(2/7) SAB (NELSON) + (ALEXANDER)

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cc: Barnes

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

February 7, 1986

OFFICE OF
THE ADMINISTRATOR

Honorable Lee M. Thomas
Administrator
U.S. Environmental Protection
Agency
401 M Street, S.W.
Washington, D.C. 20460

Dear Mr. Thomas:

The Science Advisory Board's Study Group on Biotechnology has prepared this report in response to the request to undertake a preliminary evaluation of the Agency's existing research and risk assessment capabilities associated with the field application of genetically engineered organisms. This report also fulfills the request to conduct a Research Review of the Office of Research and Development's Research Program in Biotechnology.

Since the Agency has only recently begun its research and regulatory activities, the Study Group felt that an intensive detailed report was unnecessary at this time. In researching and preparing this report, the Study Group was pleased with the cooperation and candor of Agency staff in conducting briefings and answering questions.

In general, the Study Group believes that although the Agency has increased its research staff and initiated a research program in biotechnology, a larger and broader program than that envisioned is needed by EPA decision makers. Dispersal of genetically engineered microorganisms, appropriate remedial action in the event of release of such organisms, and possible environmental effects of such a release, whether beneficial or detrimental, are critical issues which should receive high priority by EPA. Research on health effects, as presently planned, is limited in scope and should be expanded with adequate resources made available for this purpose.

The Study Group appreciates the opportunity to provide comments on this critical issue. We look forward to the Agency's response to our report.

Sincerely,

Norton Nelson

Norton Nelson, Chairman
Executive Committee
Science Advisory Board

Martin Alexander

Martin Alexander, Chairman
Study Group on Biotechnology
Science Advisory Board

cc: A. James Barnes
Don Ehreth
Jack Moore
Terry Yosie

REPORT OF THE STUDY GROUP ON BIOTECHNOLOGY

SAB-EC-86-009

U.S. Environmental Protection Agency
Science Advisory Board
Washington, D.C.

January 1986

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U.S. Environmental Protection Agency
Science Advisory Board

BIOTECHNOLOGY STUDY GROUP

Chairman

Dr. Martin Alexander, Department of Agronomy, Cornell University, Ithaca, New York

Members

Dr. Ralph Baker, Plant Pathology and Weed Science, Colorado State University, Fort Collins, Colorado

Dr. Rita Colwell, Department of Microbiology, University of Maryland, College Park, Maryland

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Mr. Robert Flaak, U.S. Environmental Protection Agency, Science Advisory Board, Washington, D.C.

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The Agency has published a preliminary policy statement for testing genetically altered microorganisms that is adequate in light of the present state of knowledge; however, attention needs to be given to developing test protocols to comply with this policy statement and future policy and regulatory requirements, while still allowing the evaluation of biotechnology products on a case-by-case basis.

The Study Group supports interagency coordination efforts to harmonize test protocols, to minimize difficulties and delays in approving biotechnology products, and to facilitate evaluations of possible health effects. International communication and cooperation in research and regulatory activities are of great importance and are needed.

The Agency should establish an advisory panel to review the adequacy and direction of research, testing procedures, and risk assessment approach to biotechnology on a continuing basis.

2. INTRODUCTION

The EPA Administrator requested that the Science Advisory Board (SAB) undertake a preliminary examination of EPA's existing research and risk assessment capabilities associated with the field application of genetically engineered organisms. The SAB's Executive Committee accepted this request and authorized the formation of a Study Group on Biotechnology.

Both the Agency and the SAB Executive Committee asked the Study Group to: (a) identify information gaps for performing risk assessments on the products of biotechnology; (b) explore the direction of EPA's research program in biotechnology; and (c) evaluate the availability of testing procedures and EPA's assessment methods for genetically altered organisms.

The Study Group held meetings on March 19, July 22-23, and December 19, 1985, at which times it was briefed by John A. Moore, Assistant Administrator for the Office of Pesticides and Toxic Substances (OPTS), and by the staff of the Office of Pesticide Programs (OPP), Office of Toxic Substances (OTS),

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The Study Group is pleased to note the completeness and frankness of the staff presentations. The EPA staffs were forthright about information gaps, problems and needs. Despite the restricted time available to meet with them, the Study Group believes that it has a relatively clear understanding of what information is needed, the current status of the EPA's research in biotechnology, and the availability of meaningful tests for evaluating genetically engineered organisms. Because the EPA has only recently begun its research and regulatory activities, an intensive detailed report by the Study Group was not deemed necessary at this time.

