

submissions even if RAC review is not required.

(3) The RAC and FDA will broaden their scope of review for human gene transfer proposals to jointly and prospectively address global issues on a regular basis, e.g., ethical consideration in the implementation of gene therapy patient registry, access for "orphan" genetic disease patients to therapies, criteria for prenatal gene therapy, and transgenic technology for xenotransplantation.

(4) The RAC, NIH/ORDA, and FDA will establish a working group to enhance data monitoring efforts.

(5) A RAC, NIH/ORDA, and FDA working group will be established to propose long-term consolidation. The working group will have input from public, academic, and corporate sources.

The RAC approved a motion to (1) accept 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); (4) the RAC prefers that any stipulation requirements should be satisfactorily met prior to forwarding its recommendation for approval to the NIH Director; and (5) 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 the revised actions to the NIH Director for approval and the FDA Commissioner for concurrence. FDA legal counsel expressed concern that implementation of these actions would require amendment 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 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 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, and (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 focused advancement of human gene therapy research. As a result of these concerns, the 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" reporting of adverse events. The compromise proposal involves simultaneous submission of human gene transfer protocols to both NIH and the FDA 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 NIH Guidelines. NIH/ORDA and the FDA will simultaneously evaluate the proposal regarding the necessity for RAC review.

These revisions to the consolidated review process were discussed during the March 6-7, 1995, RAC meeting (published for public comments in the **Federal Register**, February 8, 1995 (60 FR 7630)). The following motions were made in response to the February 24, 1995, comments submitted by Ms. Sheryl Osborne of Viagene, Inc., San Diego, California: (1) A motion to retain the current requirement for obtaining Institutional Review Board (IRB) approval prior to RAC submission. A friendly amendment was made and accepted that ORDA should notify the Director of the Office for Protection from Research Risks regarding the necessity for IRB adherence to the detailed questions contained in Appendices M-II through M-V of the NIH Guidelines (Informed Consent issues). The amended motion was approved by a vote of 17 in favor, 0 opposed, and 1 abstention. (2) A motion was made that the RAC should continue to review and approve Phase I follow-up studies, i.e., Phase II and Phase III trials. Such studies may be submitted through the Accelerated Review process; however, the RAC retains the option to require full RAC review. The motion passed by a vote of 18 in favor, 0 opposed, and no abstentions.

The RAC approved a motion to approve the proposed amendments to Sections I, III, IV, V, and Appendices C, F, G, I, and M of the NIH Guidelines regarding NIH and FDA consolidated review of human gene transfer protocols, by a vote of 18 in favor, 0 opposed, and no abstentions.

The actions are detailed in Section II—Summary of Actions. I accept these recommendations, and the NIH Guidelines will be amended accordingly.

## II. Summary of Actions

### A. Amendments to Section I, Scope of the NIH Guidelines

The amended version of Section I-A, Purpose, reads:

#### 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 NIH and the FDA. 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 NIH and the FDA 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.

### B. Amendments to Section III, Experiments Covered by the NIH Guidelines

The amended version of Section III beginning paragraphs reads: