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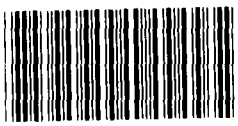
Report to the Chairman, Committee on Science and Technology
House of Representatives

March 1986

BIOTECHNOLOGY

Agriculture's Regulatory System Needs Clarification



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GAO

United States
General Accounting Office
Washington, D.C. 20548

Comptroller General
of the United States

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March 25, 1986

The Honorable Don Fuqua
Chairman, Committee on Science and Technology
House of Representatives

Dear Mr. Chairman:

Your letter dated March 29, 1984, asked us to review U.S. Department of Agriculture activities that related to biotechnology. Two reports have resulted from this request. The first one, entitled The U.S. Department of Agriculture's Biotechnology Research Efforts (GAO/RCED-86-39BR, Oct. 25, 1985), provided an otherwise unavailable inventory of biotechnology research projects funded in whole or in part by the Department of Agriculture in fiscal years 1984 or 1985. This report discusses, among other things, the Department of Agriculture's programs and activities that relate to biotechnology and affect decision-making concerning the release of genetically engineered organisms into the environment.

As arranged with your office, unless you announce its contents earlier, we plan to distribute copies of this report to other interested committees; the Director, Office of Management and Budget; and the Secretary of Agriculture, 14 days after the date of the report. Copies will also be made available to other interested parties.

Sincerely yours,

for Charles A. Bowsher
Comptroller General
of the United States

Executive Summary

Biotechnology includes "any technique that uses living organisms . . . to make or modify products, to improve plants or animals, or to develop microorganisms for specific uses." It involves new, nonsexual techniques enabling man to move genes from one organism to another, related or unrelated. (See p. 8.)

Some say that the new biotechnologies can help provide for mankind's most basic needs—from health care to food supplies. Others are concerned about the detrimental effects to public health and the environment that might occur from deliberately releasing genetically engineered organisms into the environment. Consequently, the House Committee on Science and Technology asked GAO to obtain information on the U.S. Department of Agriculture's (USDA's) (1) programs and activities that relate to biotechnology, (2) decision-making concerning the release of genetically engineered organisms into the environment, and (3) relationships with other federal agencies involved in biotechnology. GAO also obtained information on the extent to which USDA has communicated to others its views on biotechnology and the regulatory role it will play. (See pp. 12 and 15.)

Background

No evidence exists that harmful, genetically engineered organisms have been created, but few experts believe that the new biotechnologies are without risk. This potential risk and biotechnology's broad application have led several federal agencies, including USDA, to regulate the research and commercialization of biotechnology. The technique of prime interest and concern involves rearranging the DNA (a molecular substance that controls hereditary traits) of living organisms and is referred to as "recombinant DNA" or "genetic engineering." (See p. 18.)

USDA helped formulate early policy decisions concerning recombinant DNA research and has helped develop the new biotechnologies. Its future involvement will likewise be significant because much of the research in biotechnology is agriculturally oriented. Until recently, regulations required the containment of genetically engineered organisms in research laboratories, and the National Institutes of Health-Recombinant DNA Advisory Committee served as the primary regulatory agency. Now, however, much of the related regulatory oversight is shifting to various agencies, including USDA. (See p. 35.)

Results in Brief

Although its regulatory work load is expected to intensify, USDA has not formulated a well-defined regulatory structure (particularly with regard

to deliberate releases of genetically engineered organisms into the environment) or provided its Agriculture Recombinant DNA Research Committee with the authority and direction it needs to effectively act as the Department's focal point for biotechnology matters. In addition, USDA has done little to communicate to the Congress and the public both the benefits and risks of biotechnology as well as its plans to minimize those risks. Its relationship with other federal agencies involved in regulating biotechnology has generally been positive. (See pp. 36, 41, and 56.)

Principal Findings

USDA Philosophy Towards Biotechnology

USDA is confident that it can regulate and minimize the associated risks of the new biotechnologies because of its (1) many years of research and accumulation of extensive knowledge and (2) cautious approach to the containment, testing, and deliberate release of organisms into the environment. In addition, it anticipates that products developed from the new biotechnologies will be similar to conventional products and can be similarly regulated. (See p. 27.)

USDA's Regulatory Structure Needs Clearer Definition

USDA has few programs or activities that relate exclusively to biotechnology; rather, its oversight in this area is handled by agencies within the Department that were established before the new biotechnologies and that have other regulatory and/or research responsibilities. In addition, the Agriculture Recombinant DNA Research Committee was established in 1976 to oversee and coordinate matters relating to recombinant DNA research. Despite such mechanisms and certain initiatives to overcome regulatory uncertainty, USDA needs a clearer definition of its regulatory structure, particularly with regard to approving requests to deliberately release genetically engineered organisms into the environment. For instance, the first two such requests submitted to USDA for approval were handled by two different groups within USDA, although the requests were essentially identical. In general, agencies within USDA have been struggling for regulatory control, questions remain as to which agency is responsible for what, and the Agriculture Recombinant DNA Research Committee—USDA's designated focal point for biotechnology—has lacked authority and direction.

USDA has been hesitant in developing a well-defined regulatory structure because (1) it does not want to impose cumbersome regulations that

might stifle growth in biotechnology, (2) the timing and pace of its actions have been influenced by the White House's Office of Science and Technology Policy, which has been examining biotechnology regulation and coordinating the actions of many federal agencies, and (3) several lawsuits filed by opponents of biotechnology have created some anxiety.

Recently, USDA has set more firmly in place a general framework under which it will regulate biotechnology. Still needed, however, are procedural details and specificities expected in a regulatory structure—procedures that minimize questions regarding who is responsible for what but that are flexible enough to encompass an expected wide range of biotechnology research and product development. USDA also needs to more clearly establish the authority and duties of the Agriculture Recombinant DNA Research Committee, thus giving it the power to effectively act as USDA's focal point for biotechnology. (See pp. 23, 36, and 51.)

Reducing Concerns Through Improved Communication

The need for USDA to inform the Congress and the public about the benefits and potential risks of biotechnology is expected to intensify as many experiments in biotechnology move toward environmental release. Such communication would (1) lessen the fears aroused by experiments involving deliberate releases of genetically engineered organisms and (2) result in more informed discussions about the speed and restrictions under which biotechnology is allowed to proceed. (See pp. 56 and 63.)

Recommendations

GAO recommends that the Secretary of Agriculture

- Complete the development of a formalized, well-defined biotechnology regulatory structure that will identify USDA's regulatory path for licensing biotechnology products and approving requests involving deliberate releases.
- Provide the Agriculture Recombinant DNA Research Committee (or a future, central committee within USDA) with the authority and sense of direction it needs to act effectively as the Department's focal point for biotechnology.
- Look for and take advantage of opportunities to improve and increase the communication of USDA's views concerning biotechnology, both in terms of the benefits to be derived and the risks that must be considered and managed. (See pp. 52 and 63.)

Agency Comments

USDA's comments did not specifically address GAO's recommendations. GAO made a number of changes to clarify and update the report on the basis of the comments received.

USDA stated that, from a research standpoint, the report was a basically sound analysis. It stated, however, that regulatory review of the GAO study disclosed what it calls "serious errors and omissions" in that the study does not (1) clearly distinguish between regulatory and research authorities and (2) describe certain recent USDA initiatives. GAO disagrees. The report clearly distinguishes between the roles and responsibilities of the research and regulatory agencies, and recognizes pertinent initiatives recently taken by USDA. These initiatives, including additional ones identified by USDA, are important. However, they do not fully address the issues and recommendations in this report. (See app. II.)

Contents

Abbreviations

ABC	Association of Biotechnology Companies
APHIS	Animal and Plant Health Inspection Service
ARAC	Agriculture Recombinant DNA Advisory Committee
ARRC	Agriculture Recombinant DNA Research Committee
ARS	Agricultural Research Service
CBA	Committee on Biotechnology in Agriculture
CED	Community and Economic Development Division (GAO)
CSRS	Cooperative State Research Service
DNA	deoxyribonucleic acid
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FSIS	Food Safety and Inspection Service
GAO	General Accounting Office
IBC	Institutional Biosafety Committee
MOU	Memorandum of Understanding
NASULGC	National Association of State Universities and Land Grant Colleges
NBIAP	National Biological Impact Assessment Program
NIH	National Institutes of Health
NIH-RAC	National Institutes of Health-Recombinant DNA Advisory Committee
NSF	National Science Foundation
OGPS	Office of Grants and Program Systems
OSTP	Office of Science and Technology Policy
RCED	Resources, Community, and Economic Development Division (GAO)
USDA	U.S. Department of Agriculture

Introduction

In a letter dated March 29, 1984, the Chairman, House Committee on Science and Technology, asked us to review U.S. Department of Agriculture (USDA) activities that relate to biotechnology and how those activities relate to decision-making concerning the deliberate release of genetically engineered organisms into the environment. This request stemmed from a February 1984 report, The Environmental Implications of Genetic Engineering, prepared by the staff of the Committee's Subcommittee on Investigations and Oversight. The Subcommittee's report examined the potential benefits and risks associated with the deliberate introduction of genetically engineered organisms into the environment and evaluated the ability of scientists to assess the risks posed by such introductions. The report acknowledged the vast potential benefits to be derived from biotechnology, but recognized the need to provide a clear and timely process for appropriate public review and agency decision-making on the products of biotechnology. One of the report's recommendations called for a GAO review of the type the Chairman requested.

What Is Biotechnology?

Biotechnology means different things to different people. The Office of Technology Assessment, for example, has broadly defined biotechnology to include "any technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants or animals, or to develop microorganisms for specific uses." A definition derived by an informal interagency working group on biotechnology representing USDA, the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration, the National Institutes of Health (NIH), and the Food and Drug Administration (FDA), is more specific:

"Biotechnology is the application of biological systems and organisms to technical and industrial processes. The technologies employed in this area include

- classical genetic selection and/or breeding for purposes such as developing baker's yeast, conventional fermentation, and vaccine development;
- the direct in vitro modification of genetic material, e.g., recombinant DNA or gene splicing; and
- other novel techniques for modifying genetic material of living organisms, e.g., cell fusion, hybridoma technology, etc."[1]

The latter definition has been accepted and used by a variety of federal agencies, and it is particularly helpful because it makes some distinction between "classical" genetic selection and/or breeding, and the newer,

[1]Definitions of technical terms such as in vitro, recombinant DNA, and cell fusion may be found in the glossary of this report.

"novel" biotechnology techniques, such as recombinant deoxyribonucleic acid (DNA) and cell fusion. An understanding of both the traditional and more recent techniques used to modify plants, animals, and microorganisms is vital in understanding the debate about biotechnology and the implications of deliberately releasing genetically engineered organisms into the environment.

Traditional Biotechnology Techniques

Although the term biotechnology has only recently appeared in the public policy forum, genetic changes in plants, animals, and microorganisms have been occurring naturally or as a result of man's intervention since the beginning of time. In nature, for example, genetic alterations are said to be primarily due to a gradual flow of successive changes resulting in organisms that are better adapted to the environment. However, discontinuous and unpredictable events may also be important contributors to nature's evolutionary process. For instance, wheat, a food staple for mankind for thousands of years, is thought to have originated around 2500 B.C. as a result of a chance genetic combination of two wild grasses. Similar spontaneous genetic changes are offered as explanations for the sudden formations of new types of organisms that sometimes occur in nature.

Mankind's use of living organisms and their components in research and in industrial and agricultural production systems is likewise not new. Historically, the manipulation of plants and animals to benefit mankind began with primitive agricultural societies. Humans were unknowingly exploiting the ability of microorganisms to convert the sugar in grape juice into the alcohol in wine; to break down the proteins in milk to soften and flavor cheese; and to convert the starch in flour into carbon dioxide, which causes bread to rise during baking. Within the last century, the pharmaceutical and chemical industries have joined in using microorganisms in their manufacturing processes.

The modern science of genetics originated in the 1800's when Gregor Mendel demonstrated that the external characteristics of plants were controlled by internal factors (genes), which were of a particulate nature and transmitted between generations in predictable fashion. Mendel's experiments, published in 1866 but generally ignored until recognition of their importance in 1900, extended the research of a long line of biologists who had been studying the effects of unifying two different parental stocks. This newfound knowledge undoubtedly had an impact on subsequent plant and animal improvements accomplished by man largely through applying the techniques of selection and breeding.

These traditional techniques of selection and breeding involve whole plants or animals and are dependent on the sexual reproduction between the selected parents to achieve specific, desirable traits in their offspring. These techniques, however, have been characterized by some as "shotgun" approaches in which the scientist, the farmer, or whoever is using the process has only limited control over the genes in the given offspring. It is often a process of gradual improvement because more than one generation may be required to achieve the intended offspring qualities. The overall result of these techniques with respect to plants, however, has been a doubling in yields of certain major crops (wheat, rice, sugarcane, soybeans, and potatoes) and a tripling in yields of others (corn, peanuts, grain sorghum, and processing tomatoes). These techniques have effected similar gains in animal production.

New Biotechnology Techniques

Even though biotechnology in the form of genetic selection and/or breeding has been an integral part of agricultural production through the ages, the term has taken on new meaning and significance in recent years. Today, biotechnology is generally considered to be a component of high technology, and the "new biotechnologies" are those resulting from recently developed, sophisticated research techniques, including plant cell and protoplast culture, plant regeneration, somatic hybridization, embryo transfer, and recombinant DNA methods.

The new techniques focus not on the whole plant or animal, but rather on the cellular and subcellular levels of plants, animals, and microorganisms. At least some of the new techniques, such as recombinant DNA and protoplast regeneration, make it possible to move genes from one organism to another, related or unrelated, organism, bypassing the sexual reproduction process. The shift from the sexual mode of reproduction, using the traditional biotechnology techniques, to the nonsexual mode of the new biotechnologies greatly enhances both the rate and potential degree of genetic innovation.

The new biotechnologies remain a mystery and a source of concern to many people. Mankind's increasing control over the characteristics of organisms and the potential for altering inheritance in a directed fashion raise questions about the relationships of humans to each other and to other living things. Although some see such potential as a challenging opportunity, others—for ethical, moral, religious, or scientific reasons—see it as a threat or respond to it with vague unease. In this regard, the technique of prime interest and concern is recombinant DNA (often referred to as genetic engineering, although such a term certainly has

applicability to the other biotechnology techniques—both traditional and new—that have been mentioned). DNA itself is a molecular substance that controls hereditary traits. The DNA is contained in each cell of a living organism and appears, under a microscope, as a threadlike substance. The chemical makeup of DNA is essentially identical in all living organisms. This basic fact has opened up countless possibilities for rearranging, or recombining, the DNA of living organisms.

The realization starting in the early 1940's of DNA's fundamental role in determining hereditary traits was followed in 1953 by the identification of the double helix as the shape for most DNA molecules. This disclosure was a major event which, in the words of James Watson, one of the discoverers, "immediately told how DNA stores genetic information" and "suggested a chemical mechanism for the self-replication of DNA." When reproducing itself, DNA unzippers its two strands, leaving each half capable of forming a new partner similar to its previous one.

Along each strand of DNA is a series of genes, the basic units of heredity. It is estimated that each human cell may contain as many as 50,000 genes. All genes are composed of four basic kinds of molecules and, depending on their arrangement, the sequence of molecules determines the message given to the cell. A single gene can be sufficient to code for a particular trait, such as a potent toxin or growth rate. In other cases, a series of genes is required to express a specific trait; an example is the 17 genes that enable a type of bacteria to take nitrogen from the air and transfer it to a plant.