3. RESEARCH NEEDS

A biotechnology research program adequate to meet the needs of the Agency should include the following topics: (a) survival; (b) growth; (c) genetic transfer in situ; (d) dispersal; (e) environmental effects; (f) health effects; (g) remedial action; and (h) use of biotechnology for destroying environmental pollutants.

- Survival - A genetically engineered microorganism may present a problem only if it persists in natural environments, and organisms to be used for pollution control must be able to endure. Nevertheless, it is not now possible to predict survival for either regulatory purposes or for the practical exploitation of microorganisms designed for biotechnological uses.

- Growth - The few individual organisms that are released or persist are not likely to have a detrimental or beneficial effect because of their small populations, and an increase in numbers or biomass is necessary for these to have some ecological or health effect. However, the current data base must be expanded to allow for accurate prediction of which types of organisms will and which will not proliferate.

- Genetic Transfer - A genetically engineered species that is harmful might itself not survive or multiply, but the relevant genetic information could be transferred in situ to other organisms. The latter might ultimately become harmful. Although enormous progress has been made in recent years in increasing our understanding of gene transfer under highly artificial conditions, little information exists on gene transfer in nature.

• Dispersal - The site of release of a genetically engineered or nonindigenous organism is usually not the site where it can bring about some deleterious change because of the absence of suitable host animals or plants, or the absence of suitable environmental conditions. Risk assessment thus requires information on the mechanisms and likelihood of dissemination by insects or other animal vectors, through air or soil, by water transport, or by other means. Epidemiology and plant pathology have developed good bases of knowledge on known pathogens, but little attention has been given to the organisms of current or likely future interest in biotechnology, and there is limited understanding of the traits contributing to successful dispersal.

• Environmental Effects - Both the public sector and the scientific community are concerned with effects on natural communities and natural processes. The Agency has had a research program on measuring effects of chemicals on such communities and processes and has considered the influence of chemicals as part of its regulatory mission. Products of biotechnology need to be evaluated in different ways from chemicals because these organisms are highly specific for the plants, animals, and microorganisms they may invade or harm, and the generalizations so useful in toxicology probably have little meaning for potential communicable agents.

• Health Effects - EPA needs information and expertise in public health, communicable disease risks, and the relevant biomedical disciplines for its biotechnology program. Other Federal agencies, including the National Institutes of Health (NIH) and the National Science Foundation (NSF), are unlikely to fund research that meets EPA's specific information requirements in making regulatory decisions about any potential health effects of genetic engineering applications. Also, in order to develop scientifically defensible risk assessments, EPA must have in-house expertise.

Because of the large variety of possible organisms and applications, it is not feasible at this state to develop a predictive model for health effects. Instead, the Study Group recommends a case-by-case approach to considering potential health hazards related to environmental releases of genetically-altered organisms. Nevertheless, EPA must develop a biotechnology health effects research strategy and a critical mass of scientists and address how the accumulation of experience from individual cases will lead to more general guidelines in the future.

• Remedial Action - A means must be found to contain and possibly destroy a genetically engineered organism in the unlikely event that, despite the research conclusions and the testing before release, the organism is found to be harmful. Some precedents exist on means for remedial action from human and veterinary medicine and plant pathology,

but the possible differences in environmental behavior of genetically engineered microorganisms dictate that attention be given to containment and remedial action.

- Biotechnology to Destroy Pollutants - The techniques of modern genetics and environmental microbiology can aid substantially in reducing the concentration or totally destroying chemical pollutants in surface and ground waters, industrial and municipal waste-treatment systems, and possibly in other circumstances. Microorganisms have the advantage of providing a low-cost, simple, and often highly effective means for chemical destruction. The programs of the Agency could benefit greatly by increasing financial and personnel resources in this area.

As part of its recently initiated research program, the Agency has hired new personnel and initiated cooperative agreements. Research is planned in methods development to detect genetically engineered microorganisms and measure the reliability and sensitivity of these methods. Some research on survival, growth, genetic transfer in situ, and environmental effects is also planned. Modest programs on health effects and possible uses of biotechnology are also underway. However, the Study Group believes that the magnitude of the program is, at present insufficient for the Agency's needs. In addition, as the products of biotechnology move from the laboratory to commercialization, the problems and processes of scale-up need to be addressed.

