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THE WHITE HOUSE

Office of the Press Secretary
(Santa Barbara, California)

For Immediate Release April 11, 1985

FACT SHEET

Economic Policy Council
Domestic Policy Council

In order to provide better policy coordination, formulation and implementation, the President today announced the creation of two new cabinet-level councils, the Economic Policy Council and the Domestic Policy Council, to advise him on economic and domestic policy issues.

The Economic Policy Council will consider those policy issues that are primarily economic in nature; the Domestic Policy Council will consider those policy issues that are not primarily economic in nature.

These new councils build on the President's commitment to cabinet government and to the inclusion of department and agency heads in the Administration's decision-making process.

General Features

The streamlined, consolidated system will help clarify responsibility and enhance accountability for formulating and implementing economic and domestic policy.

- The two new councils will replace the following:

  Cabinet Council on Commerce and Trade
  Cabinet Council on Economic Affairs
  Cabinet Council on Food and Agriculture
  Cabinet Council on Human Resources
  Cabinet Council on Legal Policy
  Cabinet Council on Management and Administration
  Cabinet Council on Natural Resources and the Environment
  Senior Interagency Group on International Economic Policy

- The Economic Policy Council, the Domestic Policy Council and the National Security Council will serve as the primary channels for advising the President on policy.

- The Vice President and the Chief of Staff will serve as ex-officio members of both the Economic and Domestic Policy Councils.

- Executive department and agency heads who are not members of a council will be invited to attend the Council's meetings when issues involving their department or agency are under consideration.

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Economic Policy Council

The increasing interrelatedness of the U.S. and international economies illustrates the importance of establishing a process that will examine economic issues in a comprehensive integrated way. The Economic Policy Council will provide the President with a single entity to advise him on domestic and international economic policy.

Membership

The Secretary of State
The Secretary of the Treasury
The Secretary of Agriculture
The Secretary of Commerce
The Secretary of Labor
Director, Office of Management and Budget
The United States Trade Representative
Chairman, Council of Economic Advisors

Heads of the national security community departments and agencies and the Assistant to the President for National Security Affairs will participate in council meetings when international policy or budget matters are discussed.

Chairmanship

The President will chair meetings of the Economic Policy Council. In his absence, the Secretary of the Treasury, who will serve as Chairman Pro Tempore, will preside at meetings of the Council.

Responsibilities

The Council will have the responsibility for advising the President on all aspects of national and international economic policy, and for overseeing the coordination and implementation of the Administration's economic policies.

Staff

The staff of the Council shall be headed by an Executive Secretary who will report to the Chief of Staff through the Cabinet Secretary.

Like the current cabinet councils, the Economic Policy Council will rely heavily on interagency subcabinet level Working Groups. This will enable it to utilize fully the expertise and resources of the departments and agencies, and to provide a structure through which departmental initiatives can be considered fully.

Domestic Policy Council

The Domestic Policy Council will provide the President with a single entity to advise him on domestic and social policy. By focusing decision making and advice through a single channel for domestic policy issues, this will enhance the prospects for developing such policies in a comprehensive and integrated way.

Membership

The Attorney General
The Secretary of the Interior
The Secretary of Health and Human Services
The Secretary of Housing and Urban Development
The Secretary of Transportation
The Secretary of Energy
The Secretary of Education
Director, Office of Management and Budget

Chairmanship

The President will chair meetings of the Domestic Policy Council. In his absence, the Attorney General, who will serve as Chairman Pro Tempore, will preside at meetings of the Council.

Responsibilities

The Council will have responsibility for advising the President on all aspects of domestic policy issues, and for overseeing the coordination and implementation of the Administration's domestic policies.

Staff

The staff of the Council shall be headed by an Executive Secretary who will report to the Chief of Staff through the Cabinet Secretary.

Like the current cabinet councils, the Domestic Policy Council will rely heavily on interagency subcabinet level Working Groups. This will enable it to fully utilize the expertise and resources of the departments and agencies, and to provide a structure through which departmental initiatives can be considered fully.

Overall Coordination

The White House Chief of Staff will have responsibility for ensuring that the activities of the National Security Council, the Economic Policy Council, and the Domestic Policy Council are fully coordinated. He will also have the responsibility for assigning topics to a particular Council.

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EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506

May 15, 1986

MEMORANDUM FOR THE DOMESTIC POLICY COUNCIL WORKING GROUP

FROM: David T. Kingsbury David T. Kingsbury

SUBJECT: Federal Register Notice

Thank you for your comments to the May 13, 1986, draft preamble. We have attempted to accommodate your suggestions in light of slightly different points of view. Enclosed is the draft preamble being sent to the Domestic Policy Council.

Also enclosed is EPA's modified policy statement. The other agencies' policy statements remain unchanged. The USDA proposed S&E guidelines are being rewritten but will be ready on Monday (May 19).

Enclosures

OFFICE OF SCIENCE AND TECHNOLOGY POLICY

COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY:

AGENCY: Executive Office of the President, Office of Science and Technology Policy

ACTION: Announcement of Policy; Notice for Public Comment

SUMMARY: This Federal Register notice announces the policy of the federal agencies involved with the review of biotechnology research and products. As certain concepts are new to this policy, and will be the subject of rulemaking, the public is invited to comment on these aspects which are specifically identified herein.

DATE: Comments must be received on or before [insert date 60 days after date of FR Notice].

Public Participation: The Domestic Policy Council Working Group on Biotechnology through the Office of Science and Technology Policy, is seeking advice on certain refinements published herein to the previously published proposed coordinated framework for regulation of biotechnology. These new aspects include the Biotechnology Science Coordinating Committee's (BSCC's) definitions for an "intergeneric organism (new organism)" and for "pathogen." These definitions are critical to the coordinated framework for the regulation of biotechnology because they establish the types of the organisms subject to certain kinds of review.

It is the intention of the Domestic Policy Council Working Group on Biotechnology, the Biotechnology Science Coordinating Committee (BSCC), the Department of Agriculture (USDA), the Environmental Protection Agency (EPA), the Food and Drug

Administration (FDA), the National Science Foundation (NSF), and the Occupational Safety and Health Administration (OSHA) that the definitions and policies contained herein be effective immediately. In consideration of comments, modifications, if any, may be published either in a separate notice or as part of proposed rulemaking by the involved agencies.

Information submitted to an agency that is trade secret information or confidential business information should be clearly marked so that it can be accorded the protection provided to such by each respective agency.

ADDRESS: Comments specific to the BSCC definitions or overall comments to the Coordinated Framework for the Regulation of Biotechnology statements should be addressed to:

BSCC: Docket #BSCC 0001, Office of Science and Technology Policy, Executive Office of the President, NEOB-Room 5005, Washington, D.C. 20506

Comments relating to the policy statements of a particular agency should be sent directly to the agency contact identified at the beginning of the respective agency policy statement.

FOR FURTHER INFORMATION CONTACT: Dr. David T. Kingsbury, Assistant Director for Biological, Behavioral, and Social Sciences, National Science Foundation, 1800 G Street, N.W., Washington, D.C. 20550, (202-357-9854).

Jerry D. Jennings
Executive Director,
Office of Science and Technology Policy

May __, 1986

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A. INTRODUCTION

This notice describes the comprehensive federal regulatory policy for ensuring the safety of biotechnology research and products. Specifically addressed are agency policies that formed part of the previously proposed Coordinated Framework for the Regulation of Biotechnology, published in the Federal Register December 31, 1984 (49 FR 50856, hereinafter "the December 84 Notice"). These agency policies build upon experience with agricultural, pharmaceutical, and other commercial products developed by traditional genetic modification techniques.

Existing statutes provide a basic network of agency jurisdiction over both research and products; this network forms the basis of this coordinated framework and helps assure reasonable safeguards for the public. This framework is expected to evolve in accord with the experiences of the industry and the agencies, and, thus, modifications may need to be made through administrative or legislative actions.

