public, academic, and corporate sources.

The RAC approved a motion made by Dr. Miller and seconded by Dr. Zallen to accept the following: (1) the FDA proposal submitted by Dr. Noguchi; (2) adopt the Categories for Accelerated Review that were approved by the RAC at its March 3–4, 1994, meeting, as guidelines for proposals that will not require RAC review; (3) establish a working group to examine the review process for human gene transfer protocols (in response to Dr. Varmus' request to establish such a group); (3) the RAC prefers that any stipulation requirements should be satisfactorily met prior to forwarding its recommendation for approval to the NIH Director; and (4) accept the proposed amendments to the NIH Guidelines to reflect this revised consolidated review process (including acceptance of a revised Appendix M and incorporation of minor editorial changes).

The motion was approved by a vote of 15 in favor, 0 opposed, and 1 abstention.

On October 26, 1994, NIH/ORDA forwarded these actions to the NIH Guidelines (incorporating the modifications accepted by the RAC), to the NIH Director for approval and the FDA Commissioner for concurrence. FDA legal counsel expressed concern that implementation of the proposed actions would require amendments to the FDA Investigational New Drug Application Regulations (21 CFR Part 312) to accommodate the release of proprietary information. To resolve this concern, a waiver for the release of information from the FDA to the NIH was proposed. While the NIH Guidelines could require such a waiver for NIH-funded investigators, it would be voluntary for others submitting proposed human gene transfer experiments to the FDA.

The NIH expressed concern that failure to comply with the voluntary waiver procedures may result in the loss of critical information necessary to maintain: (1) The human gene therapy database, (2) ''real-time'' reporting of serious adverse events, (3) comprehensive overview (by category) by the RAC in a public forum. Public review and access to submission, review, and follow-up information is critical to the safe and focussed advancement of human gene therapy research.

As a result of these concerns, NIH and FDA agreed on a compromise proposal that would accommodate the single submission format proposed at the July 18–19, 1994, meeting of the National Task Force on AIDS Drug Development, yet maintain public access to critical information and ''real-time'' adverse event reporting. The compromise proposal involves simultaneous submission of a human gene transfer proposal to both the FDA and the NIH in a single submission format. This format includes (but is not limited) to the documentation described in Appendix M–I through M–V, of the Points to Consider. NIH/ORDA and the FDA will simultaneously evaluate the proposal regarding the necessity for RAC review.

Section I–A, Purpose, is proposed to read:

Section I–A. Purpose

The purpose of the NIH Guidelines is to specify practices for constructing and handling: (i) recombinant deoxyribonucleic acid (DNA) molecules, and (ii) organisms and viruses containing recombinant DNA molecules.

Section I–A–1. Any recombinant DNA experiment, which according to the NIH Guidelines requires approval by the NIH, must be submitted to the NIH or to another Federal agency that has jurisdiction for review and approval. Once approvals, or other applicable clearances, have been obtained from a Federal agency other than the NIH (whether the experiment is referred to that agency by the NIH or sent directly there by the submitter), the experiment may proceed without the necessity for NIH review or approval (see exception in Section I–A–1–a).

Section I–A–1–a. In the interest of maximizing the resources of both the NIH and the Food and Drug Administration (FDA) and simplifying the method and period for review, research proposals involving the deliberate transfer of recombinant DNA or DNA or RNA derived from recombinant DNA into human subjects (human gene transfer) will be considered through a consolidated review process involving both the FDA and the NIH. Submission of human gene transfer proposals will be in the format described in Appendices M–I through M–V of the Points to Consider. Investigators must simultaneously submit their human gene transfer proposal to both the FDA and the NIH in a single submission format. This format includes (but is not limited to) the documentation described in Appendices M–I through M–V, of the Points to Consider. NIH/ORDA and the FDA will simultaneously evaluate the proposal regarding the necessity for RAC review.

Section III beginning paragraphs is proposed to read:

This section describes five categories of experiments involving recombinant DNA: (i) those that require Institutional Biosafety Committee approval, RAC review, and NIH Director approval before initiation (see Section III–A), (ii) those that require NIH/ORDA and Institutional Biosafety Committee approval before initiation (see Section III–B); (iii) those that require Institutional Biosafety Committee approval before initiation (see Section III–C), (iv) those that require Institutional Biosafety Committee notification simultaneous with initiation (see Section III–D), and (v) those that are exempt from the NIH Guidelines (see Section III–E).

Note: If an experiment falls into either Section III–A or Section III–B and one of the other categories, the rules pertaining to Section III–A or Section III–B shall be followed. If an experiment falls into Section III–E and into either Sections III–C or III–D categories as well, the experiment is considered exempt from the NIH Guidelines.

Any change in containment level, which is different from those specified in the NIH Guidelines, may not be initiated without the express approval of NIH/ORDA (see Minor Actions, Section IV–C–1–b–(2) and its subsections).

Section III–A is proposed to read:

Section III–A. Experiments that Require Institutional Biosafety Committee Approval, RAC Review, and NIH Director Approval Before Initiation (see Section IV–C–1–b–(1)).

Section III–A–1. Major Actions Under the NIH Guidelines

Experiments considered as Major Actions under the NIH Guidelines cannot be initiated without submission of relevant information on the proposed experiment to the Office of Recombinant DNA Activities, National Institutes of Health, Suite 323, 6006 Executive Boulevard, MSC 7052, Bethesda, Maryland 20892–7052, (301) 496–9838, the publication of the proposal in the **Federal Register** for 15 days of comment, review by the RAC, and specific approval by the NIH (see Appendix M for submission requirements on human gene transfer experiments). The containment conditions or stipulation requirements for such experiments will be recommended by the RAC and set by the NIH at the time of approval. Such experiments require Institutional Biosafety Committee approval before initiation. Specific experiments already approved are included in Appendix D which may be obtained from the Office