

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH  
RECOMBINANT DNA ADVISORY COMMITTEE

1164

WORKING GROUP ON RELEASE INTO THE ENVIRONMENT

MINUTES OF MEETING<sup>1</sup>

APRIL 9, 1984

The Working Group on Release into the Environment was convened at 9:00 a.m. on April 9, 1984, at the Marriott Hotel, 5151 Pooks Hill Road, Bethesda, Maryland 20814. The meeting was open to the public. Dr. Gerard McGarrity was Chair. The following people were present for all or part of the meeting:

Working Group Members:

Charles Arntzen	Thomas Pirone
Royston Clowes	John Scandalios
Susan Gottesman	Frances Sharples
George Lacy	William Gartland
Gerard McGarrity	(Executive Secretary)
David Pimentel	

A working group roster is attached (Attachment I).

Government Liaison Representatives:

John Fowle, U.S. Environmental Protection Agency  
Henry Miller, Food and Drug Administration  
Sue Tolin, U.S. Department of Agriculture

Other National Institutes of Health Staff:

Stanley Barban, NIAID  
Elizabeth Milewski, NIAID

Others:

Robert Brink, Environmental Protection Agency  
Ann Hollander, Environmental Protection Agency  
Carl Maza, Environmental Protection Agency  
Jane Rissler, Environmental Protection Agency  
Mark Segal, Environmental Protection Agency

<sup>1</sup>The working group is an advisory to the RAC, and its recommendations should not be considered as final or accepted.

Dr. McGarrity, Chair, called the meeting of the Working Group on Release Into Environment of the Recombinant DNA Advisory Committee (RAC) to order at 9:00 a.m. on April 9, 1984.

Dr. McGarrity said the working group's agenda consisted of four items. These are listed below.

- (1) The working group will consider the report entitled "The Environmental Implications of Genetic Engineering" prepared by the staff of the Subcommittee on Investigations and Oversight of the Committee on Science and Technology of the U.S. House of Representatives. This report is based on joint hearings held on June 22, 1983, by the House Subcommittee on Investigations and Oversight and the House Subcommittee on Science, Research, and Technology of the Committee on Science and Technology of the U.S. House of Representatives.
- (2) The working group will consider, in light of the report entitled "The Environmental Implications of Genetic Engineering," the questions posed by Dr. Bernard Talbot, Deputy Director of the National Institute of Allergy and Infectious Diseases, in the January 5, 1984, Federal Register (49 FR 696). These questions deal with NIH's appropriate boundaries in its function of overseeing use of recombinant DNA technology.
- (3) The working group will review a draft of submission guidelines drawn up by the Plant Working Group to provide guidance for submissions under Appendix L, Release into the Environment of Certain Plants.
- (4) The working group will be asked to provide advice on a proposed workshop to deal with release into the environment of genetically engineered organisms.

Dr. McGarrity said recommendations made by the Working Group on Release into Environment would be advisory to RAC. The RAC, in turn, is advisory to the National Institutes of Health (NIH). The NIH has final authority for determining the suitability of any action.

#### DISCUSSION OF THE REPORT "THE ENVIRONMENTAL IMPLICATIONS OF GENETIC ENGINEERING"

Dr. McGarrity then began discussion of the report "The Environmental Implications of Genetic Engineering." He said the report from the staff of the Subcommittee on Investigations and Oversight (the Gore Report) drew three conclusions. These are:

- "(1) The potential environmental risks associated with the deliberate release of genetically engineered organisms are best described as 'low probability of high consequence risks'; that is, while there is only a small possibility of occurrence, the damage that could occur is great.

- "(2) Predicting the specific type, magnitude or probability of environmental effects associated with deliberate release will be extremely difficult at the present time.
- "(3) The current regulatory framework does not guarantee that adequate consideration will be given to potential environmental effects of a deliberate release."

Dr. McGarrity said he had concluded in light of what he had read that currently no agency has both expertise and regulatory authority in this area. He asked each of the agency representatives present at the meeting to describe their agency's activity in the area of genetic engineering.

Dr. Gartland said the questions posed by Dr. Talbot were one approach undertaken by the NIH. He said the NIH has approved to date three proposals involving field testing of organisms modified by recombinant DNA techniques. He gave an update on the status of the three proposals: Dr. Ronald Davis of Stanford University has suggested that he might in June 1984 field test corn which has been transformed by corn DNA or modified corn sequences; Dr. John Sanford of Cornell University will not be field testing tomato and tobacco plants transformed with bacterial and yeast DNA as growth chamber and greenhouse experiments have not been successful; and Drs. Nickolas Panopoulos and Steven Lindow of the University of California, Berkeley, have been threatened with litigation should they proceed with plans to field test bacteria lacking the genes coding for proteinaceous ice nucleation foci.

