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Report to the Chairman, Subcommittee on Regulation, Business Opportunities, and Energy, Committee on Small Business, House of Representatives

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BIOTECHNOLOGY

Delays in and Status of EPA's Efforts to Issue a TSCA Regulation

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The Honorable Ron Wyden
Chairman, Subcommittee on Regulation,
Business Opportunities, and Energy
Committee on Small Business
House of Representatives

Dear Mr. Chairman:

This report responds to your April 11, 1991, request for information on the development and potential issuance of a biotechnology regulation under the Toxic Substances Control Act (TSCA) to control certain genetically modified microorganisms used in commerce. Specifically, you asked us to address (1) the Environmental Protection Agency's (EPA) efforts to issue a TSCA biotechnology regulation and (2) the impact on the biotechnology industry of not having a TSCA biotechnology regulation.

Biotechnology has the potential to dramatically improve the health of humans and animals, the food supply, and the environment. In this process, new vaccines, pesticides, insect-resistant plants, bacteria that break down toxic wastes, and other products and services can be created by applying biological procedures, such as genetic engineering, to living organisms or their components. However, safeguards are needed to ensure that the release of these organisms created by biotechnology does not pose an unreasonable risk to public health or the environment.

TSCA was enacted in October 1976 to provide a safeguard against the introduction of harmful new chemicals into the environment and to address the risks posed by chemicals already in use. EPA considers microorganisms and their component parts used in biotechnology products to be "chemical substances" and thus subject to regulation under the act.

Results in Brief

EPA has worked since 1984 to issue a TSCA biotechnology regulation, but the agency has been unsuccessful primarily because of disagreement within the executive branch over the scope of the regulation. Specifically, during 1988 EPA developed and sent to the Office of Management and Budget (OMB) for review a proposed regulation that was based on policy issued by the Office of Science and Technology Policy (OSTP) in 1986, according to EPA officials. But, according to EPA officials, OSTP raised

concerns during OMB's review that EPA's proposal would subject more microorganisms to regulation than was warranted by their probable risk to the environment. Unable to obtain OMB's support for EPA's position, the Administrator of EPA withdrew the proposed regulation in February 1989.

In July 1990, OSTP issued new guidance defining the scope of biotechnology products to be considered for regulation. In December 1991, EPA completed drafting a revised regulation based on the scope defined in the new guidance. EPA plans to submit the regulation to OMB for review in late summer 1992. However, OSTP issued guidance in February 1992 that eliminated the definition of scope in the 1990 guidance. Rather than defining the scope, which was done in both the 1986 policy and the 1990 guidance, the 1992 guidance advises agencies to oversee the introduction of only those biotechnology products that pose an unreasonable risk to the environment. The guidance did not provide any specific direction on how agencies are to implement this risk-based approach. As a result, it is unclear whether EPA's current proposed regulation will be acceptable.

The biotechnology industry is concerned that the extended debate over the regulation is delaying the implementation of a clear regulatory process that will allow safe and effective products to be rapidly commercialized. According to industry representatives, the uncertainty over the final regulation inhibits investment in new biotechnology products because researchers and investors consider the costs of meeting regulatory requirements when they make investment decisions.

Background

Because no single statute specifically targets the regulation of biotechnology products, various federal agencies have become involved in regulating biotechnology. For the most part, these agencies apply existing laws to the products according to the purposes for which they are used, such as for pesticides or as drugs. Under TSCA, EPA has indicated that it will regulate microorganisms produced for environmental, industrial, or consumer uses except when they are manufactured, processed, or distributed for use as pesticides, foods, food additives, drugs, cosmetics, or medical devices. Examples of microorganisms that may be regulated under TSCA are those used for mining metal, degrading wastes, and producing enzymes and other proteins for nonpharmaceutical purposes.

