-Serum-Toxin Act of 1913 (VST 1913). This statute requires licensing for any virus, serum, toxin, or analogous product intended for use in the treatment of domestic animals. Under the statute no license shall be issued unless the product was prepared in compliance with regulations prescribed by the Secretary of Agriculture (VST 1913).

The USDA has enunciated what it will consider an animal biologic. A federal regulation defines the term to include "all viruses, serums, toxins, and analogous products of natural or synthetic origin . . . intended for use in the diagnosis, treatment, or prevention of disease in animals (CFRa). This language covers genetically engineered, live viruses such as the one in the controversial genetically modified pseudorabies vaccine (USDA 1986).

The Virus-Serum-Toxin Act prohibits licensing of

worthless, contaminated, dangerous, or harmful products. The USDA has therefore promulgated regulations to measure purity, safety, potency, and efficacy. Its permit system involves well established tests. Producers submit a detailed outline of production. The relevant master seed, primary cells, and cell line undergo testing. Genetic stability and purity must be established even for non-engineered entities. Host animal studies supplement laboratory tests to measure safety, potency, and efficacy (CFRa).

A controversial licensing action under the Virus-Serum-Toxin Act occurred in the spring of 1986. This concerned the gene-deleted pseudorabies vaccine developed by Biologics Corporation of Omaha, Nebraska. According to M. Bartkoski (pers. comm.), Vice President of Operations, the company conducted extensive field tests in cooperation with the USDA and state veterinary authorities. After laboratory and field tests, APHIS granted the license to market the product.

The Foundation on Economic Trends challenged the USDA's actions in federal courts. The Foundation's first claim arose under the Administrative Procedure Act. For most licensing, a federal agency must demonstrate in the record that it used reasoned decision-making. The Foundation claimed that the USDA ignored its own policies in licensing the modified pseudorabies vaccine. This, according to E. Rogers (pers. comm.), attorney for the Foundation, constituted arbitrary and capricious decision-making.

Specifically, the Foundation alleged existence of a published USDA policy for all research involving recombinant DNA molecules. Allegedly, the USDA's own policy was to withhold licensing where an applicant failed to comply with the NIH Guidelines for Research. The Foundation relied on USDA statements in the Federal Register that all research involving recombinant DNA must meet the NIH guidelines.

The USDA insisted that review channels depended completely on the type of genetic engineering used to develop the vaccine. According to Dr. D. Espeseth (pers. comm.), Chief Staff Veterinarian at USDA-APHIS-VS, the modified virus was not a true recombinant organism because no new genetic material was added to it. The vaccine was derived by using rDNA techniques to delete a Thymidine kinase gene. This category of products was exempt from the policy which might have imposed NIH guidelines. Several members of the Agriculture Recombinant DNA Research Committee disagreed with this official position (Schneider 1986).

The USDA held that the relevant issue was whether the agency complied with regulations under the Virus-Serum-Toxin Act (VST) for ensuring purity, safety, potency, and efficacy. The agency asserted that rigorous testing had established, according to regulations, those qualities. Tests on laboratory animals, host animals, and other animals compared the new virus with its parent. The altered virus, as intended, proved less virulent. The pseudorabies vaccine was the first product of its kind to undergo licensing under VST, because it contained a living virus with a single gene deleted. However, the USDA claimed considerable experience regulating non-engineered vaccines containing naturally occurring live viruses. In addition, the agency had granted 12 licenses for genetically engineered biologics. All of these licenses had involved inactive or killed viruses and organisms.

The pseudorabies litigation, including a second claim discussed below, is ongoing. During the pendency of litigation, administrative review channels within the agency appear to have clarified. Currently, the Veterinary Services Biotechnology Committee for the Veterinary Services branch of the USDA provides advice and council to the Deputy Administrator concerning the approval of environmental assessments and pending releases. This is true for all genetically engineered veterinary biologics. The agency-wide Recombinant DNA Research Committee approves research projects only (D. Espeseth pers. comm.). The vaccine has been marketed under the brand name "Omnivac" with no reported problems.

The Virus-Serum-Toxin Act originally governed only the interstate shipment and importation of products intended for use in domestic animals. Recent amendments contained in the Food Security Act of 1985 have extended this authority to products shipped intrastate and exported (USDA 1986).