Dr. Miller of the Food and Drug Administration (FDA) said FDA for the past 3 or 4 years has been regulating drugs and biologics produced using genetic engineering techniques. He said FDA has a recombinant DNA coordinating committee which functions administratively within FDA.

Dr. Tolin of the U.S. Department of Agriculture (USDA) said that USDA has been active for some time in the recombinant DNA area. She pointed out that USDA has sponsored and participated in several workshops addressing recombinant DNA issues. She said USDA has an internal administrative advisory committee, the Agriculture Recombinant Advisory Committee.

Dr. Fowle of the Environmental Protection Agency (EPA) said that EPA is attempting to increase its research activity in this area. At the moment, EPA depends on RAC for guidance, and EPA will undoubtedly work closely with NIH when jurisdictional issues have been ironed out. Dr. Hollander of EPA said EPA has not yet published its "intention to regulate," thus, EPA has not yet received any formal inquiries in the genetic engineering area.

Dr. Gartland asked how a "pest" is defined under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) statutes. Dr. Hollander replied that FIFRA grants authority to EPA to regulate the sale, distribution, and use of pesticides and defines a pesticide as any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest. A pest is defined as any virus, bacteria, or other micro-organism (except viruses,

bacteria, or other microorganisms on or in living man or other living animals) which the EPA Administrator declares to be a pest under Section 25(c)(1) of the Act. In regulations promulgated pursuant to FIFRA, microorganisms (including bacteria) and viruses which exist under circumstances that make them deleterious to man or the environment are designated as pests. Dr. Hollander said the general counsel for the EPA Office of Pesticides and Toxic Substances (OPTS) believes that EPA can regulate the release of ice nucleation bacteria under these statutes.

Dr. Hollander said EPA will attempt to regulate the release of recombinant DNA containing organisms which are not designated as pesticides under Section 5 of the Toxic Substances Control Act (TSCA).

Dr. Clowes said he was unhappy with the attempt to regulate living organisms under TSCA. He felt it naive to believe that the whole is no more than the sum of the parts. He did not think TSCA could address the appropriate questions posed by use of living organisms. When the applicability of TSCA is debated in court, scientific arguments will be considered; and use of this statute to regulate deliberate environmental releases does not make scientific sense.

Dr. Gartland added that TSCA prescribes a notification process applied to commercial releases. Dr. Hollander noted, however, that EPA's counsel believes the TSCA statutes could be interpreted to regulate research.

Dr. Pimentel said enforcement of regulations for deliberate releases will be difficult. Dr. Tolin said USDA has considered the cost and the difficulty of enforcement versus the potential risk involved in the processes, and at the present time does not believe enforcement of regulations would benefit society. The cost of enforcement would be high, and genetic technologies have not yet shown hazard.

Dr. Miller said proposals involving recombinant DNA technology are only the tip of the iceberg; there are many other genetic techniques which will be employed to modify organisms. Dr. Pirone agreed. Dr. Gottesman said the potential hazard of several different types of genetic procedures might be evaluated; however, at the moment, the working group under the RAC charter can only evaluate recombinant DNA applications. She suggested that if USDA and EPA have developed testing procedures for environmental releases these procedures should be part of RAC review.

Dr. Gottesman said RAC should not "over require" when the types of procedures to be evaluated are specified. She thought a distinction should be made between trivial and major modifications in organisms; it may be that proposals involving trivial modifications need not be reviewed.

Dr. Pimentel felt that the working group could categorize "hazard." He suggested for example that experiments involving U.S. crop plants which are tropical in origin, annual, do not easily survive without man's intervention and are large enough to control present minimal hazard. He felt deliberate releases involving

modified weeds, however, should be carefully evaluated. He also thought releases involving modified microorganisms, insects, and protozoa should be carefully controlled. He pointed out that USDA has placed stringent control requirements on use of biorational control agents which include microorganisms, insects, and protozoa.

Dr. Pirone asked if any Federal agency oversees releases of plants generated by crosses between domestic and wild species of plants. Dr. Tolin said some USDA "weed" legislation would cover this type of experiment. She pointed out that trivial applications versus important applications of the statutes have to be considered in these cases.

Dr. Pimentel said he found the RAC specifications for a P1 greenhouse disturbing. He thought quarantine regulations should be imposed on procedures involving certain organisms and the P1 greenhouse requirements do not do this. He objected particularly to the lack of language specifying air flow control. Dr. Tolin said the P1 specification for laboratories do not require control of air flow and for consistency the language defining P1 conditions for greenhouses should not specify air flow control measures.

Dr. Pimentel felt air flow control measures were necessary to contain experiments involving certain organisms. Dr. Gottesman suggested experiments involving these organisms should be assigned to P2 greenhouse containment conditions rather than modifying the P1 greenhouse specifications to address this concern.

