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HENRY A. WAXMAN
29th District, California

November 23, 1999

Dr. Harold Varmus
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Varmus:

I am writing out of concern regarding the recent deaths in a number of human gene therapy protocols overseen by both the National Institutes of Health's (NIH) Recombinant DNA Advisory Committee (RAC) and the Food and Drug Administration (FDA).

Three years ago, I wrote to you to oppose your proposal to disband the RAC. At the time, I urged you not to alter the RAC's authority, citing the "rigor, flexibility and credibility" this advisory body had historically provided to both genetic research and the biotechnology industry. Most importantly, I was concerned about changes which would jeopardize the "public accountability and oversight which are integral to the RAC." While the NIH proposed on July 8, 1996 to disband the RAC, your agency ultimately retained a modified RAC lacking the authority to approve gene therapy protocols on November 22, 1996.

The recent death of Jesse Gelsinger in a University of Pennsylvania gene therapy protocol, and the delayed disclosure of six patient deaths in the GenVec/Parke-Davis and Vascular Genetics protocols, have rekindled my concerns about the adequacy of NIH oversight and public scrutiny of such protocols. To help address these issues, I would appreciate answers to the following questions —

1. On November 5, 1999, the members of the RAC empaneled in December 1995 wrote to you and Secretary Shalala that during their review of the University of Pennsylvania protocol, "FDA assured RAC members that there would be a feedback loop from the non-public FDA review process and that any major changes in protocols reviewed by the RAC would be reported to the RAC."

   It is clear that such "feedback" never took place between the RAC and the FDA. Please explain the reasons for this failure.

2. On May 14, 1996, Dr. Thomas Shih in the NIH Office of Recombinant DNA Activities (ORDA) wrote to Dr. Mark Batshaw, a principal investigator of the University of Pennsylvania protocol, that "the RAC will no longer be engaged in case-by-case review of human gene transfer protocols. No approval from the NIH director is required for initiation of human gene transfer experiments. The new NIH policy became effective as of the date of May 9, 1996."

The letter also states that "the investigators whose protocols have been previously approved by the RAC with stipulations are not required to submit to ORDA additional data for the fulfillment of the stipulation requirements."

In waiving the RAC's right to "additional data" from the University of Pennsylvania protocol, the letter preceded the July 8, 1996 NIH *Federal Register* notice by a full month. It also directly contradicts the preliminary nature of the July 8 notice, as well as the final policies established in the November 22, 1996 *Federal Register* notice.

Why did NIH issue this apparently premature and inaccurate letter? To whom else was this letter sent?

3. In its November 22 *Federal Register* notice, the NIH announced it would maintain a "publicly available, comprehensive NIH database of human gene transfer clinical trials, including adverse events." Such a database was intended to ensure that, in lieu of RAC protocol approval authority, gene therapy adverse event reports would be publicly available.

Has the NIH created such a database? If not, why has NIH failed to fulfill this commitment to public disclosure and oversight of gene therapy protocols?

4. The principal investigators of the Vascular Genetics and the GenVec/Parke-Davis gene therapy protocols have reportedly requested that adverse event reports of deaths and illnesses from the protocol be withheld from the public. Such a request was reportedly also made by Schering-Plough, the sponsor of other gene therapy protocols.

Did the NIH comply with these requests? Please provide copies of these and any other comparable requests, as well as documentation of the NIH's decisions and background concerning the protocols.

5. On November 5, 1999, Dr. Kathryn Zoon, director of the FDA Center for Biologics Evaluation and Research, issued a letter to gene therapy sponsors and principal investigators, stating that "investigators/sponsors are expected to report all serious adverse events to both the FDA and NIH."

Have all such adverse events been reported simultaneously and in a timely manner to both agencies in the past? Please identify any cases where gene therapy investigators or sponsors have failed to comply with this regulatory requirement.

6. Dr. Zoon also stated that "FDA will notify NIH/ORDA of the receipt of an adverse event report on a gene therapy IND to enhance investigator compliance with the NIH Guidelines."

Is the NIH aware of cases in which the FDA has possessed such adverse event reports, but has delayed or failed to notify NIH of these reports? Has FDA cited trade secrecy to NIH or the RAC as a basis for its failure to comply with this regulatory requirement? Please specify which, if any, protocols and adverse event reports were involved.

The issues raised by the reported deaths and increasing secrecy surrounding gene therapy protocols are serious and implicate the health and safety of many patients. I intend to work closely with your agency and the FDA in ensuring that all novel gene therapy protocols are subjected to adequate public scrutiny.

I appreciate your attention to these matters and request a response by Friday, December 3, 1999. If you have any questions, please contact Paul Kim of my staff at (202) 225-3976.

Sincerely,

Henry A. Waxman

HENRY A. WAXMAN
Member of Congress

Enclosures