Some scientists, environmental groups, and members of the public have raised concerns about the possible environmental consequences of the many anticipated agricultural and environmental applications of

biotechnology outside a contained facility. Environmental applications of genetically engineered microorganisms were of particular concern because they are microscopic, can reproduce and proliferate, and may become established in the environment. In response to such concerns, the Reagan Administration formed an interagency working group in 1984 under the White House Cabinet Council on Natural Resources and the Environment.[1] This group concluded that although existing laws would adequately address most regulatory needs, federal regulations needed to be established for certain products, such as those to be regulated under TSCA. The group published a proposed policy statement in 1984.[2]

As part of the 1984 proposed policy statement, EPA announced that it considered microorganisms used in biotechnology products to be "chemical substances," as defined in section 3 of TSCA, and thus subject to the provisions of TSCA.[3] Under premanufacture notification requirements set forth in section 5(a) of TSCA, companies must notify EPA of any "new" chemical substance covered by the act prior to manufacture. EPA announced in the 1984 policy statement that microorganisms used in biotechnology would be considered "new" under TSCA if significant human intervention had been used in developing them. Under this "process-based" approach, microorganisms altered by certain genetic engineering techniques were presumed to be new because those techniques involved significant human intervention.

In 1986, after receiving comments on the 1984 proposed policy statement, OSTP published Coordinated Framework for Regulation of Biotechnology.[4] EPA's section of the 1986 policy statement indicated that the agency had revised its determination of which microorganisms covered by TSCA would be considered "new." According to the 1986 policy statement, all "intergeneric microorganisms"—that is, those created by the deliberate combination of genetic material from organisms of different genera[5] would

[1]The member agencies included the Departments of Justice, State, Agriculture, Commerce, Defense, Energy, Health and Human Services, Labor, and the Interior; EPA; the Council on Environmental Quality; the Council of Economic Advisors; OMB; the Office of Policy Development; the National Science Foundation; the Office of the U.S. Trade Representative; and OSTP.

[2]Office of Science and Technology Policy, Proposal for a Coordinated Framework for Regulation of Biotechnology (49 Fed. Reg. 50856-907, Dec. 31, 1984).

[3]A number of commentators on this matter have questioned the discretionary authority claimed by EPA regarding the applicability of TSCA. That issue is beyond the scope of this report.

[4]Office of Science and Technology Policy, Coordinated Framework for Regulation of Biotechnology (51 Fed. Reg. 23302-50, June 26, 1986).

[5]Genera is the plural of genus, the second level of categories in the biological classification of organisms, ranking directly above species, the narrowest category.

be considered "new."[6] EPA indicated that its policy concerning which microorganisms would be considered new was effective as of the date of publication of the policy statement. EPA also indicated that new microorganisms being manufactured for commercial purposes other than research and development would be immediately subject to the premanufacture notice requirements of TSCA. EPA further indicated that implementing other aspects of its biotechnology policy would require rulemaking, and until final rules could be made effective, it expected manufacturers to voluntarily comply with most aspects of the policy.

The definition of intergeneric organisms in the 1986 Coordinated Framework was developed by the Biotechnology Science Coordinating Committee, an interagency group established by OSTP in October 1985 to coordinate biotechnology regulatory activities.[7] According to EPA, the likelihood of creating new combinations of traits and the uncertainty regarding effects on the environment were high enough to require regulatory scrutiny of these intergeneric organisms.

In March 1989, the President established the Council on Competitiveness to minimize the burdens of regulation and encourage America's competitiveness. Among other functions, the Council, which is chaired by the Vice President, is responsible for reviewing issues raised in conjunction with the regulatory review process carried out by OMB.[8] To assist the Council in reviewing regulatory and policy issues affecting the biotechnology industry, the Vice President established a Biotechnology Working Group within the Council on Competitiveness in January 1990. The Biotechnology Working Group includes representatives of EPA and other regulatory and research agencies. The administration views biotechnology as a potential major growth industry for the United States.

[6]Excluded from the 1986 Coordinated Framework definition of "new" microorganisms were those formed by the addition of certain genetic material whose transfer does not produce new combinations of traits in the created organisms.

