

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

RECOMBINANT DNA ADVISORY COMMITTEE
WORKING GROUP FOR DEVELOPMENT OF RESPONSE TO
PRESIDENT'S COMMISSION'S REPORT ON ETHICAL AND SOCIAL ISSUES

MINUTES OF MEETING¹

JUNE 24, 1983

The Working Group for Development of Response to President's Commission's Report on Ethical and Social Issues was convened at 9:00 a.m. on June 24, 1983, in Building 31, Room 7A24, at the National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20205. The meeting was open to the public. Mr. Robert Mitchell was Chairman. The following were present for all or part of the meeting:

Working Group Members:

Susan Gottesman	Elena Nightingale
Jean Harris	Mark Saginor
John Harvin	LeRoy Walters
David Martin	William Gartland
Robert Mitchell	(Executive Secretary)

A Working Group roster is attached (Attachment I).

Government Liaison Representatives:

Herman Lewis, National Science Foundation
Charles McCarthy, National Institutes of Health
Henry Miller, Food and Drug Administration

Other National Institutes of Health Staff:

Stanley Barban, NIAID
John Fletcher, Clinical Center
Elizabeth Milewski, NIAID
Janet Sobell, OD

Other:

Carter Leonard Blakely, Blue Sheet

¹The Working Group is advisory to the RAC, and its recommendations should not be considered as final and accepted.

The Chairman, Mr. Mitchell, called the meeting of the Working Group for Development of Response to President's Commission's Report on Ethical and Social Issues to order at 9:00 a.m., June 24, 1983. He said that at its April 11 meeting the Recombinant DNA Advisory Committee (RAC) endorsed a proposal to form a working group to comment and report to RAC on the "Report on the Social and Ethical Issues of Genetic Engineering with Human Beings" issued by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. He said the Working Group for Development of Response was instituted in response to the RAC directive.

Mr. Mitchell called on Ms. Janet Sobell of the Division of Legislative Analysis at the National Institutes of Health (NIH) to review the situation regarding legislation and genetic engineering. Ms. Sobell said a bill (H.R. 2788) introduced by Representative Albert Gore (D-Tenn) to create a commission for oversight of human genetic engineering (Attachment II) had been amended to the NIH reauthorization bill (H.R. 2350) which has been cleared by committee and is awaiting action on the floor. All indications suggest that the bill will most likely be passed by the House. In the Senate, the NIH reauthorization bill (S. 77) is pending floor action. S. 77 does not contain a provision to create an oversight commission. Should H.R. 2350 and S. 77 pass as written, a conference committee will meet to develop compromise legislation. At this time, the probability that Mr. Gore's proposed commission will be accepted in compromise legislation is good.

[Ms. Sobell noted that Representative Gore had held hearings on June 22, 1983, concerning dissemination of genetically engineered organisms in the environment. The hearing produced testimony that currently there are no methods for estimating the risks of disseminating novel organisms. The Congressional panel appeared to feel more risk assessment was needed.]

Dr. Nightingale reported that she had participated in the June 2 Institute of Medicine (National Academy of Sciences) workshop on the desirability of creating an ethics commission. She said participants in this workshop appeared to support the establishment of a commission for oversight of ethical issues in medicine.

Dr. Gartland noted that the Department of Health and Human Services (HHS) had at one time an Ethics Advisory Board. He asked Dr. Charles McCarthy of the NIH Office for Protection from Research Risks (OPRR) for information on the status of that board. Dr. McCarthy said that HHS regulations specify an Ethics Advisory Board. Such a board was instituted by former Secretary Califano, but terminated in September 1980. Although technically required, that board has not been reactivated.

Dr. McCarthy said that in general presidential commissions have been constructive as they have had "action forcing" clauses; the departments are forced to act or to explain why no action has been taken. He said the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research offered recommendations rather than directives.

Mr. Mitchell suggested that few Congressmen had in-depth experience in the biomedical sciences; he asked if Congressmen educate themselves in the issues. Ms. Sobell replied that the Congressmen depend on their staff people; some Congressmen have only a superficial understanding of the issues, while others have good staff work and are well informed. Dr. Nightingale said the RAC should fill an educational function.