The discovery of DNA's physical structure was followed in the 1970's by the prediction, disclosure, and first actual use of "gene splicers," that is, enzymes that chemically cut a selective segment of genetic material from the total strand of DNA. The corresponding trait can thus be eliminated if the trait is unwanted, or, if it is wanted, it can be transferred to other DNA as a result of a further essential development—the use of vectors. Vectors are genetic agents, such as viruses, into which the appropriate segment of DNA can be spliced and that in turn can convey the DNA into the target cell, or "host," thus adding the new trait. Although the new genetic material does not always combine successfully with the target material, a successful combination does occur in a percentage of cases and the trait is then passed on to descendants. When the host cell or microorganism absorbs the virus or other vector, the combination is known as a "host-vector" system.

The following examples of recombinant DNA experiments indicate the range and results of this type of research. In one experiment, researchers succeeded in combining the rat gene producing a growth hormone with the genetic material of a mouse, resulting in offspring that were roughly twice the size of an ordinary mouse. The achievement was significant because it may set the stage for additional applications in agriculture. Another experiment focused on deleting a single gene in a microbe commonly found on certain agricultural crops. Scientists believe that by deleting the gene, they can reduce by a few degrees the freezing point of water on the leaves of the crops, thus adding a measure of protection to the crops during cold weather. A planned field test was halted by a lawsuit, as discussed in chapter 2. A final example, one of the first recombinant DNA experiments ever proposed, involved the blending of the DNA from a microbe commonly found in the human stomach, with a cancer-causing virus. The perceived risk associated with such an experiment, however, led to the formulation by NIH of initial guidelines for work with recombinant DNA. These guidelines are discussed in more detail in chapter 2.

The new biotechnologies, including recombinant DNA, have already yielded some important achievements, and more are expected. The new biotechnologies are expected to have a broad impact. They may contribute to meeting some of mankind's most fundamental needs—from health care to supplies of food and energy. At the same time, there are concerns about their potential effects on the environment, about the risks to health involved in some types of basic and applied scientific research and development, and about the ethical and moral implications of human and animal experimentation.

Benefits and Risks of the New Biotechnologies

Scientists involved in research in the new biotechnologies have said that, in terms of benefits, the potential for developments in this area is limited, for all practical purposes, only by the lack of scientific ingenuity, insight, and/or capital. Some believe that we are on the threshold of a promising era in agriculture and biologically driven processes. The new biotechnologies have already led to such breakthroughs as the bacterial production of interferon used in treating cancer and a noninfectious vaccine used to combat hoof and mouth disease. The new biotechnologies provide additional opportunities for the improvement of plants and animals, for increasing the efficiency of various agricultural production systems, and for enhancing the management of natural resources and ecosystems. It is increasingly possible, for instance, to identify genes providing a higher resistance to various physical factors

such as drought, frost, salt, or heat, and then to move these genes to unrelated plants and organisms in need of such qualities. Genes controlling nitrogen fixation in certain bacteria, for example, may be transferred to other bacteria or directly to higher plants from the bacteria. As another example, microorganisms may be tailored to enhance wine production, reduce food spoilage, and clean up the environment (i.e., eliminate or neutralize oil spills, dioxin, and other chemical hazards).

The nature of the risks associated with the new biotechnologies is less easy to define and depends largely on the nature of the organisms upon which the research is being done and the extent to which these organisms will be released into the environment. Along this line, the February 1984 report of the Subcommittee on Investigations and Oversight stated that, as the new biotechnologies have advanced, new public concern has arisen. In contrast to the previous concern about the harm that could result from the accidental escape of a new, genetically engineered organism, concern now focuses on possible effects from deliberate release.

The staff report further explained that because many new biotechnology products are designed to produce results in the field rather than in the laboratory, effective performance of these products would require their deliberate release into the environment. The report stated that the deliberate release of genetically engineered organisms could have a profound and potentially negative effect on the environment and the existing ecological balance.

With respect to microorganisms, for example, there is public concern that genetic modifications may accidentally convert a harmless microbe into one capable of (1) producing a toxin or (2) attacking other microbes or plants and animals in unintended ways. Some fear that genetic modifications may turn a harmless plant into a destructive weed; perhaps, too, a healthy plant could become vulnerable to disease or pests, yield some unforeseen by-product that decreases its value as food, or produce a toxin capable of harming important microorganisms in the soil. For both plants and animals, a major concern has been the potential narrowing of the gene pool because of increasingly selective breeding and biotechnology practices. If genetically uniform characteristics in plants or animals are suddenly adversely affected by poor weather, insects, or disease, the losses could be substantial. This was the focus of our December 4, 1981, report to the Secretary of Agriculture, entitled Better Collection and Maintenance Procedures Needed to Help Protect Agriculture's Germplasm Resources (CED-82-7).

The degree of risk associated with biotechnology research and its subsequent commercialization has proven to be controversial, and arguments can be made to justify completely opposite points of view. To illustrate, those who minimize the risk are apt to argue that

- Potential benefits exceed potential risks by a wide margin.
- New biotechnologies increase the precision with which genetic alterations can be made.
- A complex process is required to convert a known, harmless organism into a pathogen, and the probability of such an accidental occurrence is low.
- A continuity exists between the old and new biotechnologies.
- An element of risk is inherent in any technological process.

On the other hand, those who accentuate the risk would generally argue that

- At present, no reliable method exists to calculate risk and, if a problem does arise, it could prove to be widespread and intractable.
- In some instances, a very thin line exists between helpful and harmful qualities of a given organism.
- At present, only a few of the thousands of genes in a complex DNA molecule have been described, and scientists do not always understand exactly which genes control even the simplest traits of an organism.
- A major discontinuity exists between the old and new biotechnologies because of the current, much greater rate and degree of change.
- Domestic and international competition in biotechnology is likely to be intense, thus creating incentives for competitors to take risks in an atmosphere of secrecy so as to gain an edge in the marketplace.

Although no detrimental effects of any genetically engineered organism have been documented, some observers have suggested that the negative effects that have been experienced from newly introduced, naturally occurring organisms, such as the gypsy moth (which, in its caterpillar stage, preys upon leaves and has caused extensive damage to trees), are indicative of the possible effects of releasing a given genetically engineered organism into the environment.

Biotechnology's increasing range of applications and ensuing entrance into the marketplace will stir debate and should force a more open discussion of its benefits and risks by those in government who are responsible for regulating biotechnology, by those in industry who are

promoting it, by scientists who are developing it, and by the public, which is being affected by it.

Objectives, Scope, and Methodology

The Chairman, House Committee on Science and Technology, asked us to obtain information about (1) USDA's programs and activities that relate to biotechnology generally, (2) the relationship of such programs and activities to decision-making concerning the release of genetically engineered organisms into the environment, and (3) the relationship between USDA and other agencies with biotechnology regulatory responsibilities, namely NIH and EPA. We additionally obtained information on the extent to which USDA has communicated to the public and the Congress its views on biotechnology and the regulatory role it expects to play. Such communication becomes increasingly important as more biotechnology research moves from small-scale, laboratory-contained experiments into experiments involving deliberate releases of genetically engineered organisms into the environment.

The Chairman also asked us to document the extent of USDA's biotechnology research efforts. This work was done in conjunction with the National Association of State Universities and Land Grant Colleges (NASULGC), largely through the use of a questionnaire, and was the subject of our October 25, 1985, report, The U.S. Department of Agriculture's Biotechnology Research Efforts (GAO/RCED-86-39BR).

In performing our work, we held discussions with and obtained documents from officials of USDA's Animal and Plant Health Inspection Service (APHIS), Agricultural Research Service (ARS), Cooperative State Research Service (CSRS), Office of Grants and Program Systems (OGPS), and Food Safety and Inspection Service (FSIS). We also met with USDA's Deputy Assistant Secretary for Marketing and Inspection Services and with individuals from NASULGC. We talked with and obtained documentation from several NIH officials. We also talked with an official at EPA and an official at FDA who were both closely involved with their agencies' biotechnology activities. In addition, we talked with an official from a company seeking USDA's approval to release a genetically engineered organism. We attended congressional hearings and listened to the testimonies given by numerous public and private individuals both for and against the biotechnology effort. We met with Mr. Jeremy Rifkin, a leading biotechnology critic, and founder and head of the Foundation on Economic Trends (an organization discussed later). We attended three meetings of the Agriculture Recombinant DNA Research Committee (ARRC), a forum in USDA for discussing biotechnology in agriculture. In

March 1985 we visited USDA's Agricultural Research Center in Beltsville, Maryland, to discuss and observe biotechnology firsthand with scientists who are engaged in such work. One publication we found particularly useful was an August 13, 1984, special issue of Chemical and Engineering News on genetic engineering and some of the issues that were expected to arise when applications are submitted for deliberate release of genetically engineered organisms.

We did our work in the Washington, D.C., area primarily during the period from May 1984 through June 1985. To the extent practical, we obtained updated or supplemental information through November 1985. Our work was done in accordance with generally accepted government auditing standards.

Agency Comments

In commenting on our report (see app. II), USDA made several statements regarding its perception of the intent and purpose of our work in the biotechnology area and our two reports that have ensued—this report and our October 1985 report. USDA stated that (1) we have not evaluated USDA's authority to regulate deliberate releases under all relevant statutes, regulations, and executive orders and (2) a careful analysis by us of USDA regulatory methodology for assessing the hazards of release into the environment, in both USDA research projects and commercial product development, would serve the public interest.

Regarding the first point, USDA was apparently under the mistaken impression that our reports were to have presented the results of an analysis of USDA's statutory capability for regulating the processes and products of biotechnology in agriculture. The request we received from the Chairman, House Committee on Science and Technology, upon which our work was predicated, is included as appendix I. It states that the American Law Division of the Congressional Research Service, not GAO, was requested by the Chairman to conduct a review of the legal authority of USDA.

USDA also stated that those commenting on its biotechnology policy statement of December 31, 1984, understood that our report would present the results of an analysis of USDA's statutory capability and help the Congress determine whether new legislation is required to effectively regulate biotechnology products. Our review, however, of 39 of the most agriculturally oriented responses to USDA's policy statement disclosed no such reference to any expectation of a statutory review by us. We did, during the course of our work, ask various officials whether USDA

needed additional statutory authority to adequately and effectively carry out its biotechnology regulatory authorities. The consensus was that it did not.

In response to the second point, we agree that such an analysis would be very helpful and is indeed needed. During our review, however, USDA's regulatory methodology for assessing the hazards of release into the environment had not been formally expressed—a circumstance that causes difficulty in performing such an analysis. We were told repeatedly during our work that USDA's methodologies used in regulating biotechnology research and in assessing risk had evolved informally over the years and that the National Biological Impact Assessment Program (NBIAP), discussed in chapter 3, was a first attempt to articulate some of these things. An official with the Office of Technology Assessment also told us that an Office of Technology Assessment/National Science Foundation-sponsored conference held in November 1985 represented "a first pragmatic stab at risk assessment in biotechnology."

We believe that this report and our October 1985 report are responsive to the Chairman's request. Our October 1985 report provided an otherwise unavailable inventory of biotechnology research projects funded in whole or in part by USDA within the fiscal year 1984-85 time frame.

This report provides information on USDA's programs and activities that relate to biotechnology and the relationship of such programs and activities to decision-making concerning the release of genetically engineered organisms into the environment. It also provides information on the relationship between USDA and other agencies with biotechnology responsibilities. No further evaluation in response to the request we received from the Chairman, House Committee on Science and Technology, is contemplated.

Regulating Biotechnology

Although no evidence exists to suggest that harmful genetically engineered organisms have been unexpectedly created, few experts believe that the new biotechnologies are totally without risk to health and the environment. Because of this perceived and/or potential risk and because of biotechnology's broad application, several agencies within the federal government have assumed or, through various statutes, been given regulatory responsibilities with respect to biotechnology research and the subsequent commercialization of the products or processes of that research. This chapter examines briefly the complex system in which the federal government regulates biotechnology overall and then looks in more detail at USDA's approach to the subject.

USDA's organizational structure is not designed to relate exclusively to biotechnology. USDA generally addresses biotechnology issues as part of its programs and activities conceived for other purposes. USDA believes that biotechnology offers tremendous potential for agriculture and is confident that it has the ability to adequately regulate the new biotechnologies.

Regulating Biotechnology Within the Federal Government

The federal government's regulatory structure relating to biotechnology is complex. No single government agency has the expertise or authority to properly govern or direct all biotechnology activities. Rather, various statutes provide several federal agencies with regulatory authority over different areas of biotechnology. The diversity of the biotechnology industry itself makes it difficult, as one editorial stated,

". . . to classify, categorize, or codify [the regulatory structure] from scratch."[1]

Regardless of this complexity, the federal government's regulation of biotechnology has generally revolved around NIH guidelines promulgated in 1976 and federal health, safety, and environmental laws. The threat of lawsuits or common law tort actions by injured persons may also have had a regulatory influence. Additionally, the administration, recognizing its responsibility to confront the special concerns that surround modern biotechnology, formed an interagency working group under the White House Cabinet Council on Natural Resources and the Environment. Each of these aspects of biotechnology regulation is discussed in the sections that follow.

[1]McCormick, Douglas, "A Crazy Quilt to Cover Biotech," Bio/Technology, Vol. 3, (March 1985), p. 183.

NIH Guidelines

The 1976 "NIH Guidelines for Research Involving Recombinant DNA Molecules" were the federal government's initial response to the concern about risks associated with recombinant DNA research. The guidelines were developed in response to concern among scientists and the general public about the potential hazards of genetic engineering. They were formalized by an NIH Recombinant DNA Advisory Committee (NIH-RAC) following an international conference held in February 1975 at Asilomar, California, and attended by a group of eminent scientists. The guidelines originally were binding only on research supported by NIH; subsequently, all federal agencies that perform, fund, or regulate recombinant DNA research agreed to adopt the NIH guidelines and to require compliance by federally funded researchers doing work involving recombinant DNA. An agency can encourage the compliance of researchers who receive federal funds by threatening to cut off such funds in the event of noncompliance. The guidelines do not cover privately funded research but contain a section encouraging voluntary compliance by industry.

The guidelines provide an administrative framework that specifies the responsibilities of the scientists, their institutions, and the federal government. For each institution the key organization is the Institutional Biosafety Committee (IBC), comprising experts in relevant scientific disciplines and lay persons representing the public interest. More than 300 IBCs throughout the nation oversee recombinant DNA research to ensure compliance with the guidelines. At the federal level the key parties are the NIH Director, who is the final decision-maker under the guidelines, and the NIH-RAC, a diverse group of experts who advise the NIH Director on the major technical and policy issues involved.

The guidelines also classify experiments into three categories: (1) those requiring special review by the NIH-RAC, (2) those requiring containment of potentially harmful organisms and review by the IBC, and (3) those exempt from special NIH-RAC and IBC review. The NIH-RAC reviews experiments in the first category to assess risk and assign an appropriate level of containment. Those in the second category must be conducted in accordance with previously established containment standards that become more rigorous as the level of perceived hazard increases. These standards specify physical types of containment relating to special laboratory features and biological types of containment relating to the deliberate weakening of experimental organisms to reduce their chance of survival outside the laboratory. According to USDA, compliance with these standards is ensured by the IBCs at the local level.

The third category of experiments—those that are exempt from NIH-RAC and IBC review—has grown to the point where it now represents about 80 to 90 percent of all recombinant DNA experiments. Research since 1976 has led to less concern among many scientists about the risks of recombinant DNA research and, as a result, there has been a gradual but substantial relaxation of original containment requirements and oversight mechanisms through a series of formal revisions in the NIH guidelines.