EPA has already initiated work on survival, growth and genetic transfer. However, the Study Group identifies the following areas as critical to the Agency and needing additional attention:

- Dissemination - An adequate base of information needs to be developed on the dispersal of genetically engineered microorganisms.

- Remedial Action - Research should be initiated to develop methods for clean-up and containment in the event of the dissemination of a harmful organism.

- Environmental Effects - The Agency has essentially no program in this area. The EPA should mount a research effort to assess possible perturbations in natural communities related to genetically engineered microorganisms. Research also should be conducted on the use of microcosms as models for natural communities, using the microcosms to evaluate effects of viable agents, as has been done for chemicals. The feasibility of the testing protocols and the validity of the risk assessment procedures might be tested using naturally occurring or genetically engineered microorganisms specifically selected or designed to bring about the inactivation and degradation of environmental pollutants.

- Health Effects - The scientific staff should, at a minimum, be involved in the following health effects activities: (a) development of test protocols, building upon and revising the existing protocols in Subdivision-M of the Pesticide Assessment Guidelines; (b) technical assistance on current information and emerging trends in health effects and biomedical mechanisms. Staff must draw upon the relevant reference materials, published literature, computerized data bases, regular contacts with outside scientists, scientific societies, and their own research. One objective of this function is to facilitate both industrial and in-house selection of microorganims least likely to present health risks—based upon an ongoing analysis of the features of pathogenicity, including propensity for exchange of genetic material; and (c) an expanding program of well-focussed, peer-reviewed intramural research, supported in order to attract and retain able scientists who can meet the regulatory science needs and interact with extramurally-supported scientists.

The scientific staff concerned with all of these topics should serve as resource personnel to respond to technical issues raised by program officials. The staff should influence the kinds of generic questions that the program offices address to the research agenda.

4. TESTING THE PRODUCTS OF BIOTECHNOLOGY

Both OPP and OTS have developed a logical framework for obtaining information from developers of biotechnology products. The types of data sought by the staff should provide a scientifically improved basis for appropriate regulatory decisions. Despite the absence of a substantial base of information concerning environmental fate and possible environmental effects of introduced organisms, OPP and OTS staff have developed preliminary guidance addressing, on a case-by-case basis, the issues of possible consequences of biotechnology products. We encourage the interaction between EPA and industry to continue to gain information.

The absence of generally accepted tests and test methods, however, is cause for concern. Some tests do now exist in Subpart M of the Pesticide Guidelines in certain areas of risk assessment. Although EPA requires results of tests of survival, multiplication, dispersal and possible ecological effects of genetically engineered organisms, generally accepted test protocols for providing such data do not exist. This absence creates problems both for industry in the attempts to satisfy requests for information from the Agency and for EPA and the public in evaluating the potential risk.

The Study Group recommends that EPA initiate research to develop appropriate tests for evaluating survival, multiplication, dispersal and possible deleterious effects of genetically engineered organisms. We believe that certain of these tests will need to be conducted using microcosms specifically designed for biotechnology products; hence, appropriate

Among the benefits from such coordination is the identification of a lead agency for defined products and processes of biotechnology; that lead agency will be available to industry or research scientists for advice on field testing and/or registration of these systems. Related to this is the need for harmonizing minimum test protocols. The Study Group believes that a single lead agency is necessary for individual products and processes. This lead agency should use any major experience base of other agencies.

The EPA does not currently have financial resources adequate to develop protocols on the health effects of biotechnological agents. Because the need exists, however, EPA should seek to involve other agencies to participate in the necessary research and help establish the requisite test protocols.

7. INTERNATIONAL ACTIVITIES

The impact of biotechnology applications obviously has worldwide significance. Since biotechnological developments do not have geographical boundaries, international communication and cooperation is of great importance. The Study Group recognizes and commends the efforts made by EPA and other Federal agencies to emphasize cooperative research with foreign investigators and to attempt to harmonize international regulatory activities.

8. BIOTECHNOLOGY ADVISORY GROUP

We are impressed with what the EPA staff has done in the brief time of its involvement with biotechnology, and we believe that the value of the programs will be augmented by input from experienced technical personnel.