Dr. Saginor expressed concern about the influence of lobbying groups. Dr. Harris said she shared Dr. Saginor's concerns; she felt political constituencies shape legislation. She felt the Working Group must express support for oversight functions, but not for regulation.

Dr. Walters noted that the Splicing Life report proposes three possible approaches: (1) RAC's mandate could be modified to include considerations of ethical and social issues in biomedicine; (2) a genetic engineering commission could be established, or (3) the President's Commission could be reactivated with multiple oversight functions including oversight of human genetic engineering.

Mr. Mitchell asked Dr. Gartland whether RAC's charter would have to be amended, if RAC were to assume additional oversight responsibilities. Dr. Gartland replied that RAC is chartered to oversee laboratory research and to evaluate risk. RAC has rarely exceeded these responsibilities. On one occasion, RAC considered issues associated with biological warfare, but it had an entree to do so through a proposal to amend the NIH Guidelines to prohibit explicitly biological warfare. Dr. McCarthy said that at the moment HHS has not taken a position on the issues before the Working Group.

Dr. Nightingale suggested that RAC has implicitly considered ethical issues. She said participants at the Asilomar Conference had discussed the ethics of recombinant DNA research. Recognizing that their expertise was in technical areas, however, they decided to focus on biosafety issues. Nevertheless, she said the original "prohibitions" were based on ethical considerations. She added that RAC had received reports on the Martin Cline case involving the administration of recombinant DNA to humans. In light of these considerations, she questioned whether the charter would have to be amended. Dr. Gottesman noted that RAC has a certain flexibility within its charter.

Dr. Martin expressed his opinion that proposals dealing with human genetic engineering will come to RAC, and that RAC will not be able to avoid these issues. Dr. Martin argued that human genetic engineering would be covered by Section III-A-2 of the Guidelines which specifies that proposals involving "deliberate release into the environment of any organism containing recombinant DNA" require RAC review and NIH and IBC approval before initiation. Dr. Gottesman suggested that experiments involving human subjects are covered by Section III-B-4-b which states:

"For all experiments involving whole animals and plants and not covered by III-B-4-a, the appropriate containment will be determined by the IBC."

Dr. McCarthy noted that in the Cline case, the proposal describing the experiment was sent to the Institutional Review Board (IRB), and to the Institutional Biosafety Committee (IBC). At that time, Dr. Fredrickson, former NIH Director, ruled the proposal had to be reviewed first by the IRB for the protection of the particular human subjects involved prior to RAC review. This issue was never resolved as Dr. Cline left the country to perform his experiments.

Dr. Martin said his laboratory would soon submit a proposal involving somatic gene therapy with a human patient. He predicted the following course of events: the IRB will review the proposal, then the IBC will review it, and the IBC will subsequently solicit RAC's approval under Section III-A-2 of the Guidelines because of the release of recombinant DNA in the environment.

Dr. Martin said he feared public response if RAC does not evaluate ethical issues in the use of recombinant DNA technology. He suggested that RAC might evaluate such proposals in the context of the President's Commission report. He suggested RAC's composition might need to be altered to reflect this responsibility and to increase its credibility for review of ethical aspects.

Dr. Walters thought it might be premature to develop another review body to deal with general medical issues, such as reproductive decisions or mood alteration technology. Questions involving genetic engineering, which are the most immediate, can be handled by the system already in place. The system is composed of two national bodies, the RAC and OPRR, and two networks of local bodies, the IBCs and the IRBs. The IRBs and OPPR are responsible for the well being of the human subjects; RAC could be responsible for the social and ethical issues. He thought this system adequate to raise issues and bring questions to public attention. He felt, however, that it is important to evaluate the RAC's composition, and perhaps appoint a few individuals with a background in dealing with public policy issues.

Mr. Mitchell asked Dr. Martin if he had a preference concerning the type of group which would review his proposal to use gene therapy on a human patient. Dr. Martin replied that he would prefer RAC review the proposal. RAC has an excellent record and the scientific grounding to understand the proposal. He felt, however, that RAC must have public credibility as well as credibility in the scientific community. He suggested that appointment of an ethicist would increase RAC's credibility with the public.