The application of traditional genetic modification techniques is relied upon broadly for enhanced characteristics of food (e.g., hybrid corn, selective breeding), manufactured food (e.g., bread, cheese, yogurt), waste disposal (e.g., bacterial sewage treatment), medicine (e.g., vaccines, hormones), pesticides (e.g. Bacillus thuringiensis) and other uses. Federal agencies implement an array of laws which seek to ensure the safety of these products. A concise index of these U.S. laws was published in the Federal Register November 14, 1985 (50 FR 47174, hereinafter "the November 85

Notice"). These laws are product-specific because they regulate certain product uses, such as foods or pesticides. This approach provides the opportunity for similar products to be treated similarly by particular regulatory agencies.

Biotechnology also includes recently developed and newly emerging genetic manipulation technologies, such as recombinant DNA (rDNA), recombinant RNA (rRNA) and cell fusion, that are sometimes referred to as genetic engineering. While the recently developed methods are an extension of traditional manipulations that can produce similar or identical products, they enable more precise genetic modifications, and therefore hold the promise for exciting innovation and new areas of commercial opportunity.

Concerns were raised as to whether products resulting from the recently developed techniques would pose greater risks than those achieved through traditional manipulation techniques. For example, what might be the possible environmental consequences of the many anticipated agricultural and environmental applications that will take place outside the physical constraints of a contained facility? In particular, the environmental application of genetically engineered microorganisms may elicit concern because they are of microscopic size, and some may be able to reproduce, proliferate, and become established.

The underlying policy question was whether the regulatory framework that pertained to products developed by traditional genetic manipulation techniques was adequate for products obtained with the new techniques. A similar question arose regarding the

sufficiency of the review process for research conducted for agricultural and environmental applications.

The Administration, recognizing its responsibility to confront these concerns, formed an interagency working group under the former White House Cabinet Council on Natural Resources and the Environment in the spring of 1984. The working group sought to achieve a balance between regulation adequate to ensure health and environmental safety while maintaining sufficient regulatory flexibility to avoid impeding the growth of an infant industry.

Upon examination of the existing laws available for the regulation of products developed by traditional genetic manipulation techniques, the working group concluded that, for the most part, these laws as currently implemented would address regulatory needs adequately. For certain microbial products, however, additional regulatory requirements, available under existing statutory authority, needed to be established.

The existing health and safety laws had the advantage that they could provide more immediate regulatory protection and certainty for the industry than possible with the implementation of new legislation. Moreover, there did not appear to be an alternative, unitary, statutory approach since the very broad spectrum of products obtained with genetic engineering cut across many product uses regulated by different agencies.

Because of the rapid growth in the scientific knowledge base, the working group felt strongly that the federal agencies needed to have an interagency mechanism for sharing scientific information

related to biotechnology, particularly information on research and product applications submitted to the agencies.

The December 84 Notice described the regulatory framework envisioned by the working group, and recognizing the evolutionary nature of its development, asked for comments. In summary, the Notice stated that the Food and Drug Administration (FDA) would regulate genetic engineering products no differently that those achieved through traditional techniques. The Environmental Protection Agency (EPA) described existing and proposed new policies for regulating pesticidal and nonpesticidal microorganisms. The Department of Agriculture (USDA) stated that under its different legislative authorities it could broadly regulate genetically engineered plants and animals, and plant and animal pathogens. The Notice also proposed an interagency science coordinating mechanism.

Many comments were received in response to the Notice. These contributed to the refinement of both the regulatory requirements and the interagency science coordination mechanism.

The interagency coordination mechanism, the Biotechnology Science Coordinating Committee (BSCC), discussed in more detail in section C. of this Preamble, came into being while the agencies were still in process of refining their regulatory proposals. Consequently, the BSCC was able to play a helpful role in the formulation of two basic principles: (1) agencies should seek to adopt consistent definitions of those genetically engineered organisms subject to review to the extent permitted by their

respective statutory authorities; and, (2) agencies should utilize scientific reviews of comparable rigor.

The regulatory framework anticipates that future scientific developments will lead to further refinements. Experience with earlier basic scientific research has shown that as the science progressed and became better understood by the public, regulatory regimens could be modified to reflect more complete understanding of the potential risks involved. Similar evolution is anticipated in the regulation of commercial products as scientists and regulators learn to predict more precisely particular product use that require greater or lesser controls or even exemption from any federal review.

This framework has sought to distinguish between those organisms that require a certain level of federal review and those that do not. This follows a traditional approach to regulation. Within agriculture, for example, introductions of new plants, animals and microorganisms have long occurred routinely with only some of those that are not native or are pathogenic requiring regulatory approval. It should be noted that microorganisms play many essential and varied roles in agriculture and the environment and that for decades agricultural scientists have endeavored to exploit their advantages through routine experimentation and introduction into the environment; and as a rule these agricultural and environmental introductions have taken place without harm to the environment.

B. THE COORDINATED FRAMEWORK FOR THE REGULATION OF BIOTECHNOLOGY

General Comments

This notice includes separate descriptions of the regulatory policies of FDA, EPA, OSHA and USDA and the research policies of the National Institutes of Health (NIH), NSF, EPA and USDA. The agencies will seek to operate their programs in an integrated and coordinated fashion and together should cover the full range of plants, animals and microorganisms derived by the new genetic engineering techniques. To the extent possible, responsibility for a product use will lie with a single agency. Where regulatory oversight or review for a particular product is to be performed by more than one agency, the policy establishes a lead agency, and consolidated or coordinated reviews. While this preamble seeks to convey an overview of the coordinated framework, it must be noted that the regulatory requirements are highly technical; reliance only on the simplified summary statements herein could be misleading and, thus, the agency policy statements must be consulted for specific details. In the event that questions arise regarding which federal agency has jurisdiction, an information contact is provided at the beginning of this notice.

While in part certain USDA and EPA requirements are new, the underlying regulatory regimens are not new. Members of the agricultural and industrial communities are familiar with the general requirements under these laws which include the Federal Plant Pest Act, the Plant Quarantine Act, the Toxic Substances Control Act (TSCA), and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

Because this comprehensive regulatory framework uses a mosaic of existing federal law, some of the statutory nomenclature for certain actions may seem inconsistent. Certain laws, such as USDA's Federal Plant Pest Act, require a "permit" before a microorganism pathogenic to plants may be transported or imported. Under other laws such as FIFRA, the agencies "license" or "approve" the use of particular products. TSCA requires a "premanufacturing notification (PMN)". There are also some variations among the agencies in the use of the phrase "genetic engineering." Regardless of the nomenclature, the public should be aware that the reviews conducted by each of the regulatory agencies are intended to be of comparable rigor. Agencies have agreed to have scientists from each other's staff participate in reviews. Each regulatory review will require that the safety, or safety and efficacy, of a particular agricultural or industrial product be satisfactorily demonstrated to the regulatory agency prior to commercialization.

The National Environmental Policy Act (NEPA) imposes procedural requirements on all federal agencies to prepare an analysis prior to making a decision to take any action that may significantly affect the environment. Depending on the characteristics of a proposal, an environmental assessment, or a broader environmental impact statement may need to be prepared in connection with the release of genetically manipulated organisms. EPA's actions under most of its environmental statutes have been considered to be the functional equivalent of NEPA compliance.

For the handling of microorganisms, agencies of the Department

of Health and Human Services have established recommendations for the safe use of infectious agents. The CDC/NIH publication, Biosafety in Microbiological and Biomedical Laboratories, describes combinations of standard and special microbiological practices, safety equipment and facilities which are recommended for working with a variety of infectious agents in research laboratories, academic and industrial. The USDA also has issued guidance on other infectious agents.

The NIH has published guidelines for the contained use of rDNA organisms in the NIH Guidelines for Research Involving Recombinant DNA Molecules, Federal Register, May 7, 1986 (51 FR 16958, NIH guidelines). The guidelines recommend physical containment at specific levels for different experiments, and exempt other experiments from containment requirements. However, they recommend Biosafety Level 1, the least stringent level of physical containment, for some "exempt" experiments. For large-scale exempt experiments, the NIH guidelines recommend "Biosafety Level 1-Large-Scale" although following review by the Institutional Biosafety Committee, "some latitude" in the application of these requirements is permitted.