Dr. Pimentel said he was uncomfortable with the proposals to field test the genetically modified ice nucleation bacteria P. syringae and E. herbicola. He pointed out that some P. syringae strains are weak pathogens for plants and some E. herbicola strains are human pathogens. He thought caution should be exercised in evaluating proposals involving weak pathogens.

Dr. Tolin said field testing of these organisms is scheduled for a test site removed from areas where plants sensitive to P. syringae are cultivated. Dr. Tolin said Dr. Lindow had presented to RAC data on population densities, and the density of test organisms will be low. Dr. Lacy said Pseudomonas and Erwinia are very widespread in nature.

Dr. Clowes felt that setting uniform guidelines for reviewing release experiments as suggested by the second recommendation of the Gore Report could be detrimental. He thought each proposal must be reviewed by experts possessing the requisite expertise and this will vary with each proposal. Dr. Pirone agreed; he felt each proposal must be evaluated on a case-by-case basis.

Dr. Sharples asked how the framework of principles specified in the Guidelines was developed. Dr. Gottesman said the framework of principles was developed through RAC's experience and was based on the following considerations:

- (1) the inherent potential of the host organism for pathogenicity or to cause harm with changes in pathogens of greater concern than changes in nonpathogens; and

- (2) the potential of the genetically modified organism to transmit the recombinant DNA to pathogens.

Dr. Gottesman said she supported the concept that each proposal must be reviewed on a case-by-case basis. She thought arranging the administrative structure so that all proposals receive appropriate review will be the more difficult task. Dr. Fowle of the EPA noted that the Interagency Risk Management Council (IRMC) was to look at three areas (cancer risk assessment, biotechnology, formaldehyde) in which interagency cooperation is essential. The biotechnology initiative, however, has been put on hold. Dr. Tolin pointed out that the IRMC at any rate does not possess the requisite scientific expertise to review proposals in biotechnology.

Dr. Mazza of the EPA said currently there are no firm plans in government for evaluating the situation on an interagency basis; he thought the Working Group on Release into the Environment might suggest the need for such an evaluation. Dr. Fowle said EPA intends to involve RAC in EPA's procedures and will attempt to coordinate with the NIH.

Dr. Scandalios said RAC is a scientific committee; he did not think any other type of committee could adequately review proposals involving recombinant DNA containing organisms.

Dr. Scandalios felt creating another review committee would be redundant. He preferred to see RAC maintained as RAC is viable, adaptable, experienced, and has a good track record. He felt RAC should remain within the NIH. Dr. McGarrity pointed out that NIH does not have regulatory authority. Dr. Gottesman said RAC does, however, possesses the necessary scientific expertise. She suggested that structuring a committee such as RAC so that it advises several agencies might meet the perception that the review body should have regulatory authority. Dr. Gottesman suggested that the Federal agencies could use RAC as a resource in this transition period during which agencies are defining their procedures.

Dr. McGarrity asked how RAC review and approval might administratively be accepted by other agencies. Dr. Mazza said the EPA Administrator could refer to RAC for advice but would not be bound by RAC's recommendations. Dr. Gottesman pointed out that RAC is an advisory body; its recommendations are not binding on the NIH and would not be binding on other agencies.

Dr. Scandalios said there will not be a "perfect" committee, but a committee like RAC could review proposals and direct further review to the appropriate agency. The regulatory agencies could beef up their internal recombinant DNA committees.

Dr. McGarrity summarized three possible mechanisms to obtain review of proposals involving release of modified organisms to the environment: (1) the government could establish an Interagency Task Force for Environmental Release, (2) the government could create a "super-RAC," or (3) RAC would continue its oversight functions.

Dr. Clowes felt the Interagency Task Force suggested by the Gore Report would fill a function that RAC already fills. He did not think the proposed task force would function better than RAC. Dr. Gottesman said the Working Group on Release into the Environment should advise RAC to continue its oversight function. Dr. Clowes agreed. He suggested that EPA and USDA might be invited to nominate potential RAC members.

Dr. Miller opposed the creation of another review group co-equivalent to RAC and said he could not support the Gore Report suggestion to create an Interagency Task Force. He thought the Gore report to be flawed; he pointed to the statement in the Gore Report that the report would address "concerns about the potential environmental effects of genetically engineered organism created by other techniques...and other procedures...." He said the report does not define these procedures and the definition of genetic engineering offered by the report is "fuzzy;" the report and its implications were not well thought out by the authors. He said that if FDA were to interpret the Gore Report literally, FDA would stop licensing vaccines produced by any technique. FDA has no intention of ceasing to license vaccines.