We believe that the scientific basis of biotechnology, regulatory as well as research activities of EPA, would profit greatly from advice and review by specialists with knowledge and experience in the relevant scientific disciplines.

Thus, we recommend that EPA establish one advisory panel to review the intramural and extramural research programs, the adequacy of the testing procedures, and the Agency's risk assessment approach to biotechnology. The specific charge to the committee should include: a) review of selected individual risk assessments; b) review of cross media and cross program scientific issues; c) comparison of specific risk assessments to ascertain the degree of internal consistency including unnecessary duplication of effort among EPA programs; d) evaluation of trends arising from the consideration of groups of individual risk assessments and regulatory applications; e) consider the environmental and health consequences of the likely growth of the biotechnology industry; and f) recommendation of needed research.

Among the benefits anticipated from an external advisory process are enhancement of EPA's credibility with the scientific community, providing a forum for developing scientific consensus, and providing peer review of EPA's risk assessments. The panel might be an independent committee that contains representatives of both the Science Advisory Board and the Science Advisory Panel (SAP) of OPP, or it might be part of SAB or SAP. This advisory panel should include members with expertise in microbial ecology, population genetics of microorganisms, ecosystem ecology, communicable diseases of animals and plants (especially of natural populations), pest management, molecular genetics, microcosms, chemical and environmental engineering and risk assessment, as well as other disciplines that the Agency deems necessary. Such a panel should have the flexibility to recruit more specialized expertise, when needed, and establish sub-committees to carry out its review responsibilities. The advisory panel should report directly to the Administrator.

CHARGE TO THE SCIENCE ADVISORY BOARD STUDY GROUP ON BIOTECHNOLOGY

Administrator William D. Ruckelshaus requested that the Science Advisory Board (SAB) Executive Committee take a preliminary look at EPA's current capabilities in addressing several issues associated with the field application of genetically altered organisms. The Committee accepted this request and authorized the formation of a Study Group on Biotechnology. The Executive Committee chose to form a study group at this juncture based upon its belief that it would be premature to carry out any formal SAB review until the many inter-Agency jurisdictional and policy questions related to biotechnology are resolved within the Federal government.

The information to be gathered by the Study Group includes:

- Identification of information gaps for performing risk assessment;
- Exploring the direction of EPA's research program in biotechnology; and
- Assessing the availability of testing procedures for genetically altered organisms and EPA's assessment methods.

The Study Group will present its findings, options, and recommendations to the SAB Executive Committee.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

February 7, 1986

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The Study Group recommends that EPA initiate research to develop appropriate tests for evaluating survival, multiplication, dispersal and possible deleterious effects of genetically engineered organisms. We believe that certain of these tests will need to be conducted using microcosms specifically designed for biotechnology products; hence, appropriate

protocols will need to be devised with a view to applying EPA's experience with microcosms to biotechnology products. These laboratory and microcosm testing methods will also need to be validated by field trials with engineered organisms whose safety is known or by using surrogate species. Publicly owned, professionally managed "contained sites" should be identified for this testing.

The Study Group believes that the availability of generally accepted testing procedures does not minimize the importance of, or the need for, considering each organism submitted for approval on a case-by-case basis. The development of biotechnology for practical purposes is too new an endeavor to warrant a generic approach to product evaluation at this time.

5. RISK ASSESSMENT

The EPA's fundamental mission, as defined in the various statutes through which it establishes and administers environmental programs, is to identify, assess, and abate the risks of pollution to human health and the environment. The risks or perceived risks that accompany the development and introduction of chemicals into the environment create the need for research on environmental fate and effects and human health impacts of chemicals and the development of regulatory programs. From this research, scientific investigators and regulatory personnel hope to gain the knowledge to estimate the risks of chemicals to the environment and to human health. Previous research on the fate and persistence of chemicals in the environment has been used to determine appropriate test protocols and to assign risks to the chemicals developed by industry.

With the evolution of biotechnology, a new and exciting challenge has arisen to discover the principles that govern the dispersal and persistence of genetically engineered microorganisms in the environment, as well as to determine their ability to multiply; the latter issue does not pertain to chemicals. However, scientists recognize that there have been few problems because of the release into the environment of organisms produced by traditional genetic means. As with chemicals in the environment, scientists hope that after these principles are discovered, predictive models can be developed for use in preparing reliable risk assessments. Innovative research over an extended period of time by EPA, other Federal agencies, the private sector, universities, and others will be required before scientists discover these principles. Only then will definitive test protocols gain general acceptance and predictive models for health and environmental risk assessment have real relevance to private and public sector decision making.