The appropriate large-scale containment requirements for many low risk rDNA derived industrial microorganisms will be no greater than those appropriate for the unmodified parental organisms. This concept is discussed further in the Organization for Economic Cooperation and Development (OECD) document, described in the International Aspects section below.

OSHA in its Federal Register Notice of April 12, 1984 (50 FR 14468) stated that its authority under the Occupational Safety and Health Act of 1970 (29 U.S.C. et seq.) provides an adequate and enforceable basis for protecting the safety and health of employees in the field of biotechnology and that no additional regulation is necessary. After consideration of comments on the April 1984 notice, OSHA is publishing this policy statement in final form without change.

Product Regulation

Agencies involved with regulating agriculture, foods, medical devices, drugs, biologics and pesticides have had extensive experience with products that involve living organisms in their manufacture and/or ultimate use including releases into the environment for these purposes. By the time a genetically engineered product is ready for commercialization, it will have undergone substantial review and testing during the research phase, and thus, information regarding its safety should be available. The manufacture by the newer technologies of food, the development of new drugs, medical devices, biologics for humans and animals, and pesticides, will be reviewed by FDA, USDA and EPA in essentially the same manner for safety and efficacy as products obtained by other techniques. The new products that will be brought to market will generally fit within these agencies' review and approval regimens.

The regulatory scheme for products is described in Chart I Coordinated Framework -- Marketing Approval of Biotechnology Products.

CHART I -- COORDINATED FRAMEWORK --
APPROVAL OF COMMERCIAL BIOTECHNOLOGY PRODUCTS

Subject	Responsible Agency(ies)
Foods/Food Additives	FDA*, FSIS[1]
Human Drugs, Medical Devices and Biologics	FDA
Animal Drugs	FDA
Animal Biologics	APHIS
Other Contained Uses	EPA
Plants and Animals	APHIS*, FSIS[1], FDA[2]
Pesticide Microorganisms Released in the Environment	
All	EPA*, APHIS[3]
Other Uses (Microorganisms)	
Intergeneric Combination	EPA*, APHIS[3]
Intrageneric Combination	
Pathogenic Source Organism	
1. Agricultural use	APHIS
2. Non-Agricultural use	EPA*[4], APHIS[3]
No Pathogenic Source Organisms	EPA Report
Nonengineered Pathogens	
1. Agricultural Use	APHIS
2. Non-agricultural Use	EPA*[4], APHIS[3]
Nonengineered Nonpathogens	EPA Report

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* LEAD AGENCY

[1] FSIS, Food Safety and Inspection Service, under the Assistant Secretary of Agriculture for Marketing and Inspection Services is responsible for food use.

[2] FDA is involved when in relation to a food use.

[3] APHIS, Animal and Plant Health Inspection Service, is involved when the microorganism is plant pest, animal pathogen or regulated article requiring a permit.

[4] EPA requirements will only apply to environmental release under a "significant new use rule" that EPA intends to propose.

Jurisdiction over the varied biotechnology products is determined by their use, as has been the case for traditional products. The detailed description of the products and their review are found in the individual agency policy statements contained in this Federal Register Notice. The following is a brief summary of jurisdiction as described in Chart I.

Foods, food additives, human drugs, biologics and devices, and animal drugs are reviewed or licensed by the FDA. Food products prepared from domestic livestock and poultry are under the jurisdiction of the USDA's Food Safety Inspection Service (FSIS).

Animal biologics are reviewed by the Animal and Plant Health Inspection Service, (APHIS). APHIS also reviews plants, seeds, animal biologics, plant pests, animal pathogens and "regulated articles", i.e., certain genetically engineered organisms containing genetic material from a plant pest or an animal pathogen. An APHIS permit is required prior to the shipment (movement) or release into the environment of regulated articles, or the shipment of a plant pest or animal pathogen.

"Other contained uses" refers to the closed system uses of those microorganisms, subject to TSCA, that are intergeneric combinations, i.e., deliberately formed microorganisms which contain genetic material from dissimilar source organisms. These are subject to EPA's PMN requirement. EPA is considering promulgating a rule to exempt certain classes of microorganisms from this requirement.

Microbial pesticides will be reviewed by EPA, with APHIS

involvement in cases where the pesticide is also a plant pest, animal pathogen, or regulated article requiring a permit. (FDA may become involved in implementing pesticide tolerances for foods.)

"Other uses (microorganisms)" include uses involving release into the environment. For these, jurisdiction depends on the characteristics of the organism as well as its use. "Intergeneric combination" microorganisms will be reported to EPA under PMN requirements, with APHIS involvement in cases where the microorganism is a also a "regulated article" requiring a permit.

"Intrageneric combinations" are those microorganisms formed by genetic engineering other than intergeneric combinations. For these, when there is a pathogenic source organism, and the microorganism is used for agricultural purposes, APHIS has jurisdiction. If the microorganism is used for nonagricultural purposes, then EPA has jurisdiction, with APHIS involvement in cases where the microorganism is also a regulated article requiring a permit. Intrageneric combinations with no pathogenic source organisms are under EPA jurisdiction although EPA will only require an informational report.

Nonengineered pathogenic microorganisms that are used for an agricultural use will fall under APHIS jurisdiction. Those that are for a nonagricultural use come under EPA jurisdiction, with APHIS involvement in cases where the microorganism is also a plant pest or animal pathogen requiring a permit. Nonengineered nonpathogenic microorganisms are under EPA jurisdiction which will require only an informational report.

Research

The coordinated framework for the regulation of biotechnology establishes requirements for the conduct of research.

Approximately ten years ago the NIH issued the NIH guidelines describing the manner in which research with organisms derived by rDNA techniques should be conducted. Since then the guidelines have been modified many times with gradual relaxation of these requirements. The guidelines prescribe the conditions under which institutions which receive NIH funds must conduct experiments. For a very small category of NIH funded experiments including environmental release, the guidelines require that the Director, NIH, approve each experiment on an individual basis. For each of these experiments, the RAC conducts a scientific review with an opportunity for public comment, and makes a recommendation to the NIH Director. As research experiments have expanded out of the biomedical area to environmental applications both agricultural and nonagricultural, other agencies have become involved, with shifting of responsibility for research approval to NSF (described in the November 85 Notice), USDA's S&E, and EPA. These other agencies' policies build, in part, on the NIH guidelines and NIH experience.

The S&E guidelines for agricultural research published separately for comment in this issue of the Federal Register have adopted the NIH guidelines with certain modifications including expansion of the scope to manipulation techniques other than rDNA; the table included with the S&E guidelines shows where particular elements of the NIH guidelines are used.

It should be noted that not all experiments involving the environmental release of genetically engineered organisms require prior federal approval. In plant applications there is a substantial body of research indicating that such experiments are of low risk. For certain categories of microorganisms modified by traditional genetic modification techniques, there is also a substantial body of research indicating low risk for environmental experiments.

Chart II -- Coordinated Framework -- Biotechnology Research Jurisdiction shows which agency has responsibility for a particular experiment. If more than one agency has potential jurisdiction, one agency has been designated as the lead agency and it is marked with an asterisk on Chart II. The lead agency designation depends on which research agency is funding the research (e.g. NIH, S&E, or NSF) or which regulatory agency reviews specific purpose research (e.g. pesticides). In the chart and in this discussion, the authority refers to approval of the actual execution of experiments and not to their funding.