Dr. Harvin said any review committee must have the public's confidence. A review committee must demonstrate that it can make good decisions for the people. RAC has thus far maintained the public's confidence. He expressed his opinion that RAC is the best committee for review of ethical questions. He questioned the "big government" solution of forming a new committee for every issue. He felt the smaller the group, the better the decisions.

Mr. Mitchell said the President's Commission report implicitly trusts RAC's decisions in the scientific and technical areas, but does not appear to trust RAC in the "moral" areas. Dr. Harris said this is because RAC has restricted its scope of responsibility; RAC has generally declined to consider explicitly

ethical and social issues in its deliberations. She felt that social goals and oversight can be achieved within the existing structure (RAC, IBCs, and IRBs). She said she personally was biased against separating ethical considerations from scientific considerations; issues must be evaluated within a context, and the context in genetic engineering discussions is a scientific one.

Dr. Miller of the FDA questioned whether a "blurring" between oversight and regulation was occurring in RAC. He pointed out that regulation was FDA's domain. Dr. Harris replied that aspects of a proposal such as Dr. Martin's might appropriately be evaluated by FDA, but she felt the public might have fears which would be more appropriately dealt with by a committee such as RAC.

Dr. Gottesman said the difficult ethical issues are just beginning to arise. She asked Dr. Walters if the system in place is adequate to handle really difficult issues. Dr. Walters replied that a case-by-case review approach would of necessity be followed. He did not perceive a need for an additional oversight body at this time. He felt, however, that more research in the ethical and social questions was needed. Dr. Gottesman agreed that, in a practical sense, a case-by-case evaluation system would arise and that this was appropriate. She questioned whether everyone would accept the report "Splicing Life" as a standard. She suggested RAC might consider the adequacy of the report. Is this report consistent with the general view? Is it adequate to cover most questions?

Dr. Nightingale presented her view that two committees are necessary. She agreed that RAC might oversee human genetic engineering but pointed out that other topical issues, such as use of reproductive technologies, mood control technology etc., are not part of RAC's mandate. RAC, on the other hand, is and has been dealing with issues far afield from human applications, e.g., engineering of plants. Dr. Nightingale expressed her belief that RAC and a second commission could interact in the area of overlapping responsibility.

Dr. John Fletcher of the NIH Clinical Center felt RAC cannot reassure the public on all the issues associated with applications of novel biomedical technologies. He agreed that RAC has tremendous credibility in the scientific community and felt RAC should continue to review specific proposals with scientific applications. He felt, however, that RAC was not an appropriate body for overseeing the social implications of applied genetics. He thought RAC, as an advisory group of the largest funder of biomedical research, would be vulnerable to charges of favoring the scientific community or of wanting to move quickly. He said a presidential commission would report to the President and Congress and would not be vulnerable to these charges.

Dr. Harvin disagreed. He thought the scientists performing the work should have some responsibility in overseeing it. He did not think total responsibility should be assigned to individuals who do not deal with the science. He said RAC need not be located in the NIH. Dr. Miller felt RAC gained from its association with the NIH.

Mr. Mitchell said that if RAC is criticized, it is criticized for what it has not done (i.e., review proposals in an explicitly ethical context). What RAC has done, it has done well. He agreed that the scientists who perform the research must have confidence in the oversight group. If they do not, the public in time will learn of this, and public confidence in the oversight group will be eroded.

Dr. Gottesman noted that RAC will be faced in the near future with a proposal involving human gene therapy and must react to that. She pointed out that RAC's expertise and experience are not relevant to other issues such as overseeing use of reproductive technologies. RAC's experience is, however, relevant to consideration of human genetic engineering. If RAC is going to expand its purview to evaluate ethical considerations, she suggested several questions should be considered. These include: (1) What is the definition of "recombinant DNA?" She pointed out that had Dr. Cline cut the gene out of the vector, his proposal would not have been covered by the NIH Guidelines as currently written. Such a distinction may be specious, however. RAC could ask to evaluate all proposals involving human genetic engineering in which recombinant DNA technology is being applied. (2) Dr. Gottesman said that with four or five groups currently overseeing some aspect of human genetic engineering (RAC, IRBs, IBCs, OPPr, and ORDA) some confusion will occur. Some ordering of review procedures might be considered. (3) Finally, Dr. Gottesman suggested RAC must be explicit in stating its responsibilities, what it will consider, and how its decisions are reached.