Three limitations of the NIH guidelines, however, have caused some people to be concerned about their adequacy in terms of regulating the biotechnology industry: they (1) apply to nonfederally funded research on a purely voluntary basis, (2) do not apply to organisms created by genetic engineering techniques other than recombinant DNA, and (3) do not adequately address the issue of deliberate release of genetically engineered organisms into the environment. (Originally, they simply prohibited such releases, but more recently they were changed to require special review under category 1.)

Federal Statutes and Agency Oversight

Some federal statutes and oversight by several agencies in addition to NIH relate to biotechnology. For example, under authority of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301-392) and Section 351 of the Public Health Service Act (42 U.S.C. 262), FDA can regulate products of biotechnology processes such as food and food additives, human and veterinary drugs, cosmetics, and biological products for medical uses. The Department of Labor is authorized through the Occupational Safety and Health Act of 1970 (29 U.S.C. 651 et seq.) to require employers to provide safe working conditions for employees working in areas of biotechnology where a significant risk has been established. EPA has broad statutory authorities to address risk to public health and the environment and conducts a program of research and development to support its activities. The two laws most applicable to EPA's oversight of the potential risk from biotechnology are the Toxic Substances Control Act (15 U.S.C. 2601-2929) and the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136-136y).

Finally, within USDA's jurisdiction are the regulation of veterinary biologicals, organisms, and vectors; the importation of foreign plants, plant products, and other articles; and the interstate movement of plant and animal pests and noxious weeds. These provisions apply whether genetic engineering is involved or not. Pertinent statutes behind USDA's regulations include the Plant Quarantine Act of 1912 (7 U.S.C. 151-164a,

166-167), the Plant Pest Act of 1957 (7 U.S.C. 150aa-jj), and the Virus-Serum-Toxin Act of 1913 (21 U.S.C. 151-158). The relationships that exist between USDA and some of the other agencies involved in regulating biotechnology are discussed in chapter 3.

Legal Influences on Biotechnology

The judicial process in the United States has influenced biotechnology's progress during the past 2 years. In May 1984, for example, a federal district judge put a moratorium on all field tests of genetically engineered microbes supported by federal funds and approved by NIH. His decision halted what would have been the first deliberate release experiment, a University of California test involving bacteria designed to impede frost formation on plants. The decision was in response to a lawsuit against NIH filed in 1983 by the Foundation on Economic Trends. The lawsuit claimed that NIH had failed to evaluate adequately the environmental impact of deliberate release experiments. Specifically, the foundation charged that NIH violated the National Environmental Policy Act by failing to conduct an environmental assessment and a much more in-depth evaluation through an environmental impact statement. NIH argued that the NIH-RAC's review of the experiments constituted an adequate environmental analysis. NIH and the University of California appealed the federal district judge's decision.

In February 1985 a U.S. court of appeals ruled in the foundation's favor that NIH must conduct an environmental assessment of the California experiment and warned that it should do the same for other experiments. In NIH's favor, however, the court lifted the preliminary injunction that barred the agency from approving all other deliberate release experiments as long as environmental assessments are completed.

In another lawsuit filed on October 1, 1984, the foundation joined the Humane Society of the United States to challenge USDA experiments in which scientists were injecting sheep and pig embryos with DNA material from human growth hormone genes in an attempt to make the animals grow faster. The foundation considers the experiments to be "morally reprehensible" and a "violation of the rights of every species." The outcome of this suit was undecided at the time of our review. A USDA attorney told us in November 1985 that USDA had requested that the case be dismissed, but a decision by the court to do so or to proceed to trial was not expected before mid-December 1985. On March 10, 1986, the attorney told us that the court's decision was still outstanding.

Tort law may also have an indirect effect, similar to regulation, on biotechnology. Lawsuits alleging harm resulting from the use of genetically engineered organisms and seeking compensation (or the threat of such suits) could lead both the private sector and the government to take extra precautions or to be more hesitant about introducing new organisms. In our view, it helps explain why companies have apparently been willing to comply voluntarily with the requirements of the NIH guidelines.

White House Cabinet Council's Working Group on Biotechnology

In April 1984 a Working Group on Biotechnology was organized to review the government processes dealing with biotechnology. This group is under the jurisdiction of the White House Cabinet Council on Natural Resources and the Environment, working through the Office of Science and Technology Policy (OSTP). Working group members come from over 15 different federal departments and agencies (including USDA).[2] The organizers thought that such a group would provide a means of ensuring that society can reap the benefits of biotechnology, and also that public health and the environment would be protected and societal concerns promptly addressed. One of the group's goals was to minimize the regulatory uncertainties or duplications that can affect the climate for innovation that exists in the United States, which was recognized as the world leader in biotechnology.

The working group's "Proposal for a Coordinated Framework for Regulation of Biotechnology" was published in the December 31, 1984, Federal Register (Vol. 49, no. 252, pp. 50856-50907). The document included a concise index of federal laws relating to biotechnology; statements of policy by EPA, FDA, and USDA; and a proposal to revise the overall regulatory structure affecting biotechnology. The proposed revision would diminish the role played by NIH in biotechnology regulation and establish a new, centralized advisory committee to oversee biotechnology with subordinate advisory committees within each of five federal agencies (EPA, FDA, USDA, NIH, and the National Science Foundation (NSF)). The working group believed that with the evolution of biotechnology and its increasing commercialization, the complexity and scope of scientific review had correspondingly broadened and the existing mechanisms for scientific review must be expanded.

[2]Member agencies include the Departments of the Interior, Justice, State, Agriculture, Commerce, Defense, Energy, Health and Human Services, and Labor; Environmental Protection Agency; Council on Environmental Quality; Council of Economic Advisers; Office of Management and Budget; Office of Policy Development; National Science Foundation; Office of the U.S. Trade Representative; and Office of Science and Technology Policy.

The working group's proposal solicited comments from interested parties on each of the three policy statements as well as on its own suggestion of a centralized advisory committee with five subordinate agency committees. USDA received 50 comments directly on its policy statement; papers forwarded to USDA by OSTP contained 15 additional references to USDA policy. The two largest categories of respondents were from business and academia. Comments in lesser numbers were received from environmental and public interest groups, law firms, foreign governments, and the Congress.

In addition, the working group received comments on its suggestion of a centralized advisory committee with subordinate agency committees. A working group member told us that the comments were generally unfavorable because the proposed system seemed too cumbersome. The working group was considering these comments, ultimately expecting to publish its coordinated framework for regulating biotechnology in final form. This was to be done as soon as possible to ensure that a well-understood regulatory policy and process are established quickly to enable what the group considers a beneficial industry to proceed safely and efficiently. On November 14, 1985, OSTP announced in the Federal Register the establishment of a Biotechnology Science Coordinating Committee and a revised matrix of U.S. laws related to biotechnology. An additional announcement concerning OSTP's coordinated framework for regulating biotechnology is expected early in 1986.

USDA's Organizational Approach to Regulating Biotechnology

The preceding discussion deals with how biotechnology is regulated overall and it gives some idea as to where and how USDA fits into the overall scheme. Because we were asked to address USDA's role in regulating biotechnology, the remaining discussion in this report in focused primarily on USDA.

USDA has been active in the development of the new biotechnologies. Its representatives participated in meetings and workshops in the early 1970's where policy decisions were made regarding recombinant DNA research. USDA recognized early that a uniform set of guidelines should be followed for research regardless of the source of research funding.

Therefore, it endorsed and adopted the NIH guidelines governing recombinant DNA research and established an internal policy requiring compliance with these guidelines as a condition for receiving funds for research.[3]

Although USDA has been involved in the development of the new biotechnologies for a number of years, it has few programs or activities that relate exclusively to biotechnology. Rather, the oversight and other involvement it has exercised with regard to this area have come from programs and activities that generally were conceived for some other purpose before the development of the new biotechnologies. This oversight is centered primarily in two USDA agencies with regulatory missions, which are responsible to the Assistant Secretary for Marketing and Inspection Services, and in several other agencies with agricultural research missions, which are responsible to the Assistant Secretary for Science and Education. Each of these agencies is discussed briefly in the following sections.

Animal and Plant Health Inspection Service

APHIS, a regulatory agency within USDA, is responsible for protecting the nation's animal and plant resources from diseases and pests and thus preserving the marketability of U.S. agricultural products domestically and abroad. APHIS carries out this mission through (1) inspection and quarantine activities at U.S. ports of entry to prevent the entry of exotic animal and plant diseases and pests, (2) similar activities in the United States to locate and prevent the spread of agricultural pests and diseases, and (3) control and eradication programs to combat new and endemic infestations and infections. Among other things, APHIS also develops standards for, licenses, and tests animals or veterinary biologicals to ensure their safety and effectiveness.

The APHIS work force totals about 5,000 full- and part-time employees. APHIS' budget for fiscal year 1986 was estimated at $262 million. Two of its organizations, which have been and will be involved with biotechnology issues, are Plant Protection and Quarantine (1,600 employees) and Veterinary Services (2,200 employees). Overall, APHIS operates 12 regional offices and 64 area offices throughout the United States, its territories, and nations extending into Central America.

[3]In commenting on this report, USDA stated that it continues to endorse a uniform set of guidelines and that it recognizes the NIH guidelines as applicable to contained research. USDA also stated, however, that it is developing guidelines for biotechnology research covering both contained research and release into the environment.

Food Safety and Inspection Service

FSIS is another regulatory agency within USDA that is expected to have some regulatory oversight over biotechnology. Under the Federal Meat Inspection Act (21 U.S.C. 601 et seq.) and the Poultry and Poultry Products Inspection Act (21 U.S.C. 451 et seq.), FSIS is responsible for ensuring that the U.S. commercial meat and poultry supply is wholesome, unadulterated, and correctly labeled and packaged.

FSIS was established in June 1981. Its work force totals about 10,000 full- and part-time employees in offices and establishments throughout the United States and some of its territories. FSIS' budget for fiscal year 1986 was estimated to be about $386 million.

Agricultural Research Service

ARS was established in 1953 and serves as USDA's in-house agricultural research agency. The Assistant Secretary for Science and Education, to whom ARS reports, has major responsibilities for conducting and leading the national agricultural research effort. ARS' mission is to develop new knowledge and technology, which will ensure an abundance of high quality agricultural commodities and products at reasonable prices. Its research, including biotechnology research, is conducted at 140 field locations throughout the United States and in Puerto Rico, the Virgin Islands, and several foreign countries. ARS' work force totals about 8,400 full- and part-time employees. Its fiscal year 1986 budget was estimated at about $500 million.

Cooperative State Research Service

CSRS is USDA's main link with the university system of the United States for conducting agricultural research. In this context, CSRS administers federal grants for research, including biotechnology research, at state agricultural experiment stations (located at various universities) and other eligible institutions. It also participates in a nationwide system of research planning and coordination among state institutions, USDA, and the agricultural industry. Program coordination and planning are carried out by a CSRS staff of about 120. This staff serves more than 12,000 scientists in the U.S. university system. For fiscal year 1986, CSRS' budget was estimated to be about $255 million, the bulk of which goes for research and is allocated according to formula or the merit of individual research projects.

Office of Grants and Program Systems

OGPS is made up of a small central staff headquartered in Washington, D.C., which oversees six separate offices and programs. The bulk of its activity in 1985 was concentrated in its Competitive Research Grants

Office, whose main function is to provide leadership and guidance in awarding grants for basic research to a wide variety of institutions. This office received about $44 million for distribution during fiscal year 1985, of which $19 million was designated for biotechnology research.

Agriculture Recombinant DNA Research Committee

USDA formed the ARRC[4] in 1976 to support the NIH-RAC and to oversee and coordinate biotechnology matters among the various agencies in USDA and between USDA and NIH and NSF. Its membership and responsibilities as reconstituted in August 1983 by USDA's Assistant Secretary for Science and Education, to whom the ARRC reports, are as follows. Regarding membership, the Assistant Secretary requested that a representative from APHIS, ARS, CSRS, OGPS, and the Forest Service, which carries out forest-related research, be designated to serve on the ARRC. The Assistant Secretary also requested that NSF and NIH continue their representation on the ARRC. Further, he defined the ARRC's responsibilities as follows:

1. Identify issues with regard to recombinant DNA research and application activities and develop needed policy recommendations.

2. Provide input and assistance to the USDA representative to the NIH-RAC.

3. Serve as a source of technical information on scientific developments and regulatory status of recombinant DNA research and applications for all agencies.

The ARRC has no budget of its own. Its members serve the committee part-time, with the bulk of their responsibilities and attention directed towards other aspects of their employment. However, efforts to formalize and strengthen the ARRC have been made and are discussed in chapter 3. In addition, a proposal for a USDA-based Committee on Biotechnology in Agriculture (CBA) is being considered. If approved, the CBA would supersede the ARRC as the primary focus for biotechnology activities in USDA, probably in early 1986.

[4]The ARRC, at its inception, was known as the Agriculture Recombinant DNA Advisory Committee (ARAC). ARRC has been primarily used to identify the committee since about June 1984. Throughout this report, the committee is generally referred to as the ARRC.

USDA's Philosophical Approach to Regulating Biotechnology

According to USDA, the new biotechnologies, including the isolation and transfer of specific genes by recombinant DNA techniques, offer tremendous potential for agriculture. USDA has stated that it is confident in its ability to regulate the new biotechnologies. USDA anticipates that agricultural and forestry products developed by these technologies will be basically similar to conventional products and has taken the position that its existing regulatory framework, combined with the NIH guidelines applicable to recombinant DNA research, are generally adequate and appropriate for regulating research, development, testing, evaluation, production, and application of the new biotechnology products. USDA plans, however, to constantly reevaluate its regulatory position as biotechnology evolves and to amend its regulations or request additional authority as needed.

USDA gives other reasons for being optimistic about the benefits to be derived from the new biotechnologies and its ability to regulate and minimize the associated risks. In particular, USDA cites its overall experience in agricultural research, which it regards as directly applicable to the new biotechnologies, and its cautious approach to research, as reflected in its previous experience.

USDA's Experience in Agricultural Research

As a result of USDA's involvement in agricultural research for over 100 years, an immense accumulation of scientific background and knowledge guides today's researchers. For instance, huge data collections relating to seeds, grains, fungi, insects, and other organisms have been developed. The data collection relating to insects alone, a cooperative endeavor between USDA and the Smithsonian Institution, contains information on over 24 million specimens.

Sophisticated instruments, too, provide agricultural scientists with special research capabilities. During a tour of ARS facilities at Beltsville, Maryland, we examined different research equipment capable of assessing chemical composition, sorting out individual cells, and magnifying the contents of slides up to one million times.

One USDA scientist told us that she and her co-workers do not operate in a vacuum with respect to their research. She said that, from previous work by themselves or others, they know a lot about the areas of focus in their current work. To illustrate the point, she said that she could "list from memory hundreds of plant viruses and the conditions under

which they could become a threat to the environment." Such information, she indicated, often provides valuable guidance in specific research projects.

This accumulation of scientific background and knowledge is also important because, according to USDA, it is directly applicable to making informed judgments about the new biotechnologies and their products. USDA does not consider these products to be fundamentally different from products obtained by conventional technology. USDA officials told us that the new biotechnologies are simply new tools to assist them in their research efforts. They also told us that these new tools are more efficient and precise than many of the tools used in the past and that the products resulting from them, therefore, are less risky and more predictable than the products resulting from less sophisticated means.

USDA Has Exercised Caution With Regard to Containment, Testing, and Deliberate Release

USDA has historically exercised a great deal of caution with respect to containing potentially harmful organisms, testing organisms before their release, and releasing what are thus thought to be beneficial organisms into the environment.