Dr. Gottesman thought a review committee should not be "frozen" in its approach as was suggested by the Gore Report; RAC is flexible and should continue to work flexibly towards determining needs and structures.

Dr. Sharples supported the suggestion that RAC should continue its oversight function. She suggested however, that the Working Group on Release Into the Environment advise RAC that working groups with broader environmental expertise should "prereview" proposals involving release into the environment. These working groups could evaluate proposals and advise RAC, and RAC would weigh these arguments. Dr. Gottesman agreed; she said working group membership can be easily modified to meet changing needs and proposals.

Dr. Pimentel said he was dubious about the quality of an unconstituted, unknown review group such as the proposed Interagency Task Force. He felt RAC with added environmental expertise is the best review group currently available. Dr. Gartland added that RAC has access to and could use an unlimited number of ad hoc consultants.

Dr. Tolin said one advantage of RAC review is that most evaluation is accessible to the public; proposals are published for public comment 30 days prior to the RAC meeting and for the most part RAC meetings are open to the public.

Dr. McGarrity said one of RAC's strengths is that RAC's membership could be modified to meet changing needs. Dr. Gottesman thought RAC should have varying expertise so that it might evaluate proposals originating in very different areas of the technology. Dr. Miller agreed and said RAC currently intends to evaluate such disparate proposals as those involving genetic engineering in human subjects and release of modified organisms into the environment. He thought RAC should have at least one expert in these areas; RAC membership should be balanced. Dr. Scandalios warned against overloading RAC with any one type of expertise; he felt any expert should be able to marshal the arguments necessary to convince the RAC.

Dr. Gottesman said she wished to offer a motion concerning the seven recommendations made in the Gore Report. This motion would be forwarded to RAC as advice.

Dr. Gottesman suggested the working group offer no comment on the first recommendation of the Gore Report which is as follows:

- "(1) The EPA should proceed with its stated intention to extend its authority to include all deliberately released organisms not specifically identified as part of the legal obligation of another agency. In view of EPA's stated conclusion that the Toxic Substances Control Act (TSCA) does provide it with authority to oversee deliberate releases and the fact the Congress intended TSCA to be 'gap filling' legislation, no additional legislation or clarifying amendments are needed at this time. EPA should, however, establish formal communications and agreements with other agencies to ensure that gaps and redundancies in the regulatory structure do not occur. A major goal should be to permit research and commercialization to proceed with minimum interference while adequately addressing environmental and public health concerns."

Dr. Gottesman suggested the working group reject the second recommendation of the Gore Report. The working group would recommend that RAC continue its oversight function making use of expert working groups for prereview. The second recommendation reads as follows:

- "(2) Until such time as EPA's regulations are promulgated, an interagency task force should be established to review all proposals for deliberate releases. EPA should take the initiative in organizing this panel. The panel should be comprised of representatives from EPA, USDA, NIH, and any other appropriate federal agency or entity directly involved from either the scientific or regulatory perspective. The panel should establish an environmentally oriented risk/benefit assessment program to evaluate current proposals for deliberate releases and to provide a data base for decisions on future releases. The panel should also develop a uniform set of guidelines to govern deliberate releases. The panel should, moreover, serve the function of educating the public about the potential risks and benefits associated with this aspect of biotechnology. Consideration should be given to making this panel a permanent oversight body even after EPA has promulgated regulations to ensure that the broadest possible expertise is brought to bear in overseeing the technology."

Dr. Gottesman suggested that the working group reject the third recommendation of the Gore Report which reads as follows:

- "(3) No deliberate release should be permitted by EPA, NIH, USDA, or any other federal agency until the potential environmental effects of the particular release have been considered by the interagency review panel. The panel shall consider the effects of any environmental release, regardless of size or intent. Each agency should evaluate proposals for deliberate releases according to a uniform set of guidelines to be

developed by the interagency task force. It is recognized that initially decisions may be made on the basis of incomplete data."

Regarding the fourth recommendation, Dr. Gottesman suggested that RAC and its working group assume the responsibilities outlined in recommendation four. No report, however, would be issued in ninety days. Recommendation four reads as follows:

- "(4) The task force should consider the need for oversight of research scale releases and, if appropriate, develop guidelines for reviewing proposals for such releases. The task force should prepare a report containing its conclusions on this matter within 90 days of its establishment. The report should be made available to the Subcommittee."

Dr. Gottesman suggested the working group reject the fifth recommendation which is as follows:

- "(5) The NIH should cease its practice of evaluating and approving proposals for deliberate releases from commercial biotechnology companies. The NIH should review proposals only from parties engaged in NIH-sponsored research, and refer requests from industry to the appropriate agency."