6. INTERAGENCY COORDINATION

At least four agencies (EPA, FDA, NIH and USDA) have direct concerns related to developments in biotechnology, while others, such as the Department of Defense, will also be impacted by this technology. The Office of Science and Technology Policy has proposed a formal mechanism, the Biotechnology Science Coordinating Committee, to establish a coordinated framework for the regulation of biotechnology.[1]

[1] "Coordinated Framework for Regulation of Biotechnology; Establishment of the Biotechnology Science Coordinating Committee," Federal Register, November 14, 1985.

Among the benefits from such coordination is the identification of a lead agency for defined products and processes of biotechnology; that lead agency will be available to industry or research scientists for advice on field testing and/or registration of these systems. Related to this is the need for harmonizing minimum test protocols. The Study Group believes that a single lead agency is necessary for individual products and processes. This lead agency should use any major experience base of other agencies.

The EPA does not currently have financial resources adequate to develop protocols on the health effects of biotechnological agents. Because the need exists, however, EPA should seek to involve other agencies to participate in the necessary research and help establish the requisite test protocols.

7. INTERNATIONAL ACTIVITIES

The impact of biotechnology applications obviously has worldwide significance. Since biotechnological developments do not have geographical boundaries, international communication and cooperation is of great importance. The Study Group recognizes and commends the efforts made by EPA and other Federal agencies to emphasize cooperative research with foreign investigators and to attempt to harmonize international regulatory activities.

8. BIOTECHNOLOGY ADVISORY GROUP

We are impressed with what the EPA staff has done in the brief time of its involvement with biotechnology, and we believe that the value of the programs will be augmented by input from experienced technical personnel.

We believe that the scientific basis of biotechnology, regulatory as well as research activities of EPA, would profit greatly from advice and review by specialists with knowledge and experience in the relevant scientific disciplines.

Thus, we recommend that EPA establish one advisory panel to review the intramural and extramural research programs, the adequacy of the testing procedures, and the Agency's risk assessment approach to biotechnology. The specific charge to the committee should include: a) review of selected individual risk assessments; b) review of cross media and cross program scientific issues; c) comparison of specific risk assessments to ascertain the degree of internal consistency including unnecessary duplication of effort among EPA programs; d) evaluation of trends arising from the consideration of groups of individual risk assessments and regulatory applications; e) consider the environmental and health consequences of the likely growth of the biotechnology industry; and f) recommendation of needed research.

Among the benefits anticipated from an external advisory process are enhancement of EPA's credibility with the scientific community, providing a forum for developing scientific consensus, and providing peer review of EPA's risk assessments. The panel might be an independent committee that contains representatives of both the Science Advisory Board and the Science Advisory Panel (SAP) of OPP, or it might be part of SAB or SAP. This advisory panel should include members with expertise in microbial ecology, population genetics of microorganisms, ecosystem ecology, communicable diseases of animals and plants (especially of natural populations), pest management, molecular genetics, microcosms, chemical and environmental engineering and risk assessment, as well as other disciplines that the Agency deems necessary. Such a panel should have the flexibility to recruit more specialized expertise, when needed, and establish sub-committees to carry out its review responsibilities. The advisory panel should report directly to the Administrator.

CHARGE TO THE SCIENCE ADVISORY BOARD STUDY GROUP ON BIOTECHNOLOGY

Administrator William D. Ruckelshaus requested that the Science Advisory Board (SAB) Executive Committee take a preliminary look at EPA's current capabilities in addressing several issues associated with the field application of genetically altered organisms. The Committee accepted this request and authorized the formation of a Study Group on Biotechnology. The Executive Committee chose to form a study group at this juncture based upon its belief that it would be premature to carry out any formal SAB review until the many inter-Agency jurisdictional and policy questions related to biotechnology are resolved within the Federal government.

The information to be gathered by the Study Group includes:

- Identification of information gaps for performing risk assessment;
- Exploring the direction of EPA's research program in biotechnology; and
- Assessing the availability of testing procedures for genetically altered organisms and EPA's assessment methods.

The Study Group will present its findings, options, and recommendations to the SAB Executive Committee.