Containment of Potentially Harmful Organisms

Containment is a function that is generally associated with research and refers to the strict isolation of potentially harmful organisms from the environment. This isolation is achieved within specially designed laboratories for microorganisms or within experimental facilities, such as greenhouses for plants. Similarly, animals that are deliberately infected with dangerous microorganisms to permit the study of animal diseases and treatments are quarantined from healthy animals and are destroyed when the experimentation is finished. In addition, the transportation of dangerous organisms under contained conditions is required. Such precautions indicate that the prevention of an accidental or unintentional release of a potentially harmful organism is indeed a matter of concern to USDA.

Various examples of containment by USDA can be cited. For instance, special containment facilities for work with virulent animal diseases have been established. Two of the major facilities are the National Animal Disease Center in Ames, Iowa, and the Plum Island Animal Disease Center near Long Island, New York. For over 20 years, the Ames facility has conducted research on hog cholera in the midst of Iowa's

swine industry, but farmers in the area have not reported a single outbreak of the disease. The Plum Island facility, opened in 1956, offers another example. It is located on an island as a further means of guaranteeing the containment of dangerous microorganisms being studied there. The Plum Island facility has served as the site for several research projects involving recombinant DNA work with animal pathogens which, if not contained, could extensively damage the nation's livestock industry.

In addition, the NIH-RAC guidelines, which required the containment of recombinant DNA and until recently prohibited its release into the environment, have helped emphasize the importance of containment. As discussed earlier, USDA follows these guidelines. Even one of the leading critics of the new biotechnology, Jeremy Rifkin, has remarked that "containment has basically been a success."

Extensive Testing Precedes Release

In the development of a new organism or product, USDA requires extensive testing in the environment in field plots before its introduction into the agricultural system is authorized. We found many examples of long periods of time devoted to testing. For example, a report by NASULGC observes that

> "The release of a single new wheat cultivar [from an experimental research program to a commercial program as a product] may involve as many as ten years of tests at twenty cooperating State Agricultural Experiment Stations and thousands of records on performance available in public reports."[5]

As another illustration of such caution, we found reference to a small, foreign wasp, which has shown excellent results as a biocontrol agent against a certain beetle that destroys U.S. potatoes, tomatoes, and eggplants. Agricultural researchers believe that, in spite of excellent test results under contained conditions, 5 to 6 more years of study are necessary before the wasp can be released for use in pest management programs.

On several occasions USDA scientists cited examples of the length of time it takes for a new crop to be developed. For instance, at an ARRC meeting we attended, a USDA scientist stated that a variety of corn had taken 6 years to develop, a variety of soybean had taken 8 years, and a specific kind of pine seed had taken 20 years. The scientist particularly stressed

[5]NASULGC, Emerging Biotechnologies in Agriculture: Issues and Policies (Progress Report III, March 1985 Update).

the example of the 20 years to develop a small sample of the pine seed, which he said had not been planted yet.

Release of Beneficial Organisms

In contrast to the concern about unintentionally releasing harmful organisms, the release into the environment of organisms proven to be beneficial is deliberate and has, over the years, occurred on a large scale. New varieties of crops have been spread over millions of acres; improved breeds of cattle and other animals have been produced by the millions. Microbes proven to be beneficial (e.g., those that help plants grow) have been deliberately released into the soil by the billions. USDA has also been involved in developing and releasing biocontrol agents over large geographic areas. For instance, it has released billions of sterilized Mediterranean fruit flies to disrupt the mating patterns of this agricultural pest. Overall, according to the report by NASULGC, American agricultural scientists have successfully released over 7,500 new varieties of organisms. These releases have played a major role in the development of the agricultural system, and the subsequent assessment of such releases has provided scientists with a great deal of information that should help guide future releases of additional organisms.

Suppressing or Eradicating Harmful Pests or Organisms

USDA officials told us that they are proud of their ability to quickly respond to and take action against pests or organisms that periodically threaten U.S. agriculture. The use of the previously mentioned sterilized fruit flies is one example of USDA's involvement in suppressing or eradicating an agricultural pest. USDA scientists told us that the agency had taken similar action in two other instances. In the one instance the scientists had anticipated corn blight, which affected the U.S. crop in 1974. The scientists were thus able to take steps to counteract the blight as it emerged, controlling and eliminating the problem in a single growing season before it developed into a major problem. The other instance involved an outbreak of avian influenza in 1983, which decimated the Pennsylvania poultry industry. USDA scientists had found and identified in wild ducks the exact strain of influenza virus before it became a problem. Once the outbreak hit the poultry industry, USDA scientists identified three slight molecular variations that had turned the virus into a killer. The scientists were able to take steps to counteract the virus and quickly control and eliminate the problem.

Although the examples used here were not the result of new biotechnologies, USDA officials mentioned them as illustrations of their ability to identify and correct agriculturally threatening problems as they occur

and as a reason for USDA's confident attitude towards the new biotechnologies. The belief is that, if by remote chance something does go wrong, USDA could quickly respond to and correct the situation. Along this line, USDA pointed out in its December 31, 1984, statement of policy concerning biotechnology that

"To date, no unique or safety problems have been associated with products of genetic engineering, conventional or modern."

Conclusions

The federal government's regulatory structure relating to biotechnology is complex. Because of biotechnology's broad application, no single government agency has the expertise or the authority to oversee all biotechnology activities. As a result, several agencies have assumed or, through various statutes, been given regulatory authority over different facets of biotechnology. Guidelines promulgated by NIH have had a significant impact on biotechnology regulation (both inside and outside the federal government), as have several different legal influences and, most recently, the White House Cabinet Council's Working Group on Biotechnology.

USDA is one of several agencies that has responsibility for regulating biotechnology. Although few of its programs or activities relate exclusively to biotechnology, t versight and involvement it has exercised in this area come from progra ns and activities conceived for other purposes before the advent of the new biotechnologies.

USDA believes that the new biotechnologies offer tremendous potential for agriculture and is confident about its ability to regulate them. USDA anticipates that agricultural and forestry products developed by these technologies will be basically similar to conventional products and believes that its existing regulatory framework, along with the NIH guidelines, are generally adequate and appropriate for regulating the new biotechnologies. USDA has a great deal of experience in agricultural research and, over the years, has accumulated vast amounts of scientific knowledge and background. USDA has exercised considerable caution with regard to the containment, testing, and deliberate release of a wide variety of organisms produced by conventional means. USDA has also shown its ability to quickly respond to and take action against various kinds of pests that have, from time to time, threatened U.S. agriculture.

Agency Comments

In its comments on this report, USDA drew a distinction between biotechnology research and the regulation of the products resulting from that research. From the research standpoint, USDA stated that the report was a basically sound analysis. From the regulatory standpoint, however, USDA stated that its review of our study disclosed "serious errors and omissions."

USDA stated that the report discusses, among other things, USDA's organizational and philosophical approach to regulating biotechnology. However, according to USDA, the discussion does not clearly distinguish between regulatory authority (granted by statutes such as the Federal Plant Pest Act and the Virus-Serum-Toxin Act), and legislative authority to fund research. USDA stated that regulatory agencies, such as APHIS and FSIS, have the statutory authority to regulate, while the NIH-RAC and the ARRC can directly control only the research contracts funded by their respective agencies. USDA also emphasized that neither NIH-RAC nor the ARRC are regulatory agencies in the sense that FDA, APHIS, and FSIS are. Rather, they provide guidelines for the "safe and efficacious" conduct of recombinant DNA research.

We believe that both the research and regulatory sides of USDA have important, distinct roles to play as far as biotechnology is concerned, and that this chapter clearly describes the roles and responsibilities of each. For example, USDA's regulatory and research agencies (including the ARRC) are described on pages 23-26. In addition, other federal parties outside USDA, such as the NIH-RAC, are described on pages 18-23.

USDA Needs to Clarify Its Plans for Regulating Biotechnology and Related Deliberate Releases

In early 1984 concern was expressed within the Congress that USDA's biotechnology programs and activities were not well defined and that USDA might be taking its role in this regard less seriously than it should. This congressional concern was challenged by a USDA official who, at the time, chaired the ARRC. The official cited a number of actions USDA was taking to better define USDA's position on regulating biotechnology. Further, he explained that one reason for the perceived lack of activity at USDA could be that the Department had mechanisms in place for regulating modified microorganisms, plants, or animals that it had been using for years.

One of our primary objectives during this review was to determine whether USDA's policies and procedures with respect to regulating biotechnology were clearly defined and operational. This has become a particularly important issue now that USDA's regulatory work load with respect to biotechnology is growing. Until now, USDA's involvement in biotechnology has been primarily research-oriented, with only a small number of genetically engineered veterinary biologicals being submitted to APHIS for regulatory review and licensing. As of November 1985, however, USDA had received several requests relating to the deliberate release of genetically engineered organisms into the environment. As the number of cases requiring regulatory determination grows, as it is expected to, it becomes increasingly important that the regulatory structure under which USDA will operate be clearly defined and made known to those who must work and comply with it.

We generally agree with the USDA position that mechanisms are in place within APHIS and FSIS for regulating various genetically engineered products that have been or are yet to be produced. We also agree that mechanisms are in place on the research side of USDA for regulating agricultural research (genetic engineering or otherwise). USDA's regulatory structure, however, lacks formality and specificity overall and specifically with regard to handling requests for approval to release genetically engineered organisms into the environment. It has recognized this shortcoming for some time, but has yet to put such a structure in place. Meanwhile, different agencies in USDA have been jockeying for regulatory control, and USDA officials have expressed uncertainty as to which agency is responsible for different activities. A regulatory structure is being formulated and is expected to be announced early in 1986, at the time OSTP issues its statement on biotechnology regulation. (See ch. 2 for an earlier discussion of OSTP's involvement regarding biotechnology.) These issues are discussed in the remainder of this chapter as is

the relationship between USDA and other federal agencies with biotechnology responsibilities.

The Biotechnology Area Is Changing

Biotechnology is an area undergoing significant change. Until recently, the major concern about biotechnology was the safety of the experiments and the assurances given that appropriate containment precautions were being taken and that, even if the organisms used in the experiments did escape, they could not survive and thus negatively affect the environment. The overriding fear was that an accidental release from the laboratory of some new pathogenic organism could have dire consequences. Some of this apprehension has since subsided, at least within the scientific community, as additional knowledge and experience have been gained. Further, as indicated earlier, USDA's efforts over the years to contain potentially harmful organisms have been highly successful.

We are now entering a new era in biotechnology. The industry that genetic engineering spawned is looking forward to the commercialization of its products and the accompanying financial rewards that are hoped for and expected. Additional government review and analysis, however, may be required before many such products can be marketed. In many cases, this will involve the deliberate release of the genetically engineered organism, or product, into the environment as a means of further testing.

Until 1985 the NIH-RAC was the federal government's primary overseer of genetic engineering. It reviewed proposals for new research experiments and required that federally funded researchers follow its guidelines to ensure safe handling of recombinant DNA material. Additionally, with input from agencies such as USDA, EPA, and FDA, the NIH-RAC considered and approved three proposals to deliberately release genetically engineered organisms into the environment, although these experiments were placed on hold by the Foundation on Economic Trends' lawsuit discussed in chapter 2. However, as other research projects have progressed to the point of field testing, and many more private, commercial firms are seeking approval of their experiments, the NIH has expressed displeasure that it is being pushed from its desired research-oriented role into a regulatory-oriented role. For example, an NIH official attending the June 1985 meeting of the ARRC indicated that the NIH-RAC wanted to reduce its regulatory role. The NIH-RAC's dilemma may eventually be solved by OSTP's "Proposal for a Coordinated Framework for Regulation of Biotechnology," published in the Federal Register on

December 31, 1984. The proposal downplays the future role of the NIH-RAC in regulating biotechnology and shifts this responsibility to FDA, EPA, and USDA. Since the proposal was published, a small number of requests for approval to release genetically engineered organisms into the environment have gone to these agencies directly, rather than first going through the NIH-RAC.

USDA Has Been Hesitant in Defining Its Biotechnology Regulatory Structure

Although USDA has displayed confidence and optimism towards biotechnology and has had time to formulate an overall biotechnology regulatory structure, it has not done so. As a result, USDA's regulatory structure, particularly with regard to how it will handle requests for approval to deliberately release genetically engineered organisms into the environment, has been unclear. The following are a few possible explanations for why USDA has not been more aggressive in defining clearly its regulatory structure under which requests for deliberate releases will be handled.

First, USDA officials told us they did not want to impose cumbersome regulations that might stifle growth in biotechnology research or in the industries that have sprung from that research. This approach is consistent with guidance given by the Director, OSTP, with specific regard to the December 31, 1984, regulatory proposal of the Working Group on Biotechnology. Along this line, USDA officials have taken the position that the Department's existing regulatory structure over plants, animals, and microorganisms is generally sufficient and appropriate for regulating genetically engineered organisms. USDA officials have recognized the vagueness of the Department's statement of policy concerning its approach to regulating biotechnology, which was published as a part of the December 31, 1984, Federal Register regulatory proposal. On the one hand, they are aware that the industry is waiting for specific regulatory procedures to follow. On the other hand, they have concluded that adequate regulatory mechanisms exist in the agricultural community and that clarifying the existing mechanisms will be fairly simple once the process has begun.

Second, USDA has adopted a "wait and see" attitude with regard to biotechnology regulation. This attitude has undoubtedly been fostered by the existence and time frame of OSTP's involvement in this area. OSTP expects to issue a revised version of its December 31, 1984, regulatory proposal early in 1986, and USDA officials told us that the agency's decision-making in biotechnology is being influenced by OSTP's time frame. USDA's concern for the actions of other agencies such as EPA may have

also contributed to its hesitation, as shown by the following episode. In a February 21, 1984, meeting of the ARRC, for example, one member, commenting on the need for USDA action, proposed that

"... the most productive step for the ARAC or USDA to take would be to define the overall role of USDA; namely, whether USDA should play a regulatory role, if so how, what to regulate, what is [in] the best interest of agriculture as a whole, etc."

Some members at the meeting said that they agreed in spirit with the proposal and with the idea that more active steps were needed. Other members, however, expressed the opinion that the ARRC should wait for EPA's expected publication in the Federal Register of its proposed regulation of recombinant DNA-related activities. No decision was reached as a result of the discussion, and the EPA document was not published until 10 months later.

In another meeting held January 10, 1985, the ARRC recognized that soon the ARRC, or a modified ARRC, would begin to directly receive requests for approval to deliberately release genetically engineered organisms. The ARRC agreed that it should begin to formulate a formal review process based on existing regulatory mechanisms. In another ARRC meeting 5 months later, however, members still raised questions about who in USDA was responsible for what areas and in which situations. With respect to one member's proposal that specific guidelines be developed to facilitate the ARRC's review of requests for deliberate release, the ARRC vice chairman countered that appendix L to the NIH-RAC guidelines already existed to govern plants, the overall NIH-RAC guidelines govern microbes, and a document recently developed in FSIS was used to govern animals. The vice chairman conceded that appendix L had weaknesses and needed revision. In response to the proposal for ARRC guidelines, the ARRC chairman said that the committee should continue to use guidelines that already exist, suggesting that the ARRC does not want to "rush pell mell down the [regulatory] road."

A third explanation for why USDA seems to have hesitated in defining its regulatory structure relates to the lawsuits that have been filed by the Foundation on Economic Trends. These lawsuits have created some anxiety within USDA, not so much because USDA officials believe the lawsuits stand to prove the research wrong or dangerous, but because of the time and resources they believe could be involved in such suits. We were told by one USDA official and sensed from several meetings we attended at USDA that there was a high level of legal consciousness and a desire to do things so that legal questions do not become major issues.