Dr. Gottesman suggested the working group endorse the sixth recommendation as regards the NIH. The sixth recommendation is as follows:

- "(6) The NIH and USDA should revise the membership of their respective Recombinant DNA Advisory Committees (RAC) to include individuals specifically trained in ecology and the environmental sciences."

Dr. Gottesman suggested the working group offer no comment on the seventh recommendation which is as follows:

- "(7) The General Accounting Office should review the activities of USDA in overseeing biotechnology and evaluate the agency's authority to regulate deliberate releases under all relevant statutes, regulations, and executive orders."

Dr. Pirone thought recommendation two of the report should be transposed to be the first recommendation as it deals with the activities of an oversight committee. He noted that RAC already serves the function of educating the public and should continue to educate the public. Dr. Gottesman thought a preamble to her motion might address Dr. Pirone's concern.

Dr. Sharples asked if Dr. Gottesman's motion should define a period of time during which RAC would operate as the oversight committee. Dr. Arntzen felt the preamble should specify a time frame in which RAC would function as the oversight body. Drs. Clowes and Gottesman felt no period should be specified; other agencies will determine when they are ready to assume responsibilities. Dr. Clowes thought the legal, jurisdictional, and Congressional picture was too complex to plan for future events. He felt the motion should be purposely

vague regarding time frames. Dr. Arntzen feared RAC might be deluged with requests if no time frame is established. Dr. Gottesman pointed to RAC's experience in the biomedical area. She said early in RAC's history all proposals involving recombinant DNA in certain areas came to the NIH for review and approval. In time, however, RAC developed principles and procedures; responsibility for overseeing many types of procedures was then delegated to the Institutional Biosafety Committees. As more experience accumulated, responsibility was subsequently delegated to the Principal Investigator. Dr. Arntzen wondered whether the working group should mention this experience in its report to RAC.

Dr. Miller thought a preamble ought to recognize the limitation imposed by overseeing only recombinant DNA technology. He suggested the following language be incorporated into a preamble:

"In many instances, jurisdiction only over recombinant DNA technology represents an unnatural division of responsibility."

Dr. McGarrity said such language implies that RAC is requesting broader responsibility. He felt such a request would be inappropriate.

Dr. Mazza suggested the working group add as a footnote to the preamble a statement to the effect that "RAC has not discussed whether these other technologies warrant similar review."

The working group then discussed the definition of genetic engineering as it would apply to Dr. Gottesman's motion. Dr. Sharples felt the working group is cognizant of the definition of biotechnology used in the Gore Report, and this would be implied or stated in the preamble to Dr. Gottesman's motion. Dr. Miller said the Gore Report is internally inconsistent in its use of the definition of genetic engineering; he thought the working group motion should not refer to the definition used in the report. Dr. Pimentel thought the preamble should refer to the Gore Report but not use the report's definition of biotechnology. Dr. Pirone agreed. Dr. Lacy suggested that including the Gore Report definition of biotechnology in the motion might inadvertently support that definition. He did not feel the motion should support this definition.

Dr. Pimentel suggested a footnote defining recombinant DNA be added to the preamble of the motion. Dr. Gottesman said the definition implied in her motion is the definition of recombinant DNA stated in the NIH Guidelines; she would state this definition in the preamble.

Dr. Pimentel said the working group motion should question whether TSCA is the appropriate statute to regulate deliberate releases of organisms containing recombinant DNA molecules. He noted that TSCA does not cover research releases, and this failure to oversee research releases was a great concern to him.

Dr. Pimentel thought EPA should have responsibility for overseeing research activities involving deliberate release of living organisms as well as commercial releases. Dr. Tolin pointed out that research involving some of these organisms

might be covered by USDA regulatory authority and not by EPA authority. Dr. Arntzen suggested scientists might have to have a lawyer to deal with EPA should EPA regulate research releases. He expressed the opinion that the NIH and USDA should be responsible for oversight and evaluation of research protocols as these institutions have greater expertise in research; EPA should have oversight responsibilities for commercial production and applications.

Dr. Clowes said the motion might express Dr. Pimentel's concern, however, he thought the working group could not offer a legal position. Dr. Pimentel said he would accept a preamble indicating that some government agency should oversee research activities. Dr. Gottesman agreed to add language to the preamble expressing this concern.

Dr. Clowes then turned the discussion to consideration of that portion of the second recommendation of the Gore Report which suggests that uniform guidelines be developed. He thought review would best be served by a case-by-case approach. He thought the applications of the technology would be too varied to permit a standard generalized set of guidelines to be constructed. Dr. Miller agreed.

Dr. Lacy suggested that a broad set of flexible principles might be developed. Dr. Sharples suggested these flexible principles might be called "principles of approach." Dr. Pimentel thought there could be no rigid guidelines; review must evaluate each organism and how the organism is to be used. Dr. Pirone supported the concept of a flexible review process.