[7]The Biotechnology Science Coordinating Committee included representatives from the Departments of Health and Human Services and Agriculture; EPA; and the National Science Foundation. An OSTP staff member served as the Executive Secretary until the Committee disbanded around December 1989.

[8]In addition to the Vice President, the Council's members are the Secretary of the Treasury, the Attorney General, the Secretary of Commerce, the Director of OMB, the Chairman of the Council of Economic Advisors, and the President's Chief of Staff.

Review of Initial Proposed Regulation Delayed Because of Disagreements Over Scope

On the basis of the 1986 Coordinated Framework, EPA began to develop a TSCA biotechnology regulation. In May 1988, EPA sent a proposed regulation to OMB for review. However, disagreement over the scope of the proposed regulation surfaced during OMB's review. Unable to obtain OMB support for its proposed definition of scope, EPA later withdrew the proposed rule.

According to EPA officials, OSTP's Biotechnology Science Coordinating Committee disagreed with EPA's proposal in the rule to require manufacturers to notify the agency before biotechnology products made with intergeneric microorganisms—as defined in the 1986 Coordinated Framework—are introduced into commerce. The Committee believed that defining the scope of the rule to include all intergeneric microorganisms would subject more biotechnology products to regulation than warranted by the risk they pose to the environment. In response, EPA officials said that an obvious difficulty exists in predicting in advance what combinations of traits will result in risky organisms. In July 1988, after being notified that the period of review was being extended, EPA urged OMB to clear the proposed regulation for publication. The Biotechnology Science Coordinating Committee held to its position on the regulation, but it did not provide specifics about how EPA should define a regulatory approach based on risk.

In September 1988, EPA submitted a revised proposed biotechnology regulation to OMB that was still based on the 1986 Coordinated Framework policy that intergeneric microorganisms were to be considered "new" and therefore subject to TSCA's section 5 premanufacture notice requirements. In the preamble of the revised proposal, EPA attempted to clarify its rationale for requiring premanufacture notification of intergeneric microorganisms. Specifically, EPA explained that the section 5 premanufacture notification provision of TSCA is not triggered by a risk determination. Instead, it is triggered by a determination that a microorganism is new. EPA said that it expected most microorganisms would get through the section 5 screening process without the need for additional information or regulatory restrictions, thus allowing the agency to focus on those microorganisms that could present significant risks. EPA emphasized that the underlying basis for its regulatory scheme was the uncertainty associated with the release of new microorganisms into the environment. However, the Biotechnology Science Coordinating Committee still held to its view that the proposed regulation was too process-based and insufficiently risk-based.

The Administrator of EPA, lacking interagency and OMB support but believing that the agency could get support for its proposed approach to scope from the public, withdrew the proposed rule from OMB and requested public comments on scope and related issues in February 1989. However, the comments that EPA received about the proposed scope of the regulation were mixed.

Revised Guidance May Affect EPA's Latest Proposed Regulation

Following EPA's withdrawal of the proposed TSCA biotechnology regulation from OMB, OSTP issued guidance for federal agencies in July 1990 to clarify its overall policy position on regulation of the biotechnology industry. EPA believes that the latest draft of its proposed regulation, dated December 1991, is consistent with both the requirements of TSCA and the position of OSTP and others in the administration, such as the Council on Competitiveness, that biotechnology regulation should be based on risk. However, EPA began developing the proposed regulation before OSTP issued the administration's most recent regulatory policy statement, dated February 1992. This latest statement eliminates the definition of scope contained in the July 1990 guidance, on which EPA based its December 1991 regulation. Rather than including a definition of scope, the statement advises that within the authority provided by statute, agencies should exercise oversight of the introduction of biotechnology products only when the risk posed by the introduction is unreasonable.

Efforts to Resolve Disagreements Over TSCA Regulation

In an attempt to resolve the impasse with EPA that surfaced in late 1988 concerning the scope of the TSCA biotechnology regulation, the Chairman of the Biotechnology Science Coordinating Committee established a working group in mid-1989 to develop a proposed definition of scope to guide federal biotechnology rulemaking.[9] In November 1989, the working group submitted a paper to the Chairman that presented four options. The full committee discussed the options but could not reach a consensus on which option to recommend. The Chairman forwarded the draft options paper to OSTP, which then forwarded it to the President's Council on Competitiveness.