USDA Initiatives in Response to Regulatory Uncertainties

APHIS, the research side of USDA (e.g., ARS and CSRS), and the ARRC are the prime players in USDA's biotechnology regulation. The specific roles of each, however, have not been clearly defined, particularly with regard to deliberate releases of genetically engineered organisms into the environment. This has resulted during the past few years in a number of initiatives being independently advanced by the different agencies, and there have even been signs of struggle between USDA's regulators and researchers over who will be given prime responsibility for regulating biotechnology. We discuss some of these initiatives and the relationships among the various players in the following sections.

APHIS Initiatives on Regulating Biotechnology

APHIS is the regulatory agency within USDA that has had and undoubtedly will have the largest role in regulating biotechnology products. As of November 1985, for example, APHIS' Veterinary Services had approved and licensed for marketing 10 "new biotechnology" veterinary biologicals. A top microbiologist in Veterinary Services told us that dozens of additional genetically engineered veterinary biologicals were being considered for approval. He also told us that APHIS does not expect the products that had been licensed or were under review to be challenged in the same sense that the experiment involving bacteria designed to impede frost formation on plants (see ch. 2) was earlier challenged in the courts. This is because the genetically altered veterinary biologicals licensed and under review have not involved live organisms being injected into animals to treat or diagnose diseases. Such injections, therefore, are generally not considered deliberate releases of genetically engineered organisms into the environment. The microbiologist told us that the expected use of live organisms in similar injections in the future will require more caution and some regulatory or procedural changes.

In another part of APHIS, Plant Protection and Quarantine responded to a company seeking to release a genetically engineered tobacco plant into the environment for experimental purposes. In a June 1985 letter from APHIS to the company, APHIS stated that it found no problem with the proposed field test. According to a company spokesperson, the wording of the letter placed a large share of the responsibility for the release on the company. The spokesperson said that the company had decided to hold off the intended tobacco planting for another year. He expected USDA to issue more detailed regulations in the interim, and he was also expecting a response from the NIH-RAC with regard to the same experiment.

At the time of our review, USDA was considering one additional request for deliberate release. This request also involved a genetically engineered tobacco plant. Perhaps as an indication of the uncertainty and inconsistency that exist with respect to USDA's regulation of biotechnology, this request was being handled primarily by the ARRC, as opposed to APHIS, which handled the first request. According to the ARRC chairman, the company submitting the second request had preferred that the ARRC handle it, rather than APHIS.

The ARRC chairman, however, was of the opinion that the uncertainty and inconsistency have been resolved and that the respective responsibilities of APHIS and the ARRC with regard to biotechnology have been clarified. The chairman said that "ARRC responsibility carries through research and field test releases while commercial-scale releases and interstate transport are to be APHIS' responsibility. Thus, the kind of letter that APHIS sent [to one company] basically authorizing a field test release of a genetically engineered tobacco plant will originate in the ARRC in the future."

In early 1985 APHIS established an ad hoc work group on biotechnology. This group is made up of 11 people: 3 from Veterinary Services, 4 from Plant Protection and Quarantine, 3 APHIS attorneys, and 1 FSIS representative. The group will work towards integrating the biotechnology activities of Veterinary Services and Plant Protection and Quarantine and will work closely with the ARRC. As of November 1985 the group's activities had been focused on such areas as the handling of proprietary business information, the relationship of relevant laws to APHIS' process for reviewing and approving deliberate releases, and the import requirements related to genetically engineered organisms and live vectors. The group had also studied the impact that biotechnology will have in the future on APHIS' staff and other resources.

Regulatory Initiatives Taken by USDA Researchers

Researchers view themselves as experts in their chosen fields and are typically wary of the extent to which their research is regulated, claiming that too much regulation stifles initiative and imagination. In this regard, USDA researchers have expressed some concern about the regulatory authority APHIS has been seeking. One researcher in an ARRC meeting, for example, stated "There's no way that the research community is going to let APHIS assert control and tell them what they can and can't do."

As one means of perhaps controlling their own destiny, at least part of the research community within USDA is developing what is being called a National Biological Impact Assessment Program (NBIAP). The NBIAP is a concept that has been put together by the NASULGC's Division of Agriculture, Committee on Biotechnology, under the oversight of CSRS. A CSRS official told us that the NBIAP describes various procedures involving research, field testing, and commercial release of new products in agriculture, but that it goes much further. The NBIAP is proposed as a means for agriculture to assess the biological impact of the release of organisms containing recombinant DNA. It would be organized using the existing national agricultural research network which, according to NASULGC, is characterized by geographic distribution of people with expertise, depth of experience, impartiality of assessment, and proven histories of scientific accomplishment. It would build on the experience and success of the NIH-RAC and associated committees such as the IBCs; it also would complement existing federal regulatory authorities and, according to NASULGC, would be consistent with the OSTP's Proposed Coordinated Framework for the Regulation of Biotechnology (Federal Register, December 31, 1984).

In a June 1985 meeting of the ARRC, the chairman characterized the NBIAP as being in a conceptual stage, with the NBIAP document itself having few details. He said that it is not up to the NASULGC to provide the details; rather it is up to USDA to develop them. His suggestion that an ARRC subcommittee be established to transform the NBIAP concept into an operational plan was adopted during the meeting. He further credited the NBIAP with the ability to provide an

> ". . . inventory of highly competent people to review technical procedures, protocols, or even full proposals from the standpoint of safety. If a particular experiment is to be conducted, the NBIAP can identify the safest place to do it. It is also a mechanism to gather a great deal more information about living organisms, and it signs on a major component of the agricultural system—the university system."

As an initiative by the agricultural research community, the NBIAP has raised differences of opinion within USDA regarding its role. A CSRS proponent of NBIAP said he believes that its future impact in terms of biotechnology regulation could be as great as NIH-RAC's impact has been in the past. He told us that the level of expertise in the field for dealing with specialized agricultural and biotechnological problems exceeds anything that can be assembled in a centralized regulatory framework such as the one being suggested within APHIS. An APHIS official, on the other hand, described the NBIAP proposal as being of high quality and

importance but stated that, although it will give the research community an idea of what is going on, "the NBIAP cannot serve as a regulatory force." In April 1985 testimony before the Congress, USDA's Assistant Secretary for Science and Education endorsed the NBIAP as an integral part of USDA's overall plans for regulating biotechnology. In addition, in a June 1985 letter to OSTP, the same Assistant Secretary discussed the NBIAP's role in relation to the ARRC and APHIS in greater detail. Most recently, in October 1985 the Assistant Secretary indicated that the NBIAP will play an important role as a source of information for biotechnology research and regulation but that it is "not in any way a regulatory activity."

Role of USDA's Coordinating Committee Needs to Be Formalized and Strengthened

The ARRC was established in 1976 to act as a USDA focal point for issues involving recombinant DNA. It has roughly a dozen members who until recently agreed to meet on an "as needed" basis. Minutes of its meetings since late 1983 indicate that the ARRC has served as a forum for discussing biotechnology problems but that its mission beyond this is unclear. Much of the discussion within the ARRC has been informative, but somewhat informal and inconclusive regarding many points of concern. ARRC has not followed up on a number of proposals and has issued no formal documents during its 9-year existence—prior to helping USDA prepare its statement of policy at the end of 1984. One USDA official told us that the ARRC has "no authority," and another official said that the ARRC has been "just a forum."

The reason for the ARRC not accomplishing more may be explained, in part, by the fact that ARRC's business has taken up a relatively small proportion of its members' time and in some cases does not receive top priority. From October 1983 through January 1985, for example, the ARRC met approximately 10 times for about 2 hours each. The minutes of these meetings show that other duties of the ARRC chairman required him to be absent from three of the nine meetings. Efforts to increase the amount of time devoted to the ARRC are discussed later in this section.

In addition to reviewing these minutes, we attended three ARRC meetings in 1985 to gain a fuller understanding of the committee's activities. The first such meeting, held on January 29, 1985, was devoted mainly to a presentation concerning the NBIAP and a discussion as to whether the ARRC has authority to approve a request to deliberately release a genetically engineered plant into the environment. Our overall impression of the meeting was that the discussion was at an introductory or exploratory level, but that those present were genuinely interested in clarifying

the ramifications of what was being discussed. At a subsequent meeting on March 29, 1985, our impression remained unchanged. A number of basic issues were discussed in an exploratory manner, and many points of uncertainty were noted but not resolved.

At the third ARRC meeting we attended on June 20, 1985, a portion of the time was devoted to discussing how to formalize the ARRC's operations. The discussion resulted in a few specific steps being taken towards greater formalization. For example, the committee decided to meet regularly on a quarterly basis and as otherwise needed, and to establish a subcommittee whose purpose would be to work towards transforming the NBIAP from a concept into a working system.

The discussion also involved several other topics, which were left unsettled. For example, the call for formalized ARRC guidelines, which was discussed earlier, was put on hold. Another important topic, which was raised and discussed but left unsettled, had to do with which agency or entity should be the initial focal point in USDA for requests for deliberate releases and other matters relating to agricultural biotechnology. Despite a June 7, 1985, letter that was supposed to clarify such things, the discussion reflected continued uncertainty with respect to whether it should be the ARRC or APHIS, or even NIH, NSF, or EPA. At one point, reference was made to a suggestion for a central clearing committee within the White House's Cabinet Council on Natural Resources and the Environment. An APHIS official remarked that the important thing is that wherever the responsibility is placed, there must be no room for confusion. An FSIS official pointed out the difficulties in doing this because of the wide array of research in biotechnology and the fact that not all requests for deliberate releases will fit neatly into one category.

As a subsequent effort to provide a more formal and strengthened central committee for biotechnology within USDA, documents in October 1985 indicated that USDA was considering the establishment of the CBA, which would replace the ARRC. The Assistant Secretary for Science and Education said that the CBA would be consistent with OSTP's "Proposal for a Coordinated Framework for Regulation of Biotechnology." The ARRC chairman told us that the CBA would represent a major step towards formalizing and strengthening a central committee for handling biotechnology in USDA.

USDA's Statement of Policy Is Found Acceptable, but Specific Procedures Are Needed

USDA's statement of policy in the December 31, 1984, Federal Register contained a brief section entitled "Regulatory Philosophy," which summarized its fundamental approach to regulating biotechnology. The section stated

"USDA anticipates that agriculture and forestry products developed by modern biotechnology will not differ fundamentally from conventional products.

"We believe that the existing regulatory framework of USDA combined with the NIH Guidelines which are mandatory for all research grants are adequate and appropriate for regulating research, development, testing and evaluation, production, and application of these biotechnology products. Should any new processes or products be shown to require additional regulatory measures, USDA will amend its regulations or will request additional authority."

The overall statement prompted comments from a variety of sources, including academia and both large and small biotechnology companies. We reviewed 39 comments (identified by OSTP to be the most agriculturally oriented) and concluded that there was general agreement with USDA's approach to regulating the new biotechnology, but that USDA needs a clearer definition of some of the specific procedures for the review and approval of deliberate releases of genetically engineered organisms and the licensing of new biotechnology products.

USDA's view, as expressed in its statement of policy, that new biotechnology products will not differ fundamentally from conventional products, was endorsed by the private sector. Other responses indicated a high level of confidence that USDA's previous experience in agricultural research and regulation would enable it to effectively regulate the new biotechnology. Criticism of USDA's statement of policy was directed primarily to the need for greater specificity of procedures. The president of one biotechnology company, for example, stated that "We urge USDA to quickly develop the procedures to review new products . . ." In another response, the Association of Biotechnology Companies (ABC) remarked that

"The USDA has a considerable depth of biotechnology expertise in its Agricultural Research Service, Research Institutes and ongoing research, which should be integrated as a resource into any pre-market approval process for biotechnology-derived products. ABC would welcome some definitive efforts by USDA to assure the integration of these scientific capabilities into its bureaucratic approval processes. This approach would assure the USDA of sufficient in-house biotechnology capabilities to effectively and expeditiously process product licenses [and] permits and inspect food, animals or animal products developed by biotechnology."

Although USDA's approach to regulating biotechnology received widespread support, we noted a limited amount of criticism regarding EPA's statement of policy. For example, some of the comments we reviewed from the private sector reflected disagreement with EPA's approach, with the general view that such an approach would be costly, time-consuming, and unreasonable. (Additional discussion on this subject, plus the views of an EPA official, may be found later in this chapter.)

Recent Effort to Specify Procedures Taken by USDA

As a result of extensive discussions to reduce the regulatory uncertainties that we have described, USDA outlined certain procedures it plans to follow with respect to recombinant DNA in a letter sent from USDA's Assistant Secretary for Science and Education to an OSTP deputy director on June 7, 1985. USDA officials with whom we talked regarded the letter as a breakthrough in resolving key differences within USDA over how to regulate biotechnology. The importance of the letter warrants extended quotation:

"It is our commitment to cover the full range of safety and ethics in agricultural research. Oversight of the research process is the responsibility of the Assistant Secretary of Agriculture for Science and Education. Our responsibilities in recombinant DNA research will be met in two ways through: (1) the Agriculture Recombinant DNA Research Committee (ARRC), and (2) the National Biological Impact Assessment Program (NBIAP). The regulatory function which applies to products will be met by the Animal and Plant Health Inspection Service (APHIS).

"The proposed entry path for recombinant DNA research review would be directly to the Agriculture Recombinant DNA Research Committee. This committee, made up of members representing the appropriate Agriculture Department Agencies and other Executive Branch Agencies, (as is current practice), has served as an arm of the NIH-RAC and continues to assist in national coordination of recombinant DNA and related efforts.

"Provision will be made for all requests involving recombinant DNA entering at the regulatory level to also go before ARRC. The regulatory agency, e.g., APHIS, should refer, when appropriate, material to ARRC for review as outlined above. Since ARRC includes regulatory representation, it could determine expeditiously whether the products could be returned directly to a regulatory agency, e.g., APHIS, for licensing review (a process which is already well defined) and/or logged in for ongoing assessment and/or comprehensive review by NBIAP.

"The ARRC would continue to use the NIH-RAC guidelines as its basic document. Where needed, they would be expanded to cover agricultural situations not adequately defined. . . ."

Although the letter goes a long way in addressing uncertainties and specifying procedures for regulating biotechnology in USDA, the letter

acknowledged in closing that the agency's biotechnology program is a developing one, yet to be further refined, and that USDA would discuss with OSTP any substantive changes.

On July 19, 1985, USDA published in the Federal Register (50 FR 29367-68) a notice of its delegation of authority pertaining to biotechnology. The Assistant Secretary of Science and Education was given responsibility to coordinate the development and carrying out by USDA agencies of all matters and functions pertaining to agricultural research involving biotechnology. The Assistant Secretary for Marketing and Inspection Services was given similar responsibility pertaining to USDA's regulation of biotechnology. Both assistant secretaries are to act as liaisons within their respective spheres between agencies within USDA and between USDA and other governmental and private organizations. The respective delegations of authority in the notice, however, were general in nature and did not provide clear definitions or details as to how they would be carried out.

As of October 1985, USDA documents indicated that the basic interrelationships envisioned by these actions were being established. The potential replacement of the ARRC by the CBA does not appear likely to alter these interrelationships.

USDA's Relationship With Other Federal Agencies Involved in Biotechnology Regulation

We were specifically asked to examine USDA's relationship with NIH and EPA with respect to regulating biotechnology. We observed that the various agencies have joined together from time to time to solve existing problems. Although there is ample evidence of such coordination, a few areas of disagreement remain between USDA and other federal agencies with biotechnology responsibilities.