Dr. Gartland said some proposals may involve proprietary information. Will RAC maintain its credibility if, on occasion, it functions in closed session? Dr. Martin thought it would, if its composition is credible. Mr. Mitchell thought RAC could publish the reasons for the decisions it might make in closed session, without disclosing proprietary information. Dr. Martin added that he cannot imagine a company wanting to develop gene therapy; there is no market for specific gene therapies at the present time.

Dr. Harris said the establishment of a body to evaluate biomedical issues is not precluded by RAC evaluating social and ethical issues involved in human genetic engineering. She wondered whether RAC should address questions involving the organization of an oversight commission.

Dr. Nightingale suggested that a new oversight commission might be an "expert group" which could have technical panels. RAC might serve as a technical panel for the expert group. In that capacity, RAC could review issues on a case-by-case basis. The IRBs could also be "a technical panel" to the expert body. As certain IRB and IBC oversight issues overlap, a broad linkage to an "expert body" could clarify oversight responsibilities. Dr. Nightingale also suggested that when RAC renders a decision on a case-by-case basis, RAC could indicate what technical and safety issues it had evaluated; the questions which remain might then be evaluated by the "expert body" or by its other technical panels.

Dr. Martin suggested that in reviewing social and ethical issues, the report "Splicing Life" might provide guidance; RAC could determine whether a proposal is consistent with the principles offered in "Splicing Life." Dr. Nightingale pointed out that "Splicing Life" is a one-time report and the situation is not going to be static. Mr. Mitchell added that gray areas exist in the report "Splicing Life."

Dr. Walters felt that protecting human subjects is part of the work of the RAC and is part, implicitly, of RAC's deliberations. Dr. Martin agreed but pointed out that real concern will arise when RAC gives permission to proceed. To date, RAC has not evaluated such cases and thus has no track record. Mr. Mitchell asked if any other group has a track record. Dr. Martin replied that no group has yet faced these questions.

Dr. Gottesman agreed that RAC has been making implicit value judgements but said the group would be recommending that RAC now make explicit value judgements. She felt RAC would have to acknowledge that it will explicitly confront and consider social and ethical issues.

Dr. Gottesman then offered a draft proposal, which was polished by the working group to read as follows:

"The Working Group agrees that there is a need for ongoing consideration of the ethical and social implications of the application of genetic technology to humans. Within this context, RAC should be prepared to consider social and ethical issues related to the applications of recombinant DNA technologies. For specific cases which come before the committee, RAC should consider explicitly issues such as those raised in the "Splicing Life" report of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. We, therefore, recommend that:

- "(1) The membership of the RAC be modified to include adequate representation to deal credibly with these issues.
- "(2) Procedures should be developed for the coordinate consideration of experiments involving the use of recombinant DNA technology in humans by Institutional Review Boards, the Office for Protection from Research Risks, the Food and Drug Administration, Institutional Biosafety Committees, the Office of Recombinant DNA Activities, and the Recombinant DNA Advisory Committee.
- "(3) The NIH Guidelines for Research Involving Recombinant DNA Molecules should be reviewed for their adequacy and clarity in dealing with human experimentation.

"We recognize that the issues which will be dealt with by RAC represent only some of the social and ethical issues associated with the applications of genetic and biomedical technologies. In addition, we believe that the general oversight function needed for these broader issues is not easily combined with the RAC's role in setting Guidelines and reviewing specific experiments. The expertise and experience of the RAC will be available to bodies which may exercise oversight of the broader issues. We expect continuing national discussion to lend new insight in dealing with the specific cases to be considered by RAC."