In 1990, the Council on Competitiveness's Biotechnology Working Group attempted to address the differences over the appropriate scope of biotechnology regulation. The Working Group developed proposed regulatory principles to be used by agencies in regulating biotechnology

[9]This group consisted primarily of subordinate staff of Biotechnology Science Coordinating Committee members. The group was chaired by the Assistant Secretary for Science and Education, U.S. Department of Agriculture.

products. The proposed principles were published in the July 31, 1990, Federal Register by OSTP.[10]

The 1990 proposed principles stated that, to the extent permitted by law, the regulatory or oversight approach should be based on the risk posed by organisms. However, the definition of scope outlined by the proposed principles was not strictly risk-based. Specifically, the proposed scope included all organisms with "deliberately modified hereditary traits" resulting from any process or technique. To factor risk into the definition, the working group provided examples of categories of organisms that agencies could consider excluding from regulatory oversight because their introduction into the environment was (1) adequately addressed by existing regulations or (2) considered safe on the basis of available information. The proposed principles also recognized that agencies may take different approaches in promulgating specific regulations because of differences in their laws.

EPA developed its current proposed regulation, which it expects to submit to OMB in late summer 1992, in line with the proposed 1990 principles. In this version of the proposed regulation, EPA proposes to drop its earlier intergeneric definition of "new" microorganisms, which was based on OSTP's 1986 policy, and instead adopt a definition of "new" microorganisms based on OSTP's 1990 policy. The proposed regulation defines as new, and requires premanufacture notice review for, all microorganisms subject to TSCA that have deliberately modified hereditary traits, except for four categories of microorganisms. EPA has excluded these categories from the definition of "new" microorganisms because it considers them to be familiar—that is, they behave like other populations of microorganisms in nature. EPA concluded that these familiar microorganisms, as they are called, need not be addressed by regulation, either because they are of low risk or because they are already addressed by other oversight systems.

In addition to providing for these exclusions, EPA proposes to exempt certain microorganisms from screening under TSCA section 5(h)(4), which allows EPA to exempt new substances from all or part of section 5 premanufacture screening requirements if the agency determines that such substances will not present an unreasonable risk. EPA proposes under section 5(h)(4) to allow certain microorganisms to be introduced into the environment for research and development purposes after an expedited

[10]Office of Science and Technology Policy, Principles for Federal Oversight of Biotechnology: Planned Introduction Into the Environment of Organisms With Modified Hereditary Traits (55 Fed. Reg. 31113-21, July 31, 1990).

review process. EPA also proposes other section 5(h)(4) exemptions for specific microorganisms and classes of microorganisms.

Issuance of Final Principles Raise Questions About EPA's Current Proposal

EPA's current proposed regulation is in the final stages of agency review. EPA officials told us that the proposed regulation could be promulgated by October 1993, assuming that no further interagency disagreements delay promulgation. However, in reviewing EPA's proposed biotechnology regulation, OMB and the Council on Competitiveness, which resolves issues raised during OMB review, will probably consider final regulatory principles developed by the Biotechnology Working Group. These principles, which differ from the 1990 proposed principles, were published in the Federal Register in February 1992 by OSTP.[11] The final principles drop the 1990 definition of scope as including organisms with "deliberately modified hereditary traits" and instead advise that within the authority provided by statute, federal agencies should exercise oversight of the introduction of biotechnology products only when evidence shows that the risk posed by the introduction is unreasonable.