Examples of Interaction Between USDA and Other Federal Agencies

USDA has been dealing with concerns about recombinant DNA for over 10 years, and much of this involvement has been in conjunction with other federal agencies such as NIH, EPA, and FDA. During the NIH-RAC's formative stages in 1974, for example, USDA officials met with and assisted NIH officials. Agricultural scientists were named as members of the NIH-RAC and have attended its meetings since it was founded. USDA was invited to participate in the Asilomar Conference held in 1975 in which concerns about recombinant DNA were discussed. In 1976 USDA's ARRC was formed to coordinate research policies among the various agencies in USDA, and

between USDA, NIH, and NSF. Along with various USDA representatives, NIH and NSF representatives were named to serve on this committee. Further, USDA endorsed and adopted the "NIH Guidelines for Research Involving Recombinant DNA Molecules," believing that a uniform set of guidelines would facilitate interagency research review.

USDA has cooperated with other federal agencies in determining agency oversight of genetically engineered organisms that fall within the regulatory jurisdiction of more than one agency. In this regard, a Memorandum of Understanding (MOU) between USDA and FDA, published in the Federal Register on June 8, 1982, concerns resolution of jurisdictional questions involving animal biological products. An October 3, 1984, MOU between USDA and EPA defines the general principles of cooperation, coordination, and communication between the two agencies. In commenting on this report, USDA additionally informed us of a January 16, 1985, MOU between USDA, EPA, and FDA concerned with residues of drugs, pesticides, and environmental contaminants in food. USDA believes that this MOU could become particularly important for agricultural biotechnology if such efforts result in the presence of biological residues in agricultural products and foods.

We noted other instances in which USDA and other federal agencies were working together on biotechnology matters. One particularly noteworthy example was the establishment in 1984 of the White House Cabinet Council's Working Group on Biotechnology, whose members come from over 15 federal departments and agencies. According to the December 31, 1984, Federal Register statement, the fundamental purpose of this group was to ensure that the biotechnology regulatory process adequately considers health and environmental safety consequences of the products and processes of the new biotechnology as they move from the research laboratory to the marketplace. The group recognized the need for a coordinated and sensible regulatory review process that would minimize uncertainties and inefficiencies. It recognized that not only should approaches be consistent from agency to agency but within each agency, from application to application, as well. The idea that scientific review and regulatory activities needed to be adequately coordinated was so important to the group that it suggested an interagency committee be established to, among other things, foster timely, coordinated decision-making and monitor the changing scene of biotechnology. For the time being, the working group is expected to serve these needs. According to the group, when its activities are concluded, an interagency coordinating committee would, if still needed, be established to continue this effort.

Some Areas of Disagreement Exist Between USDA and Other Agencies

Although considerable interaction has taken place between USDA and various other federal agencies having biotechnology responsibilities, there remain at least a few areas where the agencies do not agree. USDA, for example, has expressed concern regarding the role EPA has sought with regard to regulating biotechnology. In October 1984 the ARRC chairman sent what USDA later labeled as highly critical comments to OSTP expressing concerns about an EPA draft statement of policy on biotechnology. USDA's concerns were divided into three areas. First, USDA was concerned that the EPA statement of policy elevated to a high level, by presumption, the overall risk of biotechnology in general and of genetic manipulation in particular. Second, USDA was concerned that the terminology used to describe what EPA was planning to regulate was confusing and often contradictory. Third, USDA was concerned that EPA's arbitrary classification of a wide variety of genetically engineered microorganisms as either pesticides or chemical substances encroached on a number of USDA programs for the quarantine, certification, licensing, registration, and inspection of agricultural commodities and other articles. In January 1985 the ARRC chairman told us that EPA's statement of policy as it appeared in the December 31, 1984, Federal Register differed only slightly from the October 1984 draft statement that he had commented on, and that he considered many of his earlier comments to still be valid.

At the time of our review, concerns such as those we have discussed plus a few additional, but related ones, were still unresolved. For example, USDA and a number of private companies have taken exception to EPA's plans (as contained in its statement of policy) to regulate small-scale field testing of genetically engineered microorganisms. One ARS scientist, commenting on this matter, explained the problem and its potential impact on agricultural research as follows:

> "EPA ordinarily grants an experimental use permit for tests of pesticides involving less than 10 acres. However, for experiments with genetically engineered microorganisms . . ., EPA plans to ask for notification and background information before granting an experimental use permit. This is not a trivial requirement because the background information is so extensive and inclusive . . . that it will be unnecessarily time-consuming and costly to obtain such information. The effect of the broad and vague definitions of genetic engineering . . ., coupled with EPA's definition of certain microorganisms as pesticides, will severely impact and hinder ARS research of microorganisms for biological control."

In this respect, EPA's decision to extend its regulatory arm over the field testing of the frost-impeding bacteria discussed in chapter 2 has proven controversial to scientists within and outside USDA. EPA has contended

that the "ice-minus" bacteria, as they are called, are, in fact, microbial pesticides because they will replace naturally occurring, ice-forming bacteria. Such an interpretation concerned many scientists, according to the ARRC vice chairman and others with whom we talked.

Genetically engineered ice-minus bacteria, however, still figure prominently in EPA's regulatory work load with respect to biotechnology. As of July 1985, for example, EPA had received five notifications of plans to field test genetically engineered microbial pesticides; one was inactive, one was withdrawn, and three were under active consideration. Two of the three notifications that were then being considered involved ice-minus bacteria. In November 1985 EPA granted an experimental use permit for a small-scale field test, which was expected to lead to the first deliberate release of a genetically engineered organism into the environment.

In September 1985 an EPA official told us that EPA was sensitive to the criticisms of its position on biotechnology and that it was taking actions to modify that position. The official noted that EPA had received a lot of criticism for imposing regulation simply on the basis that genetic engineering was used, rather than on the potential risk that might be involved (regardless of the process). The official told us that EPA was thus considering a regulatory approach based on risk rather than on the method of production. The official also said that some groups of products might be exempted from EPA regulation and that key definitions by EPA that had received criticism might be clarified and revised. In our judgment, these comments suggest a somewhat more flexible approach to regulation by EPA than was initially envisioned. In addition, EPA's regulatory approach appears now to more closely coincide with USDA's approach and belief that genetically engineered organisms should be regulated not because of how they were derived, but on the basis of potential risk.

In addition, the official said that OSTP had told EPA and USDA to begin negotiations at the staff level to sort out differences of view. As a result, a series of meetings has begun and the EPA official remarked that these meetings bring the two sides closer together and provide a means for discussing decisions that have to be made. A USDA official also told us that the two sides are working together to resolve their differences.

In the past several years, USDA and FDA had also been at odds over which agency had responsibility for regulating a product known as interferon. Interferon can be used both as a growth promoter in animals and as a

treatment for certain animal diseases. USDA believed that FDA should regulate interferon when it is used as a growth promoter (veterinary drug), but that APHIS should regulate it when it is used to treat animal diseases (veterinary biological). The issue was eventually resolved at a high level within the two agencies with FDA being given the responsibility for regulating interferon.

Diminishing Role of NIH and Need for Agriculturally Oriented Recombinant DNA Guidelines

NIH's role in regulating biotechnology during the past 10 or so years has been a very important one and NIH's association with USDA in this regard, from all accounts, has been very close. Now, however, NIH wants to reduce its role with respect to those areas of biotechnology that fall outside the biomedical field. At the ARRC's June 1985 meeting, the NIH representative told the committee that NIH wanted to remove itself from involvement in many of USDA's areas. He said that the NIH Director does not want, for example, to be responsible for authorizing the release of genetically engineered tobacco plants.

In conjunction with this issue, the NIH guidelines for governing recombinant DNA research are somewhat difficult to apply to agriculture. The NIH representative to the ARRC recently told the committee that the NIH guidelines were oriented to biomedical research but that they were being applied to all recombinant DNA research. In several discussions with us, key USDA officials concerned with biotechnology agreed with NIH's view that the NIH-RAC guidelines were oriented to biomedical research and acknowledged the need for recombinant DNA guidelines geared more specifically to agriculture.

Some consider the NIH guidelines to be complex and cumbersome. One author, for example, made the following statement in 1982 concerning the initial guidelines.

"The people who drafted the guidelines and their associates at NIH could hardly anticipate that lay persons would someday be struggling to understand them. . . . Even for those who were knowledgeable in the field of molecular biology, the guidelines represented a cumbersome document that lacked simplicity, coherence, and internal consistency."[1]

The NIH guidelines have been revised a number of times since their issuance in 1976; however, their complexity has not diminished and their applicability to agriculture has not been greatly enhanced. The main

[1]Krimsky, Sheldon, Genetic Alchemy, The Social History of Recombinant DNA Controversy, (MIT Press, 1982), pp. 191-192.

body of the guidelines now consists of 6 sections, with 12 appendixes presenting a variety of technical information. Material relating specifically to agriculture is fragmented and condensed. Appendix B-III, for example, provides a list of microorganisms of particularly high risk to agriculture, which are forbidden entry to the United States either by law or by USDA policy. No discussion relating microorganisms more clearly to agriculture occurs in the guidelines. In the only place in the guidelines that refers directly to animals, appendix F refers in general terms to "vertebrates," a term that could include farm animals but, in the context of the guidelines, more likely refers to laboratory animals such as monkeys and smaller animals. Appendix L, in a few short paragraphs, lists criteria for approving releases of genetically engineered plants. ARRC's vice chairman, who is also USDA's representative to the NIH-RAC's Plant Working Group, told us that, as a part of a recent guidelines revision, the plant criteria had been condensed to the point of creating confusion and that such guidelines had proven inadequate in terms of handling the requests for release that USDA had recently received.

Conclusions

Biotechnology is an area undergoing significant change. Until recently, emphasis was placed on containing genetically engineered organisms, and much of the regulatory oversight was assumed and conducted by the NIH-RAC according to guidelines it established for this purpose. Now, however, several experiments involving genetically engineered organisms have reached the point where, for testing purposes, the organisms need to be released into the environment. Much of the related regulatory oversight for such releases is shifting from the NIH-RAC to the agencies that are more directly involved—namely USDA, EPA, and FDA.

USDA has not prepared itself fully to accept a greater degree of regulatory responsibility. Although USDA is confident and optimistic towards biotechnology, and has had a considerable amount of time to formulate a formal, well-defined regulatory structure, it has not done so. It has been hesitant in developing such a structure for several reasons. First, it does not want to impose cumbersome regulations that might stifle growth in biotechnology. Second, the timing and pace of its actions have been influenced by OSTP, which has been examining biotechnology regulation and coordinating the actions of many federal agencies. Third, several lawsuits filed by opponents of biotechnology have created some anxiety in USDA.

Different agencies within USDA, however, recently have taken certain initiatives. One example is the development of the NBIAP, an attempt to

describe the review process for proposals involving research, field testing, and commercial release of genetically engineered organisms. The NBIAP is in a conceptual stage, with many details still undecided. Another example is the June 1985 letter from USDA's Assistant Secretary for Science and Education to OSTP, which assigned overall biotechnology research and regulatory responsibilities within USDA and which established the ARRC as somewhat of a central clearinghouse within USDA for all biotechnology matters. Despite this letter, subsequent discussion within USDA reflected continued uncertainty with respect to the regulatory path to be followed in handling requests for deliberate releases and other matters involving agricultural biotechnology.

Both of these examples represent steps in the right direction. Now USDA needs more detail on the specific policies and procedures that it will use in the future to oversee biotechnology. Many of the private sector responses to USDA's statement of policy in the December 31, 1984, Federal Register agreed with USDA's general approach to regulating biotechnology but called for specific procedures applicable to the review and approval of deliberate releases of genetically engineered organisms and the licensing of new biotechnology products. The authority and duties of the USDA coordinating committee (currently the ARRC) have not been firmly and clearly established. Establishing specific duties and the authority to act on them will give the committee the power and the sense of direction it needs to act effectively as USDA's focal point for biotechnology. Overall, USDA recognized in its letter to OSTP that its biotechnology program is a developing one, yet to be further refined.

USDA's relationship with other federal agencies involved in regulating biotechnology has generally been positive, and ample evidence exists of their interactions. A few areas of disagreement between USDA and EPA and FDA have arisen, but such differences appear to have been, or are being, worked out.

USDA needs to have its biotechnology regulatory structure in place now. It has already dealt with the licensing of a number of genetically engineered veterinary biologicals, and it has recently begun to receive requests for approval to release genetically engineered organisms into the environment. USDA's work load can only be expected to intensify as many companies with substantial investments in biotechnology research begin to push towards the commercialization of their research products. USDA can facilitate this process, thus generating the benefits of biotechnology and at the same time safeguarding the public and the environment from the related risks, only if its regulatory structure is in place,

sufficiently defined, and made known to all who must comply with or are otherwise interested in it. Along this line, USDA needs to develop its own recombinant DNA guidelines rather than to continue to rely on the NIH guidelines, which are said to be biomedically oriented, complex, and cumbersome with respect to agricultural matters.

Throughout our review we noted that there were signs of struggle between USDA's researchers and regulators over who will be given prime responsibility over biotechnology. USDA needs to resolve this issue as its ability to effectively and efficiently oversee biotechnology is dependent on all parties working together towards common goals. We believe that the ARRC, in part composed of representatives from both the research and regulatory sides of USDA, can and should provide the focal point and unity that USDA needs to conduct its activities relating to biotechnology.

Recommendations

We recommend that the Secretary of Agriculture direct the Assistant Secretaries for Marketing and Inspection Services and for Science and Education to work together to

- Complete the development of a formalized, well-defined regulatory structure over biotechnology, particularly with regard to deliberate releases of genetically engineered organisms into the environment. Such a structure should be sufficiently detailed to minimize questions about who in USDA is responsible for decisions in particular areas and flexible enough to encompass the wide range of biotechnological research and product development expected. It could, if deemed appropriate, incorporate a fully developed NBIAP and recombinant DNA guidelines geared specifically towards agriculture. Further, it should clearly identify the regulatory procedures for handling requests to license biotechnology products and approve the deliberate release of genetically engineered organisms into the environment. These procedures should help ensure the consistent handling and treatment of such requests.
- Provide USDA's coordinating committee (currently the ARRC) with the authority, prestige, and sense of direction it needs to effectively act as USDA's focal point for biotechnology. The committee should have the power to resolve differences that may arise with regard to biotechnology within USDA (e.g., between the regulators and researchers) and to act on USDA's behalf in resolving differences between USDA and other federal agencies, such as NIH, EPA, or FDA. The committee should be constituted as it is now with representatives from various agencies within and outside USDA. The various representatives should be capable of and willing to commit high priority to their committee responsibilities.

Agency Comments

USDA made no specific comments with regard to our recommendations.

USDA stated that the report does not describe any of USDA's recent initiatives in regulatory and research policy development and interagency cooperation. For example, USDA mentioned that APHIS has completed development of a well-defined biotechnology regulatory structure. It stated that APHIS' Veterinary Services has established three categories to classify new biotechnology products and is in the process of developing guidelines for the category of products that consist of live vectors carrying foreign antigens. In addition, APHIS' Plant Protection and Quarantine is drafting proposed regulations for the introduction of organisms altered by biotechnology that may be plant pests, or could harbor plant pests. Further, the APHIS administrator has established a Biotechnology and Environmental Coordination Staff to ensure that biotechnology matters receive the highest priority consideration.