CHART II--COORDINATED FRAMEWORK--BIOTECHNOLOGY RESEARCH JURISDICTION

Subject	Responsible Agency(ies)
Contained Research, No Release in Environment	
1. Federally Funded	Funding agency
2. Non-Federally Funded	NIH or S&E voluntary review, APHIS[2]
Foods/Food Additives, Human Drugs, Medical Devices, Biologics, Animal Drugs	
1. Federally Funded	FDA*, NIH guidelines & review
2. Non-Federally Funded	FDA*, NIH voluntary review
Plants, Animals and Animal Biologics	
1. Federally Funded	Funding agency*, APHIS[2]
2. Non-Federally Funded	APHIS*, S&E voluntary review
Pesticide Microorganisms	
Genetically Engineered	
Intergeneric	EPA*, APHIS[2], S&E voluntary review
Pathogenic Intrageneric	EPA*, APHIS[2], S&E voluntary review
Intrageneric Nonpathogen	EPA*, S&E voluntary review
Nonengineered	
Nonindigenous Pathogens	EPA*, APHIS
Indigenous Pathogens	EPA*[3], APHIS
Nonindigenous Nonpathogen	EPA*,
Other Uses (Microorganisms) Released in the Environment	
Genetically Engineered	
Intergeneric Organisms	
1. Federally Funded	Funding agency*, APHIS[2], EPA[4]
2. Commercially Funded	EPA, APHIS, S&E voluntary review,
Intrageneric Organisms	
Pathogenic Source Organism	
1. Federally Funded	Funding agency*, APHIS[2], EPA[4]
2. Commercially Funded	APHIS*[2], EPA (*if non-agricul. use)
Intrageneric Combination	
No Pathogenic Source Organisms	EPA Report
Nonengineered Pathogens	EPA Report*, APHIS[2]

* LEAD AGENCY

1 Review and approval of research protocols conducted either by S&E or NSF.

2 APHIS issues permits for the importation and domestic shipment of certain plants and animals, plant pests and animal pathogens, and for the shipment or release in the environment of regulated articles.

3 EPA jurisdiction for research on a plot greater than 10 acres.

4 EPA reviews federally funded environmental research only when it is for commercial purposes.

For contained federally funded research for for biomedical and agricultural purposes, research approval will granted by the funding agency. The NIH guidelines relate primarily to biomedical experiments and only to those using rDNA techniques. Research on foods/food additives, human drugs, medical devices and biologics will continue to rely on the NIH guidelines, with NIH approval required for certain experiments such as human gene therapy, and FDA permission for clinical trials.

Fashioned after the NIH guidelines, the S&E guidelines apply to agricultural research on plants, animals, and microorganisms and provide guidance for laboratory and field testing of organisms derived using rDNA manipulation and other technologies. Adherence to the appropriate set of guidelines is required for institutions receiving financial support from NIH, S&E, or NSF. These guidelines specify what type of review procedures are required for specific categories of experiments. Some experiments require individual approval by the respective agency providing institutional support. For those experiments that require agency approval, advisory committees at NIH, S&E, and NSF, composed primarily of nongovernment scientists, may be asked to provide expert review. In addition, research on plants, animals, and animal biologics will come under APHIS permit requirements if a regulated article, plant pest, animal pathogen is involved. An APHIS permit is required prior to the shipment (movement) or release of a regulated article, or the importation or shipment of a plant pest or regulated article used in any research experiment.

EPA has authority for all environmental research on microbial pesticides regardless of whether research is federally funded or not. EPA will regulate research under a two level review system based upon its evaluation of the potential risks posed by various types of microorganisms with lesser notification required for level I reporting and full review for level II.

For the "other uses" category from Chart II (research involving nonpesticide microorganisms released into the environment), jurisdiction for release may be under S&E, NSF, APHIS, or EPA depending primarily upon the source of the funding, but also upon the purpose of the research and the characteristics of the genetically engineered microorganism. Thus, federally funded research conducted for an agricultural use will require adherence to S&E guidelines and approval of certain experiments by S&E or NIH depending on which is the funding agency. EPA will review commercial research. APHIS's jurisdiction applies to issuing permits for regulated articles, plant pests, or animal pathogens.

For nonengineered pathogens EPA will require an informational report, with APHIS involvement for the review of plant pests or animal pathogens.

There may be situations where one agency may choose to defer to, or ask advice from, another agency. If experiments requiring NIH, NSF or S&E review/approval are submitted for review to another agency, then NIH, NSF, or S&E may determine that such review serves the same purpose, and based upon that determination, notify the submitter that no NIH, NSF, or S&E review will take place, and the experiment may proceed upon approval from the other agency.

C. INTERAGENCY COORDINATION MECHANISMS

The Domestic Policy Council Working Group on Biotechnology

The Domestic Policy Council Working Group on Biotechnology has been responsible for this coordinated framework for the regulation of biotechnology; it also considers policy matters related to agency jurisdiction, commercialization, and international biotechnology matters. The Working Group monitors developments in biotechnology and is ready to identify problems and make appropriate recommendations for their solution.

Although at the present time existing statutes seem adequate to deal with the emerging processes and products of modern biotechnology, there always can be potential problems and deficiencies in the regulatory apparatus in a fast moving field. The Working Group will be alert to the implications these changes will have on regulation, and in a timely fashion will make appropriate recommendations for administrative or legislative action.

The Domestic Policy Council Working Group on Biotechnology is a continuation of a similar group established under the former Cabinet Council on Natural Resources and the Environment. The chair is the Director, Office of Science and Technology Policy, who is now assisted by the Assistant Director for Biological, Behavioral and Social Sciences of the National Science Foundation, with staff support provided by the Office of Science and Technology Policy.

The Biotechnology Science Coordinating Committee (BSCC)

The BSCC is responsible for coordination and consistency of scientific policy and scientific reviews. The BSCC, established October 31, 1985 as part of the Federal Coordinating Council for Science, Engineering and Technology (FCCSET), consists of senior policy officials of agencies involved in the oversight of biotechnology research and products. FCCSET is a statutory interagency coordinating mechanism managed by the Office of Science and Technology Policy, Executive Office of the President, with a mission to coordinate federal science activities among federal agencies. The November 85 Notice described the structure and activities of the BSCC.

One of the primary activities of the BSCC has been the development of definitions because a common scientific approach is essential to a coordinated federal regulatory framework. The underlying scientific issue, therefore, was defining those organisms subject to certain types of agency review.

The definitions are included in the following section of this preamble and have been incorporated, with modification, into the individual policy notices of the involved agencies. Explanatory material is also included in the agency policy statements. As mentioned elsewhere, the BSCC is seeking comments on these definitions.

Research to develop genetically modified organisms for environmental and agricultural applications (as for research on traditionally modified organisms) generally proceeds in a step-wise manner from highly contained facilities to progressively lesser

degrees of containment as the investigator determines the safety and efficacy of experimental applications; these are conducted sequentially under controlled laboratory conditions, greenhouse testing, small field trials, and full field trials. The BSCC recognizes the need for further work to define the nature and extent of physical and biological barriers that limit or manage environmental release of modified organisms during greenhouse testing and field research.

The BSCC is authorized to hold public meetings in order to discuss public concerns about scientific and other issues. Accordingly, the BSCC will hold its first public meeting shortly after publication of this notice for discussion of the scientific aspects of this notice and the receipt of comments from the public. The public meeting will be held in July 1986. Details regarding time and location will be separately announced in the Federal Register.

D. BSCC DEFINITIONS

Any proposal to regulate the research and products of genetic manipulation techniques quickly confronts the issue of what organisms should be considered appropriate for certain types of review. The BSCC formulated definitions are effective immediately but are open to comment; the text following the definition of "pathogen" contains details of the request for comments.

Organisms meeting two different sets of criteria are proposed. First are organisms formed by deliberate combination of genetic material from sources in different genera. It was recognized,

however, that in certain precisely constructed "intergeneric organisms" the genetic material is not considered to pose an increased risk to human health or the environment; thus, such combinations are excluded from the definition. A detailed explanation of the scientific basis for these exclusions is found in the footnote after the definition of pathogen. The BSCC specifically requests comments on whether also to consider for exclusion those organisms that exchange DNA by known physiological processes, as explained in the text immediately following the definition of "intergeneric organism (new organism)."

The second definition is "pathogen." This includes microorganisms that belong to a pathogenic species or that contain genetic material from source organisms that are pathogenic. In certain precisely constructed modified organisms, the genetic material from a pathogenic donor is not considered to pose an increased risk to human health or the environment; and, therefore, such combinations are excluded from the definition.