Although the 1992 final principles published by OSTP recognize that their implementation is to be within the context of applicable laws, such as TSCA, the principles do not provide specific guidance on how agencies should address the concept of risk within the context of the relevant laws. For instance, the 1992 principles indicate that EPA has the discretion to determine what biotechnology products are "new" for purposes of TSCA, but the principles do not say how EPA should consider risk in making that determination. EPA officials told us that although they consider their proposed regulation to be risk-based and consistent with section 5 of TSCA and the 1992 final principles, they are uncertain as to whether OMB and the Council on Competitiveness will consider the regulation to be in line with the final guidelines. (A chronology of the major events surrounding EPA's efforts to issue a TSCA biotechnology regulation is contained in app. II.)

[11]Office of Science and Technology Policy, Exercise of Federal Oversight Within Scope of Statutory Authority: Planned Introductions of Biotechnology Products Into the Environment (57 Fed. Reg. 6753-62, Feb. 27, 1992).

Industry Concerns About the Lack of a Final TSCA Regulation

According to representatives of the Association of Biotechnology Companies,[12] Industrial Biotechnology Association,[13] and Applied BioTreatment Association,[14] the lack of a final TSCA biotechnology regulation has caused uncertainty and is hindering the industry's ability to conduct long-term planning and raise capital for new product research. Researchers and investors normally consider the costs of meeting regulatory criteria in investment decisions.

In October 1991, the Office of Technology Assessment (OTA) issued a report entitled Biotechnology in a Global Economy. In testimony before the Subcommittee on Environment, House Committee on Science, Space, and Technology, on December 16, 1991, an OTA official stated that "the failure to promulgate final regulations has led to complaints by industry representatives that the regulatory approval process is unclear and inhibits investment." This official told us that biotechnology industry representatives made such complaints during a 1989 workshop conducted as part of the data-gathering efforts in connection with OTA's October 1991 report.

Conclusions

EPA's efforts to promulgate a TSCA biotechnology regulation have been delayed because of disagreement between EPA and others in the executive branch over the scope of biotechnology products that should be subject to regulatory review or oversight. EPA's latest proposal, which it intends to submit to OMB for review in late summer 1992, is based on OSTP's 1990 proposed biotechnology regulatory principles. However, when reviewing the EPA proposal, OMB and the Council on Competitiveness will likely consider OSTP's 1992 final principles. The 1992 guidance eliminates the definition of scope that the 1990 guidance contained, the definition on which EPA's proposal is based. Instead, the 1992 guidance calls for agencies—within the context of their statutory authority—to use a risk-based approach to develop biotechnology regulations. Considering this change in guidance, and in the absence of specific guidance on how

[12]Founded in 1983, the Association of Biotechnology Companies is an international trade association with over 250 members. Its members include private biotechnology companies, academic and state biotechnology centers, nonprofit and government-affiliated entities, and other organizations interested in biotechnology.

[13]Founded in 1981, the Industrial Biotechnology Association was the first trade association to represent the biotechnology industry. The association represents about 115 member companies of all sizes engaged in every aspect of the emerging biotechnology industry.

[14]Founded in 1989, the Applied BioTreatment Association represents 45 entities that include both companies and individual members. Its member companies develop microorganisms that occur naturally in nature.

agencies are to implement a risk-based approach consistent with laws such as TSCA, it is uncertain whether OMB and the Council on Competitiveness will consider EPA's proposed regulation to be sufficiently risk-based. Members of the biotechnology industry have expressed concern about the uncertainty over what regulatory requirements they will have to meet in the future and have indicated that this uncertainty has hampered their long-range planning and has inhibited investments in new biotechnology activities.

Our work was conducted from October 1991 through April 1992 in accordance with generally accepted government auditing standards. Appendix I contains more information on the objectives, scope, and methodology of our review. As requested, we did not obtain written agency comments on a draft of this report. However, we discussed the facts in this report with EPA, OMB, and OSTP officials, who generally agreed with the information. Their suggestions have been incorporated where appropriate.

Unless you publicly announce its contents earlier, we plan no further distribution of this report until 30 days from the date of this letter. At that time, we will provide copies to the Administrator, EPA; the Director, OMB; and appropriate congressional committees. We will also make copies available to other interested parties upon request.

Please call me at (202) 275-6111 if you have any questions about this report. Major contributors to this report are listed in appendix III.