USDA stated that its agricultural biotechnology research policy parallels the NIH system used by USDA for the past decade and that the policy is consistent with the mandate of the 1985 amendments to the National Agricultural Research, Extension, and Teaching Policy Act of 1977. These amendments (Public Law 99-198, Dec. 23, 1985) permit the Secretary of Agriculture to establish appropriate controls with respect to the development and use of biotechnology in agriculture.

USDA also stated that USDA is in dynamic dialogue with other agencies of the federal government that is leading to a clear statement of national policy regarding biotechnology. USDA referred specifically to the Biotechnology Science Coordinating Committee with OSTP, NIH, NSF, EPA, FDA, and its own regulatory and science units.

It is important to recognize the above initiatives, just as we have recognized many other important USDA initiatives on pages 38-45. The initiatives we discuss were recent ones, some of which took place in October and November 1985. Also, on pages 45-49, we discuss a number of interactions between USDA and other federal agencies. Many of the interactions mentioned in USDA's comments were relatively recent ones. Some of the more recent ones actually occurred after the completion of our field work in November 1985.

We recognize that USDA's involvement in biotechnology is changing, but believe that its actions to date have not fully addressed the issues and recommendations in this chapter. Along this line, we believe that it was contradictory for USDA to state that APHIS has completed development of

a well-defined biotechnology structure when, in fact, it goes on to state that APHIS' Veterinary Services ". . . is in the process of developing guidelines . . ." and ". . . APHIS' Plant Protection and Quarantine is drafting proposed regulations. . . ."

Although USDA's comments did not specifically address this matter, we continue to be concerned about the struggle for biotechnology regulatory control that seems to be going on within USDA between the research and regulatory sides. USDA's ability to effectively and efficiently regulate biotechnology is dependent upon all parties working together towards common goals. We continue to believe that the ARRC can and should provide the leadership that USDA needs to conduct its biotechnology activities.

USDA Needs to Better Communicate Its Plans for Regulating Biotechnology

The need for USDA to inform the public about the benefits and potential risks of biotechnology is expected to intensify as the related research moves from small-scale, carefully contained experiments to experiments built around the deliberate release of genetically engineered organisms into the environment. Although scientists have concluded that laboratory work with recombinant DNA is safer than initially thought, the transition to an era of frequent releases into the environment of genetically engineered organisms has caught the attention and aroused the concern of the public. USDA is expected to play a prominent role in these releases. To date, all but a few proposals for such releases have involved agriculture in one way or another. As the number of proposals for release (mainly relating to modified plants and microorganisms) grows, USDA will become increasingly a focal point for public concern about the nature of activities in biotechnology.

USDA has begun to recognize its need to inform others of its views about biotechnology and the regulatory role USDA will play. As indicated in the preceding chapter, it has recently undertaken several initiatives to specify procedures for research and regulation. These initiatives represent steps in the right direction and should help to clarify regulatory procedures. USDA can do more, however, to convey the reasons for its confident outlook on biotechnology and its plans for regulation in this area.

USDA needs to balance the presentation of its own views with views that do not completely share USDA's confidence about biotechnology. Distinguished scientists and some public critics have expressed their concerns about biotechnology's potential risks. The scientific community has realized increasingly that scientists specializing in ecology and the environment do not entirely agree with scientists in other specialties relevant to biotechnology where risk is concerned.

USDA needs to explain its own views effectively and yet be fully sensitive to those scientists and critics who either agree only in part or completely disagree with USDA. These contrasting points of view and suggestions for how USDA should respond to them are discussed in the following sections.

USDA Needs to Present Its Views More Effectively

Much of the criticism of USDA that we observed concerned the lack of specificity in USDA's plans for regulating biotechnology and the need for USDA to present its own views on biotechnology more effectively. One scientist who helped draft the original NIH-RAC guidelines and who has been closely involved with recombinant DNA research, development, and commercialization for a decade, told us that "USDA has got to marshal its arguments" in making its position on biotechnology clear and convincing to the public. Without exception, USDA officials with whom we talked agreed that USDA can do more to inform the public about biotechnology. For example, one USDA scientist, in referring to the vagueness of USDA's policy statement in the December 31, 1984, Federal Register, said "we can do better than that."

Some of the difficulty USDA has encountered in clarifying its biotechnology role has been attributed to the fact that many of its past activities were not matters that typically received close public scrutiny. USDA officials told us that the Department has been involved in agricultural research for 100 years with relatively few expressions of concern about what they were doing. According to the officials, informal guidelines for research were developed over the years, but the need to explain them to others did not arise. The officials said that, as a result, USDA has been somewhat surprised by the excitement and concern about biotechnology.

The importance of communication with the public was emphasized at a major conference on biotechnology held February 27 and 28, 1985, at the National Academy of Sciences in Washington, D.C. The conference marked the tenth year since the 1975 Asilomar Conference in California and, at least in part, was held to reflect on what had transpired over the past 10 years as well as what was expected in the future. Many issues and concerns were discussed, one of which was the need for those assembled to better inform the public about biotechnology. The conference recognized that public attitude is a driving force in shaping any law or regulation and that an uninformed or misinformed public with a fear of biotechnology could cause the enactment of a more restrictive set of rules than might otherwise be warranted.

In reviewing USDA's research and regulatory activities concerning biotechnology, we found that some recent USDA documents were beginning to "marshal the arguments" and communicate how USDA approaches its work. For instance, a November 1984 NASULGC document on the NBIAP provided an overview of the reasons for the agricultural research community's confident approach to biotechnology. It cited the extensiveness

of the community's prior experience—such as the safe release of over 7,500 new varieties of organisms—and proposed plans for improving the oversight of agricultural research throughout the nation. Officials involved in USDA's research and regulatory activities emphasized the document's value; we agree that the document and its August and November 1985 revisions are helpful in presenting USDA's general philosophical approach to biotechnology and some of its future plans for reviewing research in this area.

Another of USDA's efforts during 1985 to clarify and communicate its plans for regulating biotechnology was to revise its December 31, 1984, Federal Register statement. As noted in chapter 3, USDA and OSTP received numerous letters asking USDA to spell out its regulatory plans, and the revised version is expected to be available early in 1986. If the revised statement adequately explains USDA's plans for regulating biotechnology, it undoubtedly will help to inform biotechnology companies and experts of USDA's procedures for reviewing their proposals involving research, testing, and commercial release of genetically altered organisms.

In our judgment, USDA needs to continue its efforts to clarify biotechnology both to the general public and to specialists. We believe that documents such as the NASULGC statement and the revised version of the Federal Register policy statement will help do this. Given the complexity of the subject, however, such documents are, in our opinion, only a beginning in explaining USDA's basic views and plans.

USDA Needs to Assure the Public of Its Sensitivity Towards Risk

While faced with the challenge of explaining its own views more effectively, USDA needs to assure the public that it is also sensitive to the issue of risk. This issue raises a variety of important questions and concerns. The prospect of releases of genetically altered organisms (such as viruses) that may perhaps cover large agricultural regions has stirred considerable concern that any mistakes could be costly and very difficult, if not impossible, to correct. A leading scientist in the study of bacteria told the conference at the National Academy of Sciences that he felt "uncomfortable" with the present uncertainties. One critic has cited the revolutionary nature of biotechnology, comparing the splitting of the gene with the splitting of the atom, and has tried to persuade the public to look further into the future at the potential, long-term risks of biotechnology.

Reference to the nation's experience with other technologies in the past several decades suggests that new technologies or products can create or subsequently exhibit risks that were not foreseen or adequately discussed. The problems with nuclear power, such as the incident at Three Mile Island and the conflicts over radioactive waste disposal, are cases in point. The extensive use of pesticides, which helped to promote the environmental movement and the development of environmental regulations, is another. The national debate on the American supersonic transport in the 1970's raised questions about the airplane's ability to disrupt the protective ozone layer in the upper atmosphere. Products such as asbestos, widely applied as a fire retardant in many kinds of buildings, were used with a specific benefit in mind, while the full extent of their danger was not recognized until years later.

Such experiences with the risks of other technologies suggest the importance of candid, wide-ranging debate in the public forum when facing the development of any new technology. Biotechnology is stirring such a debate. One recent example of the controversy and uncertainty surrounding risk in biotechnology is provided by an exchange of views among scientists in the July 12, 1985, issue of Science magazine. Three letters were submitted concerning an earlier article in Science on the issue of safety in genetic engineering. The first letter contained the views of several ecologists and started as follows:

"The article on safety concerns and genetic engineering in agriculture . . . is a geneticist's evaluation of potential ecological hazards. As ecologists, our evaluation is quite different."

The letter then described why, from an ecological point of view, the risks of genetic engineering may be greater than admitted in the original article.

The second letter suggested that the accidental creation of a harmful organism through genetic engineering is extremely unlikely. According to the letter,

"Events like this do not happen inadvertently in laboratories by the random mixing of genes, just as one cannot inadvertently create a television set by a random mixing of electrical components."

The third letter was a response from the author of the earlier article. He defended his article and asserted that

"There is no reason to believe that genetically engineered organisms should be treated differently from conventionally altered organisms with regard to safety evaluation."

He also pointed out that his article was based on considerable personal knowledge of ecology.

Such a disagreement among scientists indicates that the issue of risk is far from being settled. In addition, the actions taken and concerns expressed by some critics have forced a review of the plans for releasing genetically engineered organisms into the environment. We believe that USDA's philosophy of caution (described in ch. 2) with regard to containment, testing, and deliberate release of new organisms has been strengthened by the need to respond to these criticisms and concerns. USDA's communication of this caution in response to potential risks, however, remains an important issue. Until USDA fully conveys its concern for, and methods of dealing with, the factor of risk, the agency is more likely to remain vulnerable to criticism on this issue.

USDA Discussion of Biotechnology Should Address Both Benefits and Risks

In its discussion of biotechnology, USDA needs to be fully responsive to the ongoing debate about biotechnology's benefits and risks. We found that USDA has shown enthusiasm for discussing the benefits expected from biotechnology. Various documents that we reviewed and presentations by USDA that we attended indicated USDA's desire to emphasize biotechnology's benefits. USDA literature, for example, suggests that direct improvements to crops and livestock will result from applying recombinant DNA techniques or some of the other new biotechnology tools. At a USDA conference we attended, biotechnology's benefits were endorsed by senior agency officials and by other speakers. In discussions with USDA officials, they told us of successful experimentation involving plants, animals, and microorganisms.

On the other hand, USDA discussion about biotechnology's risks or the reasons it believes certain risks are less significant than some critics allege were not as apparent or prevalent. For instance, we found few references in USDA literature to the possibility of long-term risks. Admittedly, biotechnology's risks and costs in many cases (and particularly over the long term) are unknown, but critics of biotechnology, including scientists, have warned that the release of hundreds or thousands of genetically engineered organisms into the environment might have major, cumulative effects that were never envisioned. Critics have also

pointed out that, unlike toxic chemicals, genetically engineered microorganisms cannot be as easily contained or recalled once they are released.

Some critics contend that, in addition to unknown risks, there are hidden costs associated with the gains from biotechnology that must be taken into account. For example, according to one critic, increases in U.S. agriculture's productivity and efficiency resulting from biotechnology might well have to be paid for with a more rapid rate of soil depletion. Another potential consequence might be the further loss of small-scale farms. To illustrate this point, the dairy industry's likely use of bovine interferon as a growth hormone has already stirred concern that small farms, which are not apt to use it, may be put out of business by larger farms, which will use it and become more productive.

We believe that in trying to improve its communication with the public, USDA needs to focus on both the potential benefits of biotechnology and its plans for dealing with risks. In past USDA communications, the potential benefits of biotechnology appear to have received greater attention than USDA's efforts to ensure a cautious approach to risks. We did not find any evidence, however, to suggest that USDA has been insufficiently cautious in its approach to biotechnology's risks. Nevertheless, in our opinion, any signs of a pattern of communication that puts too much emphasis on the benefits and too little emphasis on the plans for dealing with risks may create the impression that USDA is not being as sensitive to risks as some scientists and critics of biotechnology believe it should be.

Alternative Ways for USDA to Communicate Its Views on Biotechnology

USDA has taken steps in recent months to more openly communicate its biotechnology activities. These include its policy statement in the December 31, 1984, Federal Register, NASULGC's and USDA's ongoing development of the NBIAP, USDA's participation in various conferences and congressional hearings, and its plans to more clearly define its policies and procedures early in 1986. We believe that in addition to these activities, there are other means by which USDA might convey its activities in biotechnology. The means discussed in the following sections do not constitute a complete listing; rather, they suggest what might be done.

Brochures and Pamphlets

Brochures and pamphlets could summarize and highlight USDA's most important activities in biotechnology research or regulation. One such pamphlet issued by ARS in November 1984 was entitled "Agricultural

Biotechnologies: Strong Acceleration of Research Programs at Beltsville." ARS also issued a brochure in August 1985 entitled "Solving Agricultural Problems With Biotechnology." We found both documents to be enlightening with regard to ARS' biotechnology activities. APHIS officials told us that they were preparing a brochure describing their biotechnology activities, but they did not expect to issue it until early 1986.

Newsletters

Because biotechnology is growing in importance and attracting wider attention, a USDA newsletter published periodically and devoted to the subject might help keep the public and the Congress informed of USDA's biotechnology activities. Without divulging proprietary or confidential information, such a publication might describe some of the proposals for research or for deliberate release that USDA has under consideration. Through case study examples, it might show the caution and extensive testing USDA insists upon before agricultural organisms are released into the environment. If an organization other than USDA publishes such a newsletter, USDA could play an active role in contributing to it.

Public Conferences and Debates

Although several conferences on biotechnology have been held, none of them has focused exclusively on agricultural concerns. To promote public discussion about biotechnology, particularly with a focus on agricultural matters, USDA might want to host such a conference. Experts from all sides of the debate could be invited to participate. Such a conference would give USDA the opportunity to make better known its views on biotechnology and, if appropriately reported, could help the public more clearly understand all sides of the debate.

Yearbook of Agriculture

USDA publishes an annual yearbook that contains considerable information on a specific, agriculturally oriented theme. For example, the themes of the yearbooks in 1983 and 1984, respectively, were "Using Our Natural Resources" and "Animal Health: Livestock and Pets." The yearbooks make wide use of photographs and various kinds of graphics.

A yearbook devoted to the subject of biotechnology could cover in some depth the many facets of this topic, including the scientific disciplines that are behind it; the structure that regulates it; and the benefits, products, risks, costs, and ethical concerns that have, or are expected to, come from it.

Conclusions

Biotechnology is entering a new era. Many of the small-scale, carefully contained experiments conducted in research laboratories have progressed to the point where USDA has received proposals for licensing or further testing, through deliberate release into the environment, of the genetically engineered organisms that have been produced. Such activity has caught the attention and aroused the concern of the public. A public uncertain of the potential benefits and possible risks and costs of biotechnology could impede biotechnology's progress in the United States through the imposition of laws and regulations that may be more restrictive than necessary. The need for federal agencies, including USDA, to communicate with the public about biotechnology is expected to intensify as experiments in biotechnology move towards the release of genetically altered organisms into the environment.

Historically, many of USDA's research activities were not the type that drew a lot of close public scrutiny; therefore, the need for USDA to explain these activities to others did not arise. USDA officials have been surprised by the excitement and concern about the new biotechnologies and, admittedly, have not been very effective in communicating to others their views on biotechnology. USDA officials have begun to recognize the need to do this, however, as the public's concerns about biotechnology have persisted and, perhaps, even grown. In their ensuing attempts to communicate more effectively with the public what they are doing with respect to biotechnology, USDA officials need to effectively explain the reasons for their confident outlook on biotechnology as well as be fully sensitive to those scientists and critics who do not entirely share their confidence. While discussing biotechnology's potential benefits, USDA officials also must acknowledge the possible risks and costs and explain more clearly their plans for dealing with risks.