Dr. Walters asked how RAC's scope of oversight should be defined. Is the current scope adequate? Dr. Martin felt those therapies which use recombinant DNA molecules should be within RAC's purview. He and Dr. Gottesman agreed that RAC should discuss the logic of evaluating all human engineering proposals using recombinant DNA technology: i.e., the guidelines probably should regard DNA molecules which have been treated with restriction nucleases to separate the gene from the vector as recombinant DNA molecules. Dr. Walters said his personal preference would be that RAC review all proposals in which recombinant DNA technology has been used at some point, including the situation where molecules introduced into a patient have been treated with nucleases.

Dr. Martin asked if RAC should review use in humans of proteins produced by recombinant DNA technology. Dr. Walters felt only the cases involving gene insertion should be considered. Dr. Gottesman agreed; the self-perpetuating nature of the gene distinguishes it from protein. Dr. Martin asked if somatic therapy will be distinguished from germ line therapy. He argued that somatic gene therapy will be self limiting, while germ line therapy will not be. For the patient, somatic therapy appears to be equivalent to germ line therapy in the benefit to be gained. Germ line therapy may provide no advantage and may involve unsolvable ethical questions. Dr. Saginor felt RAC will have to evaluate both somatic and germ line therapy.

Dr. Walters asked if embryo modification would be covered under RAC's mandate. Dr. Martin said it would be if recombinant DNA were used. He argued, however, that somatic therapy would be preferable. He felt somatic gene therapy does not present ethical questions different from those associated with bone marrow transplants. On the other hand, in germ cell therapy, who decides which characteristics will be changed? How does one distinguish between disease and eugenics?

Dr. Nightingale said she would like to call for a straw vote to determine whether the working group supports the concept of an oversight body to deal with applications of new genetic and biomedical technology. Dr. Martin seconded the motion.

Dr. Harvin said he could not support the motion. He said the motion does not specify the oversight purview of the new body; he feared such a committee would control too many groups (including RAC). Dr. Walters said he saw no need

for an oversight body; Representative Gore's hearing on June 22 provides a model for the type of oversight Congress can exert. Other committees already in place such as RAC and IRBs provide oversight.

Dr. Miller said he was not convinced of the value of an oversight group but suggested political realities require that some body be in place to provide oversight. Dr. Harvin replied that just because something is inevitable does not mean one should support it.

Dr. McCarthy felt that currently there are not enough issues to occupy such an oversight body. However, as issues arise, some oversight body should be in place to evaluate them. The HHS Ethics Committee might fill this function.

To permit a vote on the Gottesman language, Dr. Nightingale withdrew her motion, and Dr. Martin withdrew his second.

Dr. Saginor called for a vote on Dr. Gottesman's proposed language. By a vote of seven in favor and none opposed, the motion carried. It was the unanimous recommendation of the Working Group that the proposal be published in the Federal Register for comment.

Dr. Nightingale then moved the following:

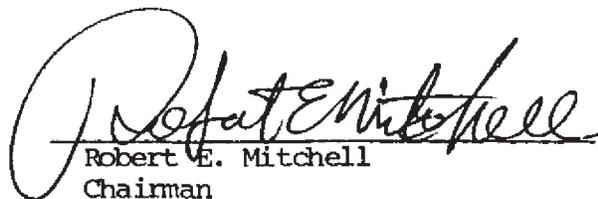
"The working group recommends to RAC that RAC support the creation of a national committee to review and discuss the human applications of genetic and other biomedical technologies."

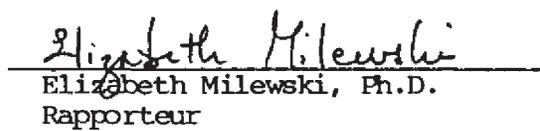
Dr. Gottesman seconded the motion.

Dr. Walters pointed out that the language of Dr. Nightingale's motion was broader than the language specifying the commission proposed by Representative Gore. By a vote of four in favor and three opposed, the working group recommended Dr. Nightingale's motion. Mr. Mitchell, however, cast his vote to make a tie.

Dr. Harvin moved the meeting be adjourned. Mr. Mitchell adjourned the meeting at 3:20 p.m., June 24, 1983.

Respectively submitted,


Robert E. Mitchell
Chairman


Elizabeth Milewski, Ph.D.
Rapporteur


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

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JUNE 24, 1983

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