The BSCC definitions of "intergeneric organism (new organism)" and "pathogen" describe the combinations genetic material that would cause a modified organism to come under review. This does not mean to suggest that the behavior of a genetically manipulated organism exempted from these definitions is wholly predictable (since any biological organism is never 100% predictable), but that the probability of any incremental hazard compared to the unmodified organism host is low. This does not mean that any product manufacture or research experiment using an organism

exempted from the definition should be conducted without adherence to proper manufacturing standards or research guidelines.

Given the statutory differences in the laws that they administer, the agencies adopted the principles underlying the definitions in ways consistent with their legislation. EPA, APHIS, and S&E are using the definitions to identify levels of review for microbial products within their jurisdiction. EPA, APHIS, FDA, S&E, and NSF are using the definitions as factors to consider in the review of products or experiments.

The BSCC is attempting to define what constitutes "release into the environment." The BSCC is establishing a working group on greenhouse containment and small field trials in order to develop scientific recommendations. The concept of "containment" has traditionally been used to describe physical conditions which severely limit release (for example, a contained laboratory fermentation facility). Containment can also be "biologic" because the ability of an organism to reproduce, exchange genetic information, or become established can be effectively limited biologically. Thus, the BSCC's exploration of the conditions that constitute release into the environment will consider circumstances of both physical and biological containment for particular organisms and the circumstances of their release. While the concept of physical containment may imply the high containment conditions found in certain laboratories and greenhouses, in agricultural practice many simpler effective barriers are routinely used; these include microplots for soil bacteria and fungi, paddocks for

noninfective animals, and removing or covering the reproductive parts of plants and animals.

Release into the environment, for the time being, will have somewhat varying definitions for the regulatory and research review of the different agencies. There may be minor differences between agricultural and nonagricultural approaches and between macro- and microorganisms.

Intergeneric Organism (New Organism)

Those organisms deliberately formed to contain an intergeneric combination of genetic material; excluded are organisms that have resulted from the addition of intergeneric material that is well-characterized and contains only non-coding regulatory regions such as operators, promoters, origins of replication, terminators and ribosome binding regions.

"Well-characterized and contains only non-coding regulatory regions" means that the producer of the microorganism can document the following:

a. the exact nucleotide base sequence of the regulatory region and any inserted flanking nucleotides;

b. the regulatory region and any inserted flanking nucleotides do not code independently for a protein, peptide or functional RNA molecules;

c. the regulatory region solely controls the activity of other sequences that code for protein or peptide molecules or act as recognition sites for the initiation of nucleic acid or protein synthesis.

Pathogen

A pathogen is a virus or microorganism (including its viruses and plasmids, if any) that has the ability to cause disease in other living organisms (i.e., humans, animals, plants, microorganisms).

A microorganism (including viruses) will be subject to regulatory policies regarding pathogens if:

a. the microorganism belongs to a pathogenic species, according to sources identified by the agency, or from

information known to the producer that the organism is a pathogen; excepted are organisms belonging to a strain used for laboratory research or commercial purposes and generally recognized as non-pathogenic according to sources identified by a federal agency, or information known to the producer and the appropriate federal agency (an example of a nonpathogenic strain of a species which contains pathogenic strains is Escherichia coli K-12; examples of nonpathogenic species are Bacillus subtilis, Lactobacillus acidophilus, and Saccharomyces species); or

b. the microorganism has been derived from a pathogen or has been deliberately engineered such that it contains genetic material from a pathogenic organism as defined in item a. above. Excepted are genetically engineered organisms developed by transferring a well-characterized, non-coding regulatory region from a pathogenic donor to a non-pathogenic recipient.

"Well-characterized, non-coding regulatory region" means that the producer of the microorganism can document the following:

a. the exact nucleotide base sequence of the regulatory region and any inserted flanking nucleotides;

b. the regulatory region and any inserted flanking nucleotides do not code independently for a protein, peptide, or functional RNA molecules; and,

c. the regulatory region solely controls the activity of other sequences that code for protein or peptide molecules or act as recognition sites for the initiation of nucleic acid or protein synthesis.

This definition excludes organisms such as competitors or colonizers of the same substrates, commensal or mutualistic microorganisms, or opportunistic pathogens.

The footnote contains the scientific basis for exempting non-coding regulatory regions from the definitions of intergeneric organisms and pathogen.*

[footnote]

* The BSCC has based the exemption of intergeneric transfers of regulatory regions on their lack of coding capacity for the production of proteins, peptides or functional RNA molecules. It has been recommended by other members of the scientific community that there should be additional exemptions such as ribosomal proteins, ribosomal RNAs and transfer RNAs. The BSCC has chosen to examine these suggestions in more detail during the next few months. At the present the BSCC has excluded:

1. Origins of replication;
2. Ribosome binding sites;
3. Promoters;
4. Operators; and,
5. Terminators.

The basis for these exemptions is as follows. Each of these regulatory elements has no coding capacity for the production of any gene product and therefore does not promote the production of any new material. What these elements are responsible for is the initiation and modulation of nucleic acid synthesis at the specific region where they appear in the chromosome.

Bacterial genes are precisely regulated and this regulation is based on a series of regulatory elements. The principal regulatory unit is the operon. Operons are controlled primarily, but not exclusively, through the regulation of the rate of initiation of messenger RNA synthesis. This regulation is based on the interaction of two short nucleotide sequences in the DNA, the promoter, which is the site of RNA polymerase binding and the operator, which follows closely and acts as an off-on switch for the movement of the polymerase into the structural gene which follows. The function of the operator is to bind a cellular repressor protein which is synthesized in response to changing nutritional stimuli. Terminator regions are short nucleotide sequences which signal the termination of mRNA synthesis by the polymerase. They act as a signal for the dissociation of the polymerase from the DNA.

Replication of DNA in every biological system that has been examined is initiated at a specific site or group of sites in the chromosome. Those sites have broad specificity and a DNA molecule without the appropriate site will not be replicated. The sites which are critical to the initiation of replication are known as origins of replication. These regions are short nucleotide sequences which serve as initiation sites for specific enzyme action during the DNA replication process. For example, in order for mammalian DNA to replicate in bacteria, it must be associated with a bacterial origin of replication and vice versa.

Ribosome binding sites are short nucleotide segments at the beginning of messenger RNA molecules which signal the attachment of ribosomes for the initiation of protein synthesis. Functioning in this role they are not translated into the protein or peptide being processed.

The BSCC is requesting comments on these definitions during the period of sixty days following the date of this notice and specifically seeks comments addressing the following:

1. The suitability and applicability of these definitions to applications involving release into the environment, contained industrial large-scale applications, foods/food additives, drugs, medical devices, and other possible products.

2. Whether combinations of genetic material from organisms that exchange DNA by known physiological processes should be excluded from the definition of intergeneric organisms: i.e., should organisms be excluded which contain intergeneric combinations of certain specified rDNA molecules that consist entirely of DNA segments from different genera that exchange DNA by known physiological processes? As certain rDNA organisms are exempted under Section III-D-4 of the NIH guidelines, the question was raised whether these organisms when used in the environment should be similarly exempted from federal product review. This exemption would not, however, exclude from review such "natural exchangers" that are also pathogens or plant pests. In the event that the exclusion of such different species that exchange DNA by known physiological processes is accepted as appropriate, a list of such species combinations that has been maintained and updated by the Office of Recombinant DNA Activities of the National Institutes of Health will be updated, in light of environmental use.

3. What are the most appropriate definitions of "release into the environment" for macro- and microorganisms.

E. INTERNATIONAL ASPECTS

The United States seeks to promote international scientific cooperation and understanding of scientific considerations in biotechnology on a range of technical matters. These activities add to scientific knowledge and ultimately contribute to protection of health and the environment.

The United States also seeks to reduce barriers to international trade. U.S. agencies apply the same regulation and approval procedures on domestic and foreign biotechnological products. We are seeking recognition among nations of the need to harmonize, to the maximum extent possible, national regulatory oversight activities concerning biotechnology. Barriers to trade in biotechnological products should be avoided as nations join together in working toward this mutual goal.

