AD HOC REVIEW COMMITTEE

RECOMBINANT DNA ADVISORY COMMITTEE

Executive Summary of Findings and Recommendations

SEPTEMBER 8, 1995

Dr. Harold Varmus, Director, National Institutes of Health, appointed an *ad hoc* review committee to review the activities of the NIH Recombinant DNA Advisory Committee (RAC). The Director asked the committee to provide recommendations about the changing role of the RAC, the ways it may need to modify its operations, and how it should function to coordinate and facilitate productive gene therapy research.

The committee finds that:

1. Gene therapy represents a special development in medical research because of its potential for modification of the human genome and for the creation and dissemination of novel transmissible pathogenic vectors. In addition, there is the possibility of controversial extensions of this work, such as modification of the germline or the use of gene transfer for enhancement purposes. Thus gene therapy differs in major ways from other clinical technologies in use or under development and is, therefore, deserving of continued public scrutiny.

2. The RAC has served -- and continues to serve -- several important purposes for the scientific community, patients, and the general public. In particular, by focusing its attention on the emerging field of gene therapy research and helping to set appropriate scientific safety and informed consent guidelines for investigators. As a public forum of discussion, RAC has provided an enormous service not only to the general public, researchers at academic and similar institutions and within the biotechnology industry, but also to officials at the Food and Drug Administration (FDA). In addition, RAC continues to be a credible forum for airing a wide range of public concerns about this emerging field of medical research.

Based on these findings, the committee recommends that:

1. To avoid duplication of effort and unnecessary delay, RAC should no longer carry out case by case review of every clinical gene transfer protocol. This function is carried out by the FDA, which is required by statute to review all such protocols before approval.

2. Review of protocols by the RAC in an open public forum should continue in several areas of concern in which a particular protocol or new technology represents a significant degree of departure from familiar practices. Such departures include, but are not limited to, the use of novel vectors, particularly in cases in which modified human pathogens (such as herpes viruses or lentiviruses) are being evaluated; gene

transfer in utero, potential germ line modification, and other similar manipulations; and gene transfer in normal volunteers. In addition, review of protocols by the RAC is warranted in other situations which could lead to the formulation of significant new policy.

3. The RAC should define the criteria and work out procedures for identifying specific protocols requiring public review.

4. The RAC should continue to provide advice on policy matters revolving around gene therapy and other recombinant DNA issues to the NIH Director, individual members of the research community, institutional review boards, and the public. Moreover, that critical function should be extended, enabling RAC explicitly to provide advice and recommendations on policy matters to FDA. However, the committee recommended against reconstituting RAC or a comparable advisory body within the FDA, pointing out that several important policy functions of RAC are outside the mission of that agency.

5. A mechanism should be devised to enable Office of Recombinant DNA Activities (ORDA), NIH and the RAC to continue to be provided with the data needed for monitoring clinical gene transfer protocols. Hence, the committee recommends that theNIH Director urge the FDA Commissioner to exempt the broad area of gene therapy from many of the proprietary restraints reserved for ordinary therapeutic drug product and biologics that come under FDA review. Such a broad exemption, similar to the one now in place for products being developed for the treatment of individuals infected with HIV, would greatly expedite efforts to monitor and evaluate gene transfer protocols and, ultimately, would accelerate progress in the clinical application of gene therapy.

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CHAIR

VERMA, Inder M., Ph.D.
Molecular Biology & Virology Laboratory
The Salk Institute
10010 N. Torrey Pines Rd.
La Jolla, California 92037

MEMBERS

AGUILAR-CORDOVA, C. Estuardo,
Ph.D. Department of Pediatrics
Texas Childrens Hospital
1102 Bates Street, MC 3-2374
Houston, Texas 77030

BLAU, Helen M., Ph.D.
Department of Molecular Pharmacology
Stanford University, Room R354

Stanford, California 94305-5332

DESNICK, Robert J., M.D., Ph.D.
Department of Human Genetics
Mt. Sinai School of Med., Box 1203
One Gustav L. Levy Place
New York, New York 10029-6574

EPSTEIN, Charles J., M.D.
Department of Pediatrics
University of California, San Francisco
San Francisco, California 94143-0748

HESLOP, Helen E., M.D.
Division of Bone Marrow Transplantation
St. Jude Childrens Hospital
332 N. Lauderdale
Memphis, Tennessee 38105

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HIRANO, Susan S., Ph.D.
Department of Plant Pathology
University of Wisconsin-Madison
1630 Linden Drive
Madison, Wisconsin 53706-1598

JONSEN, Albert, Ph.D.
Dept. of Medical History & Ethics, SB20
University of Washington School of Medicine
Seattle, Washington 98195

PARKMAN, Robertson, M.D.
Division of Res. Immunology--BMT
Childrens Hospital of LA
4650 Sunset Boulevard, Room 226
Los Angeles, California 90027

ZALLEN, Doris T., Ph.D.
Science Studies & Humanities
VA Polytechnic Inst. & State University
Humanities Center, Lane Hall

Blacksburg, Virginia 24061

EXEC. SECRETARY

WIVEL, Nelson A., M.D.
Office of Recombinant DNA Activities
National Institutes of Health, MSC 7010
6000 Executive Boulevard, Suite 302
Bethesda, Maryland 20892-7010