Sincerely yours,

Richard L. Hembra
Director, Environmental
Protection Issues

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Abbreviations

BSCC	Biotechnology Science Coordinating Committee
EPA	Environmental Protection Agency
OMB	Office of Management and Budget
OSTP	Office of Science and Technology Policy
OTA	Office of Technology Assessment
TSCA	Toxic Substances Control Act

Objectives, Scope, and Methodology

The Chairman of the Subcommittee on Regulation, Business Opportunities, and Energy, Committee on Small Business, requested that we examine (1) the Environmental Protection Agency's (EPA) efforts to issue a biotechnology regulation under the Toxic Substances Control Act (TSCA), including the reasons why its efforts have not been successful, and (2) the potential impact on the biotechnology industry of not having a TSCA biotechnology regulation.

With regard to the history of and prospects for a TSCA biotechnology regulation, we reviewed the TSCA statute and implementing regulations and various biotechnology policies published in the Federal Register. We obtained further information through discussions with officials from EPA's Office of Prevention, Pesticides and Toxic Substances, the Office of Management and Budget (OMB), and the Office of Science and Technology Policy (OSTP) within the Executive Office of the President. We also reviewed various documents provided by officials of these agencies, including the two drafts of EPA's proposed TSCA biotechnology regulation submitted to OMB in 1988 and EPA's current proposed TSCA biotechnology regulation. The Council on Competitiveness declined our requests for an interview and declined to review a draft of this report. As a result, the report does not reflect the Council's (1) perspective on its role in the events surrounding EPA's efforts to promulgate a TSCA biotechnology regulation and (2) views on prospects for promulgation of EPA's current draft of the proposed regulation.

We also interviewed officials of three biotechnology associations —The Association of Biotechnology Companies, The Industrial Biotechnology Association, and The Applied BioTreatment Association—to obtain their views on the impact that the lack of a TSCA biotechnology regulation is having on the industry.

We conducted our work between October 1991 and April 1992 in accordance with generally accepted government auditing standards. We discussed the information in this report with EPA officials in the Office of Prevention, Pesticides and Toxic Substances, OSTP, and OMB officials, who generally agreed with the factual information. We made changes where appropriate. As requested, we did not obtain written agency comments on a draft of this report.

Chronology of TSCA Rulemaking Activity

Date	Event
12/84	*Proposal for a Coordinated Framework for Regulation of Biotechnology* published by the Office of Science and Technology Policy (OSTP) in the *Federal Register.*
11/85	Biotechnology Science Coordinating Committee (BSCC) established under OSTP.
6/86	*Coordinated Framework for Regulation of Biotechnology* (1986 Coordinated Framework) published by OSTP in *Federal Register.*
6/86 to 5/88	Environmental Protection Agency (EPA) prepared draft TSCA regulation based on definitions developed by BSCC and contained in the 1986 Coordinated Framework.
5/88	First draft of TSCA proposed rule sent to BSCC and OMB for review.
9/88	Second draft of TSCA proposed rule sent to BSCC and OMB for review.
2/89	EPA Administrator withdrew proposed rule from OMB.
3/89	President established Council on Competitiveness.
7/89	BSCC formed a working group to develop an appropriate scope approach.
12/89	Policy oversight functions of BSCC assumed by President's Council on Competitiveness.
1/90	Vice President established Biotechnology Working Group (within Council on Competitiveness).
7/90	OSTP published *Principles for Federal Oversight of Biotechnology: Planned Introduction into the Environment of Organisms with Modified Hereditary Traits* in *Federal Register.*
2/91	President's Council on Competitiveness issued Report on National Biotechnology Policy.
6/91	EPA completed revised TSCA proposed rule based on July 1990 OSTP proposed principles.
12/91	Revised TSCA rule sent for final internal review at EPA.
2/92	OSTP published *Exercise of Federal Oversight Within Scope of Statutory Authority: Planned Introductions of Biotechnology Products into the Environment* in *Federal Register.*

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