The U.S. agencies that have published separate policy statements as part of this notice are committed to the policy described in this section on international harmonization and have incorporated by reference the language in this International Aspects section as part of their respective agency policy statements.

Organization for Economic Cooperation and Development (OECD)

The approach of the comprehensive framework contained in this notice takes into account, inter alia, the broad goals described by an Ad Hoc Group of Government Experts convened by OECD in their recent report entitled, "RECOMBINANT DNA SAFETY CONSIDERATIONS, Safety Considerations for Industrial, Agricultural and

Environmental Applications of Organisms Derived by Recombinant DNA Techniques." The United States is pleased to have had the opportunity for its experts to work with those of other governments in the preparation of this report. The report includes the following concepts:

Summary of Major Points

Recombinant DNA techniques have opened up new and promising possibilities in a wide range of applications and can be expected to bring considerable benefits to mankind. They contribute in several ways to the improvement of human health and the extent of this contribution is expected to increase significantly in the near future.

The vast majority of industrial rDNA large-scale applications will use organisms of intrinsically low risk which warrant only minimal containment, Good Industrial Large-Scale Practice (GILSP).

When it is necessary to use rDNA organisms of higher risk, additional criteria for risk assessment can be identified and furthermore, the technology of physical containment is well known to industry and has successfully been used to contain pathogenic organisms for years. Therefore, rDNA microorganisms of higher risks can also be handled safely under appropriate physical and/or biological containment.

Assessment of potential risks of organisms for environmental or agricultural applications is less developed than the assessment of potential risks for industrial applications. However, the means for assessing rDNA organisms can be approached by analogy with the existing data base gained from the extensive use of traditionally modified organisms in agriculture and the environment generally. With step-by-step assessment during the research and development process, the potential risk to the environment of the applications of rDNA organisms should be minimized.

I. General Recommendations

1. Harmonization of approaches to rDNA technology can be facilitated by exchanging: principles or guidelines for national regulations; developments in risk analysis; and practical experience in risk management. Therefore, information should be shared as freely as possible.

2. There is no scientific basis for specific legislation

for the implementation of rDNA technology and applications. Member countries should examine their existing oversight and review mechanisms to ensure that adequate review and control may be applied while avoiding any undue burdens that may hamper technological developments in this field.

3. Any approach to implementing guidelines should not impede future developments in rDNA technology. International harmonization should recognize this need.

4. To facilitate data exchange and minimize trade barriers between countries, further developments such as testing methods, equipment design, and knowledge of microbial taxonomy should be considered by both national and international levels. Due account should be taken of ongoing work on standards within international organizations such as: World Health Organization; Commission of the European Communities; International Standards Organization; Food and Agricultural Organization; and, Microbial Strains Data Network.

5. Special efforts should be made to improve public understanding of various aspects of rDNA technology.

6. For rDNA applications in industry, agriculture and the environment, it will be important for OECD Member countries to watch the development of these techniques. For certain industrial applications and for environmental and agricultural applications of rDNA organisms, some countries may wish to have a notification scheme.

7. Recognizing the need for innovation, it is important to consider appropriate means to protect intellectual property and confidentiality interests while assuring safety.

II. Recommendations Specific for Industry

1. The large-scale industrial application of rDNA technology should wherever possible utilize microorganisms that are intrinsically of low risk. Such microorganisms can be handled under conditions of Good Industrial Large-Scale Practice (GILSP).

2. If, following assessment using the criteria outlined in the document, a rDNA microorganism cannot be handled merely by GILSP, measures of containment corresponding to the risk assessment should be used in addition to GILSP.

3. Further research to improve techniques for monitoring and controlling non-intentional release of rDNA organisms should be encouraged in large-scale industrial applications requiring physical containment.

III. Recommendations Specific for Environmental and Agricultural Applications

1. Considerable data on the environmental and human health effects of living organisms exist and should be used to guide risk assessments.

2. It is important to evaluate rDNA modified organisms for potential risk, prior to applications in agriculture and the environment. However, the development of general international guidelines governing such applications is premature at this time. An independent review of potential risks should be conducted on a cases-by-case basis prior to application. Case-by-case means an individual review of a proposal against assessment criteria which are relevant to the particular proposal; this is not intended to imply that every case will require review by a national or other authority since various classes of proposals may be excluded.

3. Development of organisms for agricultural or environmental applications should be conducted in a stepwise fashion, moving, where appropriate, from the laboratory to the growth chamber and greenhouse, to limited field testing and finally, to large-scale field testing.

4. Further research to improve the prediction, evaluation, and monitoring of the outcome of applications of rDNA organisms should be encouraged.

DRAFT

MAY 14

ENVIRONMENTAL PROTECTION AGENCY

[OPTS-00049A]

STATEMENT OF POLICY, MICROBIAL PRODUCTS SUBJECT TO THE FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT AND THE TOXIC SUBSTANCES CONTROL ACT

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice describes how EPA is addressing certain microbial products of biotechnology under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Toxic Substances Control Act (TSCA). The notice outlines EPA's plan for review of microbial pesticides under FIFRA with particular emphasis on small-scale field testing of genetically engineered, nonindigenous, and pathogenic microbial pesticides. It also announces EPA's policy for addressing new microbial products that fall under TSCA authority. This includes EPA's interpretation of the new chemical premanufacture notification (PMN) provisions of TSCA section 5 for new genetically engineered microorganisms used for commercial purposes, and the Agency's intentions to develop, under TSCA, a significant new use rule for pathogenic microorganisms; a rule modifying the PMN research and development exemption so that small scale field testing of microorganisms for TSCA purposes is subject to PMN; a section 8(a) reporting rule for other microorganisms prior to their release in the environment; and section 5(h)(4) exemptions as appropriate.

DATES: The following policies and requirements announced in this notice are effective (insert date of publication in the FEDERAL REGISTER): (1) the notification and reporting requirements for small-scale field tests and the experimental use permit and registration requirements for microbial pesticides under FIFRA, described in Unit II.D of this notice; (2) premanufacture notice requirements under TSCA for "new" microorganisms, as defined in Unit III.C.1 and Unit IV of this notice, except those produced only in small quantities solely for research and development; (3) TSCA section 8(e) reporting requirements for information on substantial risks posed by microorganisms subject to TSCA, as described in Unit III.C.5 of this notice; and (4) FIFRA section 6(a)(2) reporting requirements for information on unreasonable adverse effects posed by microbial pesticides. EPA requests that persons voluntarily comply with other policies announced in this notice, as summarized in Unit I.C, until rules implementing them are promulgated.

ADDRESS: Comments on this EPA notice should be identified by Docket Number OPTS-00049A and addressed to:

Document Control Officer (TS-793),
Office of Toxic Substances,
Environmental Protection Agency,
Rm. E-209,
401 M St., SW.,
Washington, D.C. 20460.

Information submitted as comments on this EPA notice may be claimed confidential by marking any part or all of that information as "Confidential Business Information." Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR Part 2. A sanitized copy of any material containing Confidential Business Information must be provided by the submitter for inclusion in the public record. Information not marked confidential may be disclosed publicly by EPA without prior notice.

Comments received on this notice, except those containing Confidential Business Information will be available for review and copying from 8 a.m. to 4 p.m. Monday through Friday, except legal holidays, in the TSCA Public Information Office, Rm. E-107 at the address given above.

FOR FURTHER INFORMATION CONTACT: For general information including copies of this EPA notice and related materials:

Edward A. Klein,

Director, TSCA Assistance Office (TS-799),

Office of Toxic Substances,

Environmental Protection Agency,

Rm. E-543,

401 M St., SW.,

Washington, D.C. 20460,

Toll-free: (800-424-9065),

In Washington, D.C.: (202-554-1404),

Outside the USA: (Operator-202-554-1404).

For technical information regarding the FIFRA section of the EPA policy:

Frederick S. Betz,

Hazard Evaluation Division (TS-769C),

Office of Pesticide Programs,

Environmental Protection Agency,

401 M St., SW.,

Washington, D.C. 20460.