Dr. Mazza asked if Dr. Gottesman would add language to the preamble concerning the use of working groups to prereview proposals. Dr. Pirone agreed with Dr. Mazza's suggestion. Dr. McGarrity supported this suggestion as working groups can be more flexible in their composition. He asked if representatives from interested federal agencies would be invited to participate and to vote in working groups. Dr. Gottesman agreed to add such language.

Dr. Miller questioned whether the motion might list procedures such as breeding race horses or developing roses which would not be considered "other procedures" as defined in the Gore Report. Dr. Sharples felt such a listing would confuse the situation.

Several other points of language in the motion were also discussed. Dr. Gottesman's final motion read as follows:

"Introduction

I move that we recommend to RAC the following responses to the seven recommendations of the Gore Report:

"The responses are based on the assumption that at least for the immediate future, RAC should continue to review and, if appropriate, approve proposals for release to the environment of genetically engineered organisms. That review would include consideration of the specific proposal by a working group of the RAC with appropriate expertise.

"Recombinant DNA represents only one technique for 'genetically engineering' organisms. This group has not addressed the question of whether other techniques warrant similar review. In responding to the Gore Report, our deliberations have centered on organisms which are created by alteration of DNA by recombinant DNA techniques as defined by the NIH Guidelines.

"Whatever the mechanism for review of "deliberate release" of genetically engineered organisms, we believe that both research and commercial releases should be subject to prereview.

"Responses

"(1) No comment.

"(2) We endorse the concept of a single task force with the responsibility and expertise to consider release of genetically engineered organisms, but for recombinant DNA-containing organisms, we believe the RAC currently best serves this function.

While there is a need for a set of general principles which should be considered for all deliberate releases, we are skeptical of the feasibility of developing a uniform set of testing requirements for all organisms and all environmental situations. We believe an appropriately constituted review group to consider specific cases will be both flexible and responsive to the particular problems posed by particular releases.

"(3) See above.

"(4) The Plant Working Group and this working group have contributed to an evolving set of procedures for evaluating experiments with plants and associated microorganisms. This process should continue and be applied to 'deliberate release' of other genetically engineered organisms as well.

"(5) We reject this proposal.

"(6) NIH is already responding to this suggestion in three ways: (1) changes in RAC membership; (2) use of ad hoc consultants to the full RAC; and (3) use of environmental experts on working groups of the RAC.

"(7) No comment."

By a vote of 10 in favor, none opposed, and one abstention the working group accepted Dr. Gottesman's motion.

QUESTIONS CONCERNING NIH'S APPROPRIATE OVERSIGHT BOUNDARIES

Dr. McGarrity said Dr. Bernard Talbot, Deputy Director of the National Institute of Allergy and Infectious Diseases, had requested that a series of questions be issued for public comment and placed on the agenda for the February 6, 1984, RAC meeting. Dr. Talbot wrote:

"The NIH Guidelines for Research Involving Recombinant DNA Molecules were originally written to deal with NIH grantees doing biomedical research in the laboratory. They were subsequently adopted by other Federal agencies. Most of the meetings of the NIH Recombinant DNA Advisory Committee (RAC) have been entirely open to the public. At the last RAC meeting, a portion of the meeting was closed (not open) to deal with a request to field test (not confine in the laboratory) an agricultural (not biomedical) submission from an industrial company (not an NIH grantee). Questions have been raised as to whether NIH should not redefine more circumscribed boundaries for NIH and RAC oversight, and possibly encourage other Federal agencies to provide oversight and/or regulation beyond these boundaries.

"I request that the following questions be issued for public comment, and placed on the agenda of the next RAC meeting. NIH would benefit from the views of the public and of the RAC before formulating an agency position on NIH's proper future role and steps to be taken before promulgating any changes from the current role.

- "1. Should the NIH Guidelines be limited strictly to work done in the laboratory? In this case, release to the environment including field tests would fall outside the jurisdiction of the Guidelines.
- "2. Should NIH accept for review only individual proposals funded by NIH or only proposals funded by the Federal government? In this case, review of individual proposals from industry would fall outside the Guidelines.
- "3. Should all portions of all RAC meetings be open to the public? In this case, NIH could cease to accept any proprietary data for review and such would fall outside the boundaries of the Guidelines.
- "4. Should the NIH Guidelines be limited strictly to biomedical research? In this case, agricultural and other studies would fall outside the jurisdiction of the Guidelines.

"Each of these proposals would create a new 'boundary' for the NIH Guidelines. It should be noted that an unusual 'boundary' already exists, since two pieces of DNA spliced together outside living cells constitute 'recombinant DNA' and fall under the Guidelines, but if the same two pieces of DNA were spliced together within a living cell they would not be considered recombinant DNA and, therefore, would not currently fall under the Guidelines."