LITIGATION TO PREVENT DELIBERATE RELEASE EXPERIMENTS. Deliberate release of a new organism involves the grandfather of environmental statutes, The National Environmental Policy Act (NEPA 1969). This statute, passed in 1969, proclaimed a national policy to pursue harmony between man and nature and called upon all federal agencies to cooperate toward this end. Prior to NEPA some federal agencies had claimed that their enabling statutes granted no authority in environmental matters (NEPA 1969).

The National Environmental Policy Act requires federal agencies to weigh the environmental consequences of all major actions that significantly affect the human environment by compiling an Environmental Impact Statement (EIS). An EIS is a document containing detailed descriptions of expected environmental or human health effects of undertaking a particular alternative. Compilation of an EIS can take several years. It must set out all known risks from the federal action and must describe alternative actions (NEPA 1969). The EPA monitors compliance. Each week the EPA publishes a notice in the Federal Register of all EISs received. The public, other agencies, and higher level agency officials can review the document upon request. The agency wanting to take action can make no decision until the required time for comment has expired.

The National Environmental Policy Act requires a full EIS only for major federal actions having a significant effect on the human environment or human health (NEPA 1969). For actions that are not categorically excluded, federal agencies must employ an abbreviated review called an Environmental Assessment (EA). An EA determines whether the potential impact of a proposed alternative is so great that an EIS must be written. The EA may result in a finding of no significant impact on human health or the environment. In that event the proposed action may proceed immediately.

Like the more comprehensive analysis, an EA is supposed to be a public document (CFRf). The delay associated with an EA can be quite short for new biotechnology products. According to M. Bartkoski (pers. comm.) of Biologics Corporation, an EA can be assembled in several weeks. Instead of having to start from scratch, the staff can assemble data from tests already

conducted. It is important to note that the public must have access to the EA upon request. The USDA's Animal and Plant Health Inspection Service, for instance, publishes the availability of the EA 30 days prior to the commencement of field testing.

It is well established that federal regulating and licensing can constitute major federal action. Determination of whether a biotechnology project results in significant risk to human health or the environment is more difficult. If the resulting life form is new, regulators lack a broad data base. Scientists must compare survivability and other behavior of the modified life form with that of the parent.

In 1984, EPA scientists articulated the view that modern biotechnology techniques increase the risk of creating a broader host range, a new toxin, enhanced virulence, greater survivability, or greater competitiveness. Further, even if experts could perfectly predict the behavior of new life forms, they lack methods to predict the ultimate effect on the ecosystem (EPA 1984). This has never been the position of the USDA, which has stated that it does not believe most genetically engineered products will differ significantly from conventionally produced products (USDA 1984).

Early litigation involved the failure of federal agencies to conduct adequate EAs under NEPA. Two of the first three field tests approved by the Recombinant DNA Advisory Committee (RAC) involved plants. Presumably, these experiments eventually went forward under revised guidelines. The third, the field test of a frost-inhibiting bacterium, became ensnared in litigation involving the National Environmental Policy Act (NEPA 1969). Dr. S. Lindow and his colleagues at the University of California at Berkeley had developed the bacterium. In 1984, environmental activist J. Rifkin, with the Foundation on Economic Trends and others, brought a lawsuit that halted small scale field-tests.

In federal court, the plaintiffs alleged that the NIH had failed to perform an adequate EA on the Lindow experiment. Plaintiffs also alleged that a programmatic EIS was needed on the NIH decision to allow deliberate release experiments on a case-by-case basis. The U.S. District Court Judge issued a preliminary injunction against the Lindow experiment. The Court also prohibited the NIH from approving more field tests until a programmatic EIS was completed. In 1985, the U.S. Court of Appeals upheld the injunction regarding the Lindow experiment. The Court of Appeals based its decision on the absence from the record of any formal EA, deeming the RAC review procedurally inadequate. However, the Court of Appeals lifted the injunction against all NIH approval of deliberate release experiments (Foundation on Economic Trends v. Heckler 1984).

Because the RAC lacks jurisdiction over private companies not receiving NIH funds, the federal injunction specifically exempted private firms. Nevertheless, it is believed that two other firms, Cetus Madison and Biotechnica, voluntarily suspended their proposed field tests.

The Foundation on Economic Trends again charged noncompliance with NEPA as its second claim in the suit against the USDA over the pseudorabies vaccine (discussed earlier). Like the NIH, the USDA enjoys no exemption from NEPA. Therefore, the USDA must prepare an EA on its actions that are not categorically excluded.