Office location and telephone number:

Rm. 1128, Crystal Mall #2,

1921 Jefferson Davis Highway, Arlington, VA 22202,

(703-557-9307).

For technical information regarding the TSCA sections of the EPA policy:

Anne K. Hollander,
Office of Toxic Substances (TS-794),
Environmental Protection Agency,
Rm. E-511,
401 M St., SW.,
Washington, D.C. 20460, (202-382-3852).

SUPPLEMENTARY INFORMATION:

Index

Following is an index to the EPA portion of this notice:

I. OVERVIEW

A. PURPOSE

For centuries, humans have used organisms to generate commercial products or to perform useful functions. During the last decade, advances in the biological sciences have increased the ability of humans to change or combine the inherited characteristics of microorganisms, plants, and animals. These advances, along with more traditional genetic engineering and biological techniques, are expected to lead to a wide variety of useful products. Among these are microorganisms that will be used to degrade toxic pollutants, leach minerals, enhance oil recovery, produce industrial chemicals, and act as pesticides. As with chemicals used for the same types of purposes, many of these microorganisms will be reviewed by EPA for potential health and environmental risks.

Specifically, EPA reviews and may register pesticide products under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and reviews chemical substances (except those used as pesticides, foods, food additives, cosmetics, drugs, and medical devices) under the Toxic Substances Control Act (TSCA). EPA's Office of Pesticides and Toxic Substances (OPTS) is responsible for implementing both FIFRA and TSCA.

This notice describes how EPA plans to address microbial products that are subject to FIFRA and TSCA, and explains the scope of coverage and procedures for review of these products under both statutes. The following questions are addressed in this notice:

1. What microbial products are subject to review under FIFRA and how will they be reviewed? (Unit II)

2. What microbial products are subject to review under TSCA and how will they be reviewed? (Unit III)

3. What definitions will be used to identify the products that will be addressed by the appropriate statute? (Unit IV)

In reviewing products, the Agency is required under both FIFRA and TSCA to consider the potential benefits to society as well as any potential risks. EPA will take both risks and benefits into account in its regulatory decisions concerning these products, and will implement the two statutes in as consistent a fashion as possible within statutory constraints.

B. BACKGROUND

1. December 1984 Proposal. EPA published for comment a "Proposed Policy Regarding Certain Microbial Products" as part of the Office of Science and Technology Policy's "Proposal for a Coordinated Framework for Regulation of Biotechnology." This proposal was published in the FEDERAL REGISTER of December 31, 1984 (49 FR 50880) and is hereafter referred to as the

proposed a mechanism for review of genetically engineered and nonindigenous microbial pesticides under FIFRA. It also described how EPA proposed to address certain genetically engineered microorganisms subject to the new chemical substance premanufacture notification (PMN) provisions of section 5 of TSCA.

2. Comments on the December 84 Notice. EPA received comments on the December 84 Notice from 68 organizations and individuals. All the comments received by EPA are available for review and copying from 8 a.m. to 5 p.m. Monday through Friday, except legal holidays, in the TSCA Public Information Office, Rm. E-107, Environmental Protection Agency, 401 M St., SW., Washington, D.C., 20460.

The Agency has carefully evaluated these comments. Several of the proposed policies set forth in the December 84 notice have been revised or clarified in this notice in response to these comments and as a result of the regulatory experience EPA has gained over the past year.

One of the most frequent comments addressed EPA's authority under TSCA and FIFRA. The Agency has continued to evaluate the extent and limit of its statutory authority and has concluded that TSCA and FIFRA provide sufficient authority for the Agency to meet its goals and responsibilities in regulating biotechnology products. However, some new regulations will be required and others will have to be modified in order to fully

implement certain aspects of EPA's policies. These regulations and modifications are discussed in Units II and III of this notice.

Numerous commenters addressed the scope of EPA's policy and raised questions about which microbial products are subject to TSCA and FIFRA. In Units II.B and III.B, the Agency provides detailed explanations of which microorganisms are and are not subject to FIFRA and TSCA, and from among the products that are subject, which are subject to regulatory review prior to any environmental application.

Many commenters expressed concern that the Agency was relating a microorganism's potential for risk to the process by which it was made, particularly in the definition of which microorganisms are "new" and therefore subject to PMN under TSCA. First, commenters suggested that the process by which an organism was modified was too indirect as an indicator of its newness. They pointed out that while certain processes can be used to produce new combinations of traits in microorganisms, their use does not necessarily mean that new combinations of traits have been formed. Second, the process-based approach was believed to be an insufficient indicator of risk, because genetic engineering processes do not necessarily produce organisms that present risks, nor are non-engineered organisms necessarily safe. Finally, because the process-based approach would single

out certain techniques for regulation, it would result in market distortions that favored the more traditional techniques even though the newer techniques could be as safe or safer.

After reviewing the comments, the Agency considered a number of alternatives to the "process-based" approach. In choosing among these alternatives, EPA carefully considered how well the options approximated risk (there was uncertainty with all the options in this respect), whether they could be implemented and enforced through criteria that were unambiguous to all affected persons, and (in the case of organisms subject to TSCA) the TSCA mandate to review "new" substances. The alternative EPA has chosen gives particular attention, under both FIFRA and TSCA, to microorganisms that (1) are used in the environment, (2) are pathogenic or contain genetic material from pathogens, or (3) contain new combinations of traits (e.g., organisms that are genetically modified to contain genetic material from dissimilar source organisms and organisms that are nonindigenous). EPA believes these categories have sufficiently high potential for widespread exposure, adverse effects, or uncertainty concerning potential effects to deserve particular regulatory scrutiny. This approach takes a significant step towards separating products on the basis of potential risk.

The Agency also received comments on the information and data to be submitted by companies filing notifications of intent to conduct field tests with certain microbial pesticides. These

requirements have been clarified and additional references have been cited in the FIFRA unit of this notice that should provide useful guidance on what information to submit. The TSCA unit contains similar guidance on the submission of information.

Finally, several commenters addressed issues pertaining to confidential business information (CBI). Some expressed concern that CBI be adequately protected from disclosure, while others stressed the need for public access to information on new biotechnology products. EPA has summarized its position with respect to CBI and public disclosure later in this overview (Unit I.G).

A background document providing more detail on the Agency's response to comments on the December 84 Notice has been placed in the public record for this notice and is available in the TSCA Public Information Office (address listed in Unit VI of this notice).

C. SUMMARY OF EPA POLICY

This notice focuses on oversight and review procedures for microorganisms that are subject to FIFRA or TSCA. Microorganisms intended for use as pesticides are subject to FIFRA, and many microorganisms intended for general commercial and environmental applications (e.g., metal leaching, pollutant degradation,

enhanced nitrogen fixation) are subject to TSCA. This notice addresses the rationale for various requirements and provides guidelines for compliance.

Specifically, EPA's policies that apply to microbial products subject to FIFRA or TSCA jurisdiction will include the following specific requirements:

1. Microorganisms deliberately formed to contain genetic material from dissimilar source organisms (inter-generic) will be subject to review before any environmental release, including small-scale field testing and other environmental research and development (R&D). Under the statute, those that are subject to TSCA and used in closed systems (i.e., never intentionally released to the environment) must be reported before they are manufactured for non-R&D commercial purposes. However, EPA is considering promulgating a rule to exempt certain contained uses from this requirement.

2. Microorganisms formed by genetic engineering other than inter-generic combinations will be subject to the following provisions: (a) If any source organism is a pathogen, the resulting microbial products are subject to review under FIFRA or TSCA prior to any environmental release, except if used solely for non-pesticidal agricultural uses, in which case they are subject only to U.S. Department of Agriculture (USDA) review (see the USDA notice in this FEDERAL REGISTER); (b) If source organisms are not pathogens, the resulting microbial products are

subject to abbreviated review under FIFRA (if they are pesticides) before any small-scale environmental release, or will be subject to the reporting requirements of sections 8(a) and (e) of TSCA.