Dr. Gottesman felt that RAC and the NIH should continue their current activities. Dr. Arntzen suggested that NIH might take a broader view of what constitutes a "laboratory." He said ecologists frequently refer to a forest plot as a laboratory. Other members of the working group did not feel this was a feasible approach for all proposals.

Dr. McGarrity asked if the working group felt RAC should restrict its review to NIH funded proposals. Dr. Gottesman felt RAC should review proposals from all sources. Dr. Arntzen pointed out that certain funding institutions are neither

federal agencies nor industrial concerns. He feared proposals funded by such entities would not be reviewed if RAC restricted review to NIH grantees' proposals. Dr. Miller pointed out that NIH is now granting funds to for-profit institutions. This process blurs the distinction between "industrial" and "university" proposals. Dr. Miller thought the most important argument in favor of NIH continuing to review all proposals is that NIH and RAC perform a useful, valuable function in overseeing recombinant DNA technology and should continue to do so.

Dr. McGarrity asked the working group whether all portions of RAC meetings should be open to the public. Dr. Clowes felt meetings should be as open to the public as possible. He supported the concept that companies should minimize the amount of proprietary material submitted for review. He felt RAC should, however, hold closed sessions as necessary. Dr. Gartland said NIH would have to respect a company's request for confidentiality if the company says public knowledge of what they are doing would be prejudicial to them. He pointed out that NIH can only protect proprietary information under a broad general statute; it has no special statutes to protect proprietary information such as those assigned to EPA under TSCA.

Dr. Miller argued that public divulgence of information would have serious repercussions on patent issues for the research company. He said the government has many precedents for maintaining the confidentiality of proprietary information. He pointed out that FDA reviews are not open to the public, and EPA will protect all proprietary information except for cleansed data. RAC, thus, would simply be following accepted procedures.

Dr. Gottesman said the procedures and thought processes employed by RAC in developing procedures to evaluate proprietary proposals would be public knowledge, and the scientific arguments will be the same in public and in private sessions. Thus, specific proprietary proposals might be reviewed confidentially as RAC has lay members to represent public interests, publicly-known criteria, and procedures for evaluating proposals. Dr. Gottesman felt it was reasonable, nonetheless, to urge companies to minimize the amount of information they wish treated confidentially.

Dr. Arntzen agreed with Dr. Gottesman that procedures and guidelines by which proposals are evaluated should be public knowledge but proprietary proposals can be reviewed in private.

#### GUIDELINES FOR PROPOSAL SUBMISSIONS UNDER APPENDIX L

Dr. Gottesman said the Plant Working Group was attempting to develop guidelines (Attachment II) for evaluating proposals under Appendix L, Release into the Environment of Certain Plants, of the Guidelines. The list developed by the Plant Working Group had been discussed by RAC at its February 6, 1984, meeting. At that meeting, comments and suggestions (Attachment III) had been made concerning the contents of the list. Dr. Anne Vidaver of the University of Nebraska, a member of the Plant Working Group, has since addressed these comments and suggestions (Attachment IV). Dr. Gottesman said that as the list was a working document which would continue to evolve these materials had been forwarded to the Working Group on Release Into the Environment for comment.

Dr. Gartland asked the working group to put this material into a form which would be published for comment in the Federal Register.

Several members of the Working Group on Release Into the Environment felt the specifications on the list were confusing as they referred to both plants and associated organisms. Dr. Toblin suggested the working group construct several separate lists; one list would deal with plants under Appendix L, a second with associated microorganisms, and a third with weeds. Dr. Pirone suggested the first list should deal only with cultivars.

Dr. Pirone suggested that item 6 of the Plant Working Group List be modified. Item 6 reads as follows:

"(6) Give criteria and methods by which the host microorganism will be monitored. If live host microorganisms are required to be present in field trials, indicate the means of strain identification and retrieval. If microorganisms are used to introduce vectors, the assessment of subsequent absence of the microorganisms should be specified."

Dr. Pirone thought that experiments in which a microorganism will be present in field tests would not fall under Appendix L which deals with plants. He thought such questions should be dealt with on another list. He suggested that the last sentence of item 6 be retained, but that the first two sentences be deleted.

Dr. Gottesman suggested the title of the list be changed to "Items for Consideration to be Included in Proposal Submissions Under Appendix L." The items to consider could be categorized under three major headings: (1) description of plant materials; (2) vectors and method of introduction; and (3) characteristics and monitoring of plant.

Dr. Pimentel suggested that morphological data on plants observed for at least two generations in the greenhouse should be requested under the category description of plant materials.