The Foundation questioned the adequacy of containment measures for live viral vaccines, and maintained that injection into animals constituted a release into the environment (E. Rogers pers. comm.). The USDA has always contended that in normal husbandry and laboratory practices, veterinary biological products are not considered released into the environment. The USDA suspended the license for 2 weeks, however, while an EA was prepared. This document contained a finding of no significant impact; subsequently, the vaccine was marketed under the name "Omnivac."

Litigation continues regarding the licensing of the pseudorabies vaccine; arguments are ongoing. In the interim, the USDA has approved field trials of a second live, viral vaccine. This product has two genes deleted. For the second product USDA conducted an EA. Notice in the Federal Register asserted no significant impact on human health or the environment. Field tests of this product remain unchallenged.

Mr. J. Rifkin and The Foundation on Economic Trends have alleged NEPA violations in several other lawsuits concerning modern biotechnology. In 1985, Retired Admiral G. La Rocque and Major General W. Fairborn (USMC RET) joined the Foundation in suing the Department of Defense. The plaintiffs sought to enjoin construction of a biological test laboratory which would house aerosol experiments. In 1985, the plaintiffs obtained a permanent injunction, based on inadequacy of the EA. The defendants are now conducting a full environmental assessment. Mr. Rifkin and the Foundation filed suit against the FDA to require an EIS for Bovine Growth Hormone (Foundation 1986). This litigation is ongoing.

The USDA has on several occasions conducted an EA after suit by Mr. Rifkin and the Foundation. One suit alleged negligence as well as NEPA violations regarding USDA management of the gene bank program (Foundation 1985a). Another complaint, still under litigation, attacked licensing procedures for a genetically engineered pseudorabies vaccine (New York Times 1986).

One criticism of NEPA is that it can become a perfunctory requirement. Frequently, a lawsuit brought under NEPA serves to delay, but not change, federal action. The statute by its terms requires only investigation and consideration of a project's expected impact. Decision-making remains with the federal agency. Where a private firm has applied for federal licensing, that firm will usually provide the data necessary for an EA. Undeniably, experts hired by the government or by private industry have an economic incentive not to undermine their employers. The agency will often conduct an EA in order to comply with NEPA and subsequently will proceed with the project.

The National Environmental Policy Act is a federal procedural statute that requires compliance by all agencies, unless their actions are found to be functionally equivalent to the NEPA requirements. Actions by the Environmental Protection Agency itself do not require publication of an EIS. This implied exemption recognizes the EPA's regulatory and statutory mission to protect the environment.

CONCLUSIONS

Representative J. J. Florio, at a Brookings Institute Conference, has called the federal biotechnology policy "sham regulation" which will lull the public into a false sense of security. According to Mr. Florio, the EPA is already burdened with obligations exceeding its resources, and, even if biotechnology products are excluded, has failed to cure the toxic chemicals problem in the United States (Florio 1985). The latter comment is probably unfair because the toxic chemicals crisis developed before the EPA got jurisdiction under TSCA and other statutes. In contrast, regulators have been involved from the outset in monitoring novel products of biotechnology.

A second criticism has been leveled at federal biotechnology policies by scientists involved in basic research. The scientists complain that regulation interrupts their research projects capriciously and unnecessarily, even where risk is low, and potential for human progress is high. This has been a valid criticism, particularly for early projects. Additionally, many scientists have questioned the scientific basis for regulating genetically engineered products any differently from identical products created through traditional means.

With their unified policy statements, existing federal agencies have attempted to establish regular review channels to expedite federal evaluation. The federal review process is unpopular with scientists, often understandably so. However, most scientists agree that federal control is preferable to a patchwork of state and local policies that would almost certainly result in the absence of federal action. The alternative of creating a new federal bureaucracy to approve all biotechnology products is unworkable, and has never been seriously considered. Biotechnology products are too diverse for such a solution.

Release of genetically engineered microorganisms into the environment raises several valid concerns. Their ability to mutate quickly in nature and to multiply rapidly under favorable conditions distinguishes them from other organisms. This, together with the already overwhelming problems concerning traditional commercial chemicals, suggests that the largest portion of new dollars for environmental regulation ought to support EPA activities under TSCA. In addition, APHIS now regulates many genetically engineered microorganisms that are or may be plant pests. These activities also demand adequate funding.

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——— e Title 7, Part 340, effective June 16, 1987.

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