3. Nonengineered microorganisms: (a) Indigenous pathogens will be reviewed under FIFRA or TSCA prior to use on greater than ten acres of land and greater than one acre of water, except those that are solely for non-pesticidal agricultural purposes, which will be subject only to USDA authority; (b) Nonindigenous pathogens will be reviewed under FIFRA prior to any environmental release, and under TSCA prior to release at greater than ten acres, unless they are pathogens used solely for non-pesticidal agricultural purposes in which case they will be reviewed by USDA (see USDA notice in this FEDERAL REGISTER); (c) Nonindigenous microbial pesticides that are not pathogens will be subject to abbreviated review under FIFRA before any small scale environmental release; (d) Indigenous microbial pesticides that are not pathogens will be reviewed under FIFRA prior to use on greater than ten acres.

4. All other microorganisms used or intended for use as pesticides and not covered in 1-3 above, regardless of source, mode of action, or method of manufacture will be reviewed under FIFRA prior to use on greater than ten acres unless exempted by regulation.

5. Manufacturers and importers of microorganisms under TSCA

that are not otherwise subject to review will be required to submit general information before environmental release that the Agency can use to monitor environmental uses and to determine if additional requirements are necessary in the future. EPA will gather such information by means of a TSCA section 8(a) reporting rule.

6. Manufacturers and importers of all microorganisms subject to TSCA must report any information on substantial risks under TSCA section 8(e). Registrants of microbial pesticides must report any information regarding unreasonable adverse effects of the pesticide on the environment under FIFRA section 6(a)(2).

A table at the end of Unit I summarizes the policies for prior notification and review of microorganisms applied in the environment.

This policy is immediately effective for microbial pesticides under FIFRA and for "new" microorganisms subject to premanufacture notification under TSCA. Implementing other aspects of the policy for TSCA substances, however, will require rulemaking. Until final rules are effective, EPA expects manufacturers to comply with most aspects of the policy voluntarily. The one exception is that manufacturers of

microorganisms, described in point 5 above, that are excluded from other TSCA notification requirements are not expected to report until a final section 8(a) rule is promulgated.

This notice also describes the types of information EPA expects to receive from persons subject to these policies to permit an evaluation of possible risks. EPA will determine specific information needs on a case-by-case basis, and will frequently use non-Agency experts with specific knowledge of the relevant microorganisms and uses to assist in reviews. In addition, EPA is establishing a biotechnology Science Advisory Committee (SAC) to provide peer review of specific cases and advice on technical issues. The SAC will be composed of non-Agency scientists and members of the lay public. More information on the SAC may be found in Unit I.F.

Although many of the policies described in this notice are immediately effective, the Agency recognizes that biotechnology is a rapidly developing field and that newly available information may affect the judgments underlying these policies. Accordingly, EPA recognizes that modifications of these policies may be necessary in the future, and it is willing to make such modifications as may be appropriate. Therefore, EPA encourages all interested persons to provide comments on the policies described in this notice. Comments should be submitted to the address provided at the beginning of this EPA notice. The public will have additional opportunities for comment when the Agency

proposes rules for those parts of its policy that require rulemaking procedures. These parts are specifically indicated in Units II and III.

D. RATIONALE FOR APPROACH

This unit provides a discussion of EPA's rationale for giving special focus to environmental release, pathogens, and microorganisms with new characteristics (e.g., containing genetic material from dissimilar source organisms or nonindigenous organisms).

1. Environmental releases. Physical containment can be used to mitigate undesirable or unexpected characteristics of a microorganism by providing the means to control a microorganism's growth, reproduction, and exposure to other organisms. However, microorganisms meant to be released in the environment are not subject to this control mechanism. Although many microorganisms will be biologically contained, that is, they will have existing and inherent limitations on their growth and survival, some of them may reproduce and thereby increase in number in the environment beyond the amounts originally released. Some will also have independent mobility, or may be spread beyond the area in which they are used. Thus, to ensure that environmental releases of microorganisms do not pose unreasonable adverse effects, the Agency has determined that it should review and evaluate proposals for certain environmental releases before they

are allowed to proceed. The microorganisms to be subject to review before any environmental release are described in the following paragraphs, and in Units II and III of this notice.

The Agency acknowledges the difficulty of defining environmental release. For now, the Agency's approach will focus on when an organism is considered to be contained rather than when it is released. Guidance is provided in Unit IV on how to determine whether a microorganism is considered to be contained. The definition of environmental release will be refined in subsequent rulemaking activities.

2. Pathogenic microorganisms. Given their ability to cause disease in plants, animals, humans, and microbes, EPA generally believes pathogenic microorganisms should be reviewed before they are released in the environment.

As used in this notice, a "pathogen" is a microorganism that has the ability to cause disease in living organisms. This includes previously documented pathogens, and microorganisms deliberately formed to contain genetic material from pathogens (e.g., through genetic engineering techniques). A complete discussion of the definition of pathogenicity is included in Unit IV, as well as guidance to aid in the determination of whether a particular microorganism falls within the scope of the EPA policies that address pathogens.

Pathogens are a clearly defined category of organisms known to cause adverse effects. In addition, because of the increased uncertainty about behavioral changes that may be associated with genetically engineered pathogens, the Agency has decided to review genetically engineered pathogens prior to any environmental release (including small-scale field testing). However, the Agency will defer review of nonengineered indigenous pathogens until they are used in larger scale applications (greater than ten acres), because ample experience indicates that nonengineered, indigenous pathogens are sufficiently well controlled by natural mechanisms in small-scale environmental applications. Further, the Agency will not review pathogens used solely for non-pesticidal agricultural purposes (except those formed through inter-generic combinations, which are "new") because these are adequately reviewed by the USDA (see the USDA notice in this FEDERAL REGISTER).

The Agency's decision to focus on pathogens does not mean that EPA has concluded that nonpathogens are necessarily safe or that all pathogens present unreasonable risks. In fact, the Agency expects to identify widely varying degrees of risk among different uses of pathogens. It should be clear that other considerations besides pathogenicity will affect the evaluation of risk, e.g., functions of the recombined genes, possibilities for genetic transfer, environmental fate, and potential competition with other organisms. When other considerations

indicate that it is appropriate, the Agency will consider excluding specific categories of pathogens from review, or may provide guidance that would limit the information requirements associated with its reviews of pathogens. As explained in Unit IV, the Agency has already exempted from review as pathogens organisms that only incorporate certain genetic material from pathogens.

3. Microorganisms with new characteristics. A third factor that makes potential adverse effects of microorganisms less predictable is the existence of new traits or characteristics. These traits may be new to the organism, or new to the environment in which the organism is released.

a. Microorganisms having significant potential to exhibit new traits. Modern genetic engineering techniques permit genetic material to be intentionally combined in organisms that would not normally share that genetic material. Some of these genetically engineered microorganisms may exhibit new or altered traits affecting, for example, their survivability, host range, substrate utilization, competition with other organisms, or protein or polysaccharide production. In some cases such microorganisms may be able to evade or overcome natural controls on their growth, or controls on their ability to cause adverse effects. In many other cases, their natural hardiness will be reduced.

In addition to the possibility that certain engineered organisms may exhibit new traits, if they are released they may be transported through natural dispersal mechanisms to other areas in the environment that have not previously contained organisms having these new combinations of traits.

Because of these considerations, EPA's policies will give particular regulatory attention to organisms that have a significant probability of exhibiting a new trait or combination of traits (standards for this are explained below). This approach accomplishes two important objectives. First, it identifies a group of microorganisms whose behavior in the environment poses significant uncertainty and thus warrants regulatory review. Simultaneously, it provides a way of defining "new" microorganisms that are subject to PMN requirements under TSCA (see Unit III.C.1).

EPA's policy, specifically, focuses on microorganisms that have been deliberately altered to contain genetic material from dissimilar source organisms, because such organisms are more likely to exhibit new combinations of traits and their behavior is therefore less predictable. Given this conceptual basis, the question then becomes how dissimilar two organisms must be before combinations of genetic material between them are likely to produce "new combinations of traits."