Recommendation

We recommend that the Secretary of Agriculture look for and take advantage of opportunities to improve and increase the communication of USDA's views on biotechnology, both in terms of the benefits to be derived and the risks that must be considered and managed. In this regard, the Secretary should consider a variety of approaches for doing this, including brochures, newsletters, public conferences and debates, and a Yearbook of Agriculture devoted to biotechnology. The purpose of all such communication should be to foster a more open, frank, and informed discussion about USDA's views on biotechnology and how USDA will address the related risks.

Agency Comments

USDA's comments did not specifically address our recommendation.

In its comments relating to this chapter, USDA stated that the report does not describe its considerable efforts to communicate within the public and private sectors about agricultural biotechnology. It stated that ARS has sponsored symposia devoted exclusively to biotechnology applications of agricultural interest, sponsored a 3-day symposium on Hybridoma Technology in Agricultural and Veterinary Research, and helped organize an international conference on genetic engineering of animals. USDA also stated that its research and regulatory staff members have actively participated in the majority of national and international symposia on biotechnology issues, including the newly formed committees on biotechnology of the American Society for Testing and Materials.

We believe that the report does describe a number of important efforts USDA has taken with regard to communication. For example, the report describes on pages 57, 58, 60, and 61 a number of different means by which USDA has communicated to others its views about agricultural biotechnology. While we acknowledge the additional examples USDA provided, as discussed above, we note that such examples address the uses and benefits of biotechnology rather than the risks associated with biotechnology and the plans USDA has for managing those risks. This is the same point we make in this chapter on pages 60 and 61 concerning much of USDA's communication about biotechnology in the past. As a result, we continue to believe that USDA can and should do more to communicate to the public not only why it is confident about the prospects of biotechnology but also what actions it is taking to protect the public and the environment from any harm that might result from biotechnology.

Request Letter From the Chairman, House Committee on Science and Technology

March 29, 1984

Hon. Charles A. Bowsher
Comptroller General of the United States
General Accounting Office
441 G Street, GAO Bldg.
Washington, D.C. 20548

Dear Mr. Bowsher:

The purpose of this letter is to request that the General Accounting Office undertake a review of the programs of the U.S. Department of Agriculture in the area of biotechnology generally, and specifically, how such programs relate to decision making concerning the deliberate release of genetically engineered organisms into the environment.

The Committee on Science and Technology recently printed the attached report, "The Environmental Impacts of Genetic Engineering." One of the recommendations in the report calls for a review of the activities of U.S. Department of Agriculture in overseeing biotechnology and an evaluation of the Agency's programs to regulate deliberate releases under all relevant statutes, regulations, and executive orders. We have requested that the American Law Division of the Congressional Research Service conduct a review of the legal authority of USDA. We would appreciate GAO's evaluation of the Agency's organization, programs, budget, research, and personnel to implement its authorities and undertake the necessary activities to make decisions concerning the release into the environment of genetically engineered organisms. The task also includes documentation of R&D activities in biotechnology, which are being supported or conducted by the Agency, as well as an analysis of the relationship between U.S. Department of Agriculture, the National Institutes of Health, and the Environmental Protection Agency.

Robert B. Nicholas, Staff Director/Counsel, and Dr. Morris Levin, a LEGIS Fellow, of the Subcommittee staff have discussed the overall scope of the review with Walter Hess, Gerald Killian, and Bob Sevigny of your staff.

We appreciate your assistance in this effort. If you have any questions, Mr. Nicholas and Dr. Levin can be reached at 226-3636.

Sincerely,

DON FUQUA
Chairman

DF/Ltk
Attachment

Advance Comments From the Department of Agriculture

Note: GAO comments supplementing those in the report text appear at the end of this appendix.

DEPARTMENT OF AGRICULTURE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20250

Februrary 4, 1986

Mr. J. Dexter Peach, Director
Resources, Community and
Economic Development Division
U.S. General Accounting Office
Washington, D.C. 20548

Dear Mr. Peach:

The U.S. Department of Agriculture (USDA) is furnishing the following comments on the draft of the proposed General Accounting Office (GAO) report, Biotechnology: Agriculture's Regulatory System Needs To Be Clarified and Communicated.

From a research standpoint, the report was found to be a basically sound analysis. Some suggested corrections and constructive comments are included below.

Regulatory review of the GAO study discloses serious errors and omissions. The USDA comments are summarized below.

I. Content of the Report - The GAO transmittal letter states that "the report discusses, among other things, USDA's organizational and philosophical approach to regulating biotechnology." However, the discussion does not clearly distinguish between the regulatory authority granted by statutes such as the Federal Plant Pest Act (FPPA) and the Virus-Serum-Toxin Act, and the legislative authority to fund research. The regulatory agencies such as the Animal and Plant Health Inspection Service (APHIS) and Food Safety and Inspection Service (FSIS) have the statutory authority to regulate, while the NIH Recombinant DNA Advisory Committee (NIH-RAC) and the Agricultural Recombinant DNA Advisory Committee (ARAC) can directly control only the research contracts funded by their respective agencies. It is important to emphasize that neither NIH-RAC nor ARAC are regulatory agencies in the sense of the Food and Drug Administration (FDA), APHIS, or FSIS. Rather, they provide guidelines for the safe and efficacious conduct of rDNA research which may be made a condition for the conduct of such research, especially that funded by the agency. (The National Science Foundation (NSF) is yet another research agency which has the same obligation to provide guidelines, but they should be consistent across research agencies.) It should be noted that the 1985 Farm Bill does provide statutory support for the agriculture research guidelines. (The 1985 amendments to the National Agricultural Research, Extension, and Teaching Policy Act (NARETPA) of 1977 permit the Secretary of Agriculture to "establish appropriate controls with respect to the development and use of the application of biotechnology to agriculture" (Public Law 99-198, December 23, 1985).)

Mr. J. Dexter Peach 2

II. Omissions - The report does not describe recent USDA initiatives in regulatory and research policy development, communication, and interagency cooperation. For example, APHIS has completed the development of a well-defined biotechnology regulatory structure. APHIS' Veterinary Services has established three categories to classify new biotechnology products and is in the process of developing guidelines for the category of products which consist of live vectors carrying foreign antigens. In addition, APHIS' Plant Protection and Quarantine is drafting proposed regulations for the introduction of organisms altered by biotechnology which may be plant pests, or could harbor plant pests, pursuant to the authority of the FPPA and the Plant Quarantine Act. Further, the Administrator of APHIS has established a Biotechnology and Environmental Coordination Staff to ensure that biotechnology matters receive the highest priority consideration.

USDA's agricultural biotechnology research policy parallels the NIH system used by USDA for the past decade. The policy is consistent with the mandate of the NARETPA amendments of 1985.

Comment #1.

These regulatory and research policy initiatives will be fully described in a Federal Register notice published in early 1986 and must be included in the GAO report.

The GAO report also does not describe the considerable effort made by USDA agencies to communicate within the public and private sectors about agricultural biotechnology. The Agricultural Research Service (ARS), USDA, has sponsored a series of Beltsville Symposia devoted exclusively to biotechnology applications of agricultural interest, sponsored a 3-day symposium on Hybridoma Technology in Agricultural and Veterinary Research, and helped organize an international conference on genetic engineering of animals at the University of California at Davis in September 1985. USDA research and regulatory staff members have actively participated in the majority of national and international symposia on biotechnology issues, including the newly formed committees on biotechnology of the American Society for Testing and Materials.

Comment #2.

The report should describe the delegations of authority for biotechnology research and regulation reported in the Federal Register on July 19, 1985 (50 FR 29367-68), the publication of the APHIS policy on the protection of confidential business information of September 23, 1985 (50 FR 38561-63), and the USDA-Food and Drug Administration-Environmental Protection Agency (EPA) memorandum of understanding (MOU) of January 16, 1985 (50 FR 2304). The triagency MOU was concerned with residues of drugs, pesticides, and environmental contaminants in food, and it could become particularly important for agricultural biotechnology if bioengineering and gene manipulation result in the presence of biological residues in agricultural products and foods.

Comment #3.

III. Proposed Revisions - USDA feels that the draft report needs work on form, as well as on content, beginning with the title chosen for the draft. How does one clarify a regulatory system, and how does one communicate a regulatory system? We suggest that a modification of the short title that appears on the bottom of each summary page would be more appropriate - "USDA Biotechnology Oversight and Regulation." We also suggest that the excessive use of terms such as "with regard to" and "with respect to" be deleted and that the use of "less easy" be replaced with "more difficult."

USDA agency reviewers also noted that certain statements should be corrected, such as the reference to Gregor Mendel's experiments having been undisclosed until 1900 when, in fact, they were published in 1866. The GAO report notes that the comments contained a limited amount of criticism on the EPA policy statement on biotechnology, when, in fact, the comments were highly critical of EPA's proposed policies.

Comment #4.

USDA continues to endorse a uniform set of guidelines and recognizes the NIH Guidelines as applicable to contained research while developing USDA Guidelines for Biotechnology Research covering both contained research and release into the environment. USDA views intentional release into the environment in a positive manner as a beneficial agricultural application of biotechnology, rather than in the negative manner suggested by use of the term "deliberate release." On pages 22-23, the following changes are suggested to accurately reflect current procedures:

Now on pp. 19 and 20.

- For Category (2) experiments, add ". . .and review by the Institutional Biosafety Committee (IBC)."
- For Category (3) experiments, insert "and IBC" after NIH-RAC.
- Add an additional sentence at the end of the last paragraph on page 22: "Compliance with these standards is assured by the IBC's at the local level."
- Change last sentence in paragraph 2, page 23, after -- to read: "originally, they simply prohibited such releases and, more recently, required special review under Category (1)."

Now on p. 19.

Now on p. 20.

The sentence reading "ARS has major responsibilities for conducting and leading the national agricultural research effort" (pp. 29-30) should be corrected to read "The Assistant Secretary for Science and Education has major responsibilities. . . ." It must also be noted that all staff associated with the Cooperative State Research Service is not located entirely in the Washington, D.C., area. In the discussion of containment, testing, and deliberate release on pages 33-36, it should be made clear on page 35 that the extensive testing illustrated occurs in field plots (i.e., in the environment) and that release in this context means release of a cultivar or organism from an experimental research program to a commercial program as a product. To more accurately describe the corn blight incident on pages 36-37, we suggest the following: "The scientists were able to take steps to counteract the blight and quickly control and eliminate the problem."

Now on p. 25.

Now on pp. 28-30.

Now on p. 30.

It is also important to recognize that the USDA is in dynamic dialogue with other agencies of the Federal Government which is leading to a clear statement of national policy regarding biotechnology. We refer specifically to the Biotechnology Science Coordinating Committee with OSTP, NIH, NSF, EPA, FDA, and USDA's regulatory and science units.

IV. Intent and Purpose of the GAO Report - While it is acknowledged that the report does not purport to be more than a discussion of the USDA organizational approach to regulating biotechnology, there is no doubt that further discussion is needed. The February 1984 staff report prepared by the Subcommittee on Investigations and Oversight, "The Environmental Implications of Genetic Engineering" stated that USDA's regulatory capability and perception need to be made clear. It was understood by commenters on the USDA

biotechnology policy statement of December 31, 1984 (49 FR 50856-50907), that the GAO report was to have presented the results of an analysis of the USDA's statutory capability for regulating the processes and products of biotechnology in agriculture. The stated need for such an analysis was to help Congress determine whether new legislation was required to effectively regulate biotechnology products. The GAO has not evaluated USDA's authority to regulate deliberate releases under all relevant statutes, regulations, and executive orders. The first section of the GAO report published in October 1985 listed and described the biotechnology research funded by USDA. This effort was succinct and useful. The draft report that is the subject of these comments could serve as background for a revised evaluation.

The evaluation should provide an analysis of the major regulatory statutes administered by USDA, including the scope and applicability of such statutes to the regulation of genetically engineered products. Of particular importance would be an examination of the scope and applicability of the 1985 amendments to the NARETPA of 1977 which permit the Secretary of Agriculture to "establish appropriate controls with respect to the development and use of the application of biotechnology to agriculture" (Public Law 99-198, December 23, 1985).

A careful analysis of USDA regulatory methodology for assessing the hazards of release into the environment, in both USDA research projects and commercial product development, would also serve the public interest. This analysis would be expected to give full credit to the 10-year record of research oversight experience that the Science and Education Administration expects to use in developing the National Biological Impact Assessment Program.

In summary, USDA urges that the draft report be used only as background preparation for the evaluation which should help resolve any questions about the capability of USDA to deal with safety and regulatory issues in agricultural biotechnology.

Sincerely,

JOHN R. NORTON
Acting Secretary

The following are GAO's comments on the Secretary of Agriculture's letter dated February 4, 1986.

GAO Comments

1. As of March 3, 1986, the details and specificities concerning USDA's approach to regulating biotechnology had not yet been published in the Federal Register. However, issuance of our report is not contingent upon publication of the Federal Register notice.

2. The publication of APHIS' policy on the protection of confidential business information in September 1985 was, we understand, in response to concerns expressed by the business community. It was not a main issue, though, with regard to the scope of our work.

3. The title of our report was modified slightly based on USDA's comments. The other editorial changes as suggested by USDA were made as we deemed appropriate.

4. Nowhere in the report did we observe that USDA's comments on the EPA policy statement on biotechnology were not critical of the EPA position. Pursuant to USDA's wishes, however, we now describe USDA's comments on EPA's policy statement as discussed on page 47 as having been "highly critical."

Glossary

Biocontrol Agent	A microorganism or insect which, for agricultural purposes, preys on harmful organisms.
Cell Fusion	Formation of a single hybrid cell by combining different cells.
Cultivar	An organism of a kind originating and persistent under cultivation.
Deoxyribonucleic Acid (DNA)	The genetic material found in living organisms.
Ecosystem	The sum total of interacting elements in a limited universe, including both the living and environmental components.
Embryo Transfer	The removal of a fertilized egg in an early developmental stage from its genetic mother's reproductive tract and its transfer to another female's reproductive tract for development and subsequent birth.
Host-Vector System	A compatible combination of host (e.g., bacterium) and vector (e.g., virus) that allows a stable introduction of DNA into foreign cells.
Hybridoma	A product of fusing a cell capable of continuous division with an antibody-producing cell; the resulting hybrid can be used to produce large amounts of antibodies for treating diseases.
Interferon	A substance produced by virus-infected cells that, in turn, can be used to inhibit multiplication of the virus.
In Vitro	Outside the living body and in an artificial environment such as a test tube; distinguished from in vivo, in the living body.
Microbe	A minute life form; microorganism.

Nitrogen Fixation	The assimilation of atmospheric nitrogen by soil microorganisms and its release for plant use following the death of the microorganisms.
Pathogen	A specific agent, such as a bacterium or virus, causing disease.
Plant Cell and Protoplast Culture	The growth of the whole cell or the internal components of the cell minus its surrounding wall.
Plant Regeneration	The development of an entire plant from a single cell or tissue of the plant.
Recombinant DNA	The hybrid DNA produced by joining pieces of DNA from different organisms or synthetic DNA together in vitro.
Somatic Hybridization	The fusion of cells composing parts of the body other that a germ cell.
Vector	DNA molecule used to introduce DNA into host cells. A virus can be used as a vector.
Veterinary Biological	A vaccine or other product used in the treatment or diagnosis of diseases; distinguished from a veterinary drug, which is used for other purposes such as stimulating growth.

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