Dr. Sharples called the attention of the group to item 9 of the list which reads as follows:

"(9) If the vector is likely to survive independently of the hosts, refer to this possibility; if the answer is in the realm of reasonably high probability, provide data to assess such transfer to likely microorganisms."

She thought the phrase "realm of reasonable high probability" was vague and not well defined. She thought the sentence would better read:

"If the vector is likely to survive independently of the host, refer to this possibility and assess the probability of transfer to likely microorganisms."

Dr. Miller suggested the term "provide any available data" be added to this language.

Dr. Arntzen said DNA transfer will occur with many of the vectors used to transform plants. He offered the example of Cauliflower Mosaic Virus (CMV) engineered to express antibiotic resistance. When the plant is infected with the CMV vector, resistance to the antibiotic becomes systemic. The vector probably is present when the plant dies and decays. Dr. Arntzen did not feel this process would present hazard and felt the public should be educated as to the safety of these procedures.

The working group agreed on the following language:

"Items for Consideration to be Included in Proposal Submissions Under Appendix L.

"These annotated items were presented for consideration by prospective proposal submitters to facilitate the process of approval. The working group has found that the proposals so far submitted for their consideration have omitted information that is considered minimal and essential for their approval. Basically, the group would like to see detailed objectives, materials, and methods, including methodology for monitoring the experiments, and expected results. At a minimum, summary data should be submitted to support the proposal. A check list of detailed requirements should include but is not limited to:

"A. Description of Plant Materials.

- "1. Give common and scientific names of plants and cultivars, if appropriate. 'Tomato plants will be inoculated' is insufficient.
- "2. If appropriate, give data or information on the relative homogeneity of the plant cultivar, and specific genetic markers the cultivar is known to possess.

"B. Vectors and Method of Introduction.

- "1. Describe the cloned DNA segment and its expression in the new host.
- "2. Give the method(s) by which proposed DNA vector will be or has been constructed. Diagrams are very helpful and may be necessary for adequate understanding of the construct. Explain the advantages (and disadvantage(s), if appropriate) of your vectors, if other candidate vectors could be considered.
- "3. If microorganisms are used to introduce vectors or are vectors themselves, indicate how they compare with wild-type strains. If disabled pathogens are used to transmit the vector, indicate measures that will most likely prevent these microorganisms from regaining or acquiring pathogenic potential. If the vector is likely to survive independently of the hosts, refer to this possibility and provide any available data to assess the probability of such transfer to likely organisms.

- "4. If microorganisms are used to introduce vectors, the assessment of subsequent absence of the microorganisms should be specified. Indicate the means of strain identification and retrieval.

"C. Characteristics and Monitoring of Plants.

- "1. Provide data from greenhouse and/or growth chamber studies under simulated field conditions to support prospective field studies. Data should include morphological data for at least two generations of plants.

"Specify plant monitoring procedures; frequency; types of data to be obtained including leaf, seed, fruit, or root characteristics.

- "2. Provide data for field plot design on the following:

"a. total area;

"b. location: where, how many;

"c. plot design: replication, row spacing, planting, border rows, etc.;

"d. name cultivar(s), if appropriate;

"e. specify plant monitoring procedures: frequency; types of data to be obtained including leaf, seed, fruit, or root characteristics; abnormalities, such as diseases; insect population monitoring; collection of meteorological data, etc; types of data to be sought, such as yield, resistance to stress, lodging, etc.;

"f. specify monitoring of the vector and/or introduced DNA; and

"g. specify access and security measures."

Dr. Segal of the EPA said the working group should stress that similar lists should be developed for microorganisms and weeds.

RISK ASSESSMENT WORKSHOP

Dr. Tolin said the NIH and the USDA were intending to hold a risk assessment workshop in the fall of 1984 to address questions on deliberate release of organisms containing recombinant DNA molecules. Dr. Tolin hoped this workshop would deal with state of the art research. She asked the working group to identify individuals to serve on a steering committee.

Dr. Lacy suggested one aspect of a risk assessment workshop might involve Ti plasmids. Dr. Fowle said EPA was particularly interested in questions such as monitoring, approaches for developing probes, etc.

Dr. Tolin asked the working group to think about possible topics and approaches for the workshop and to contact either herself or Dr. Gartland.

Dr. McGarrity adjourned the meeting at 4:50 p.m., April 9, 1984.

Respectively submitted,

*Elizabeth A. Milewski*

Elizabeth A. Milewski, Ph.D.

Rapporteur

*William J. Gartland, Jr.*

William J. Gartland, Jr., Ph.D.

Executive Secretary

I hereby certify that, to the best of my knowledge, the foregoing Minutes and Attachments are accurate and complete.

\_\_\_\_\_  
Date

\_\_\_\_\_  
Gerard J. McGarrity, Ph.D.  
Chair