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Congress of the United States
House of Representatives
Washington, DC 20515–0529

HENRY A. WAXMAN
29th District, California

Ranking Member
Committee on Government Reform

Member
Committee on Commerce
Democratic Steering Committee

January 10, 1999

Dr. Ruth Kirschstein
Acting Director
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Kirschstein:

I am writing to express my concerns regarding the December 21, 1999 letter from your predecessor, Dr. Varmus, concerning the National Institutes of Health's (NIH) oversight of human gene therapy trial protocols.

I applaud the Recombinant DNA Advisory Committee (RAC) for acting expeditiously to revise the NIH Guidelines governing recombinant genetic research. Such revisions are needed to ensure that the RAC and the NIH are informed of all serious adverse events in gene therapy trial protocols. I am also pleased that the Food and Drug Administration (FDA) revised its policies on December 6 and will now inform NIH of such adverse events on a weekly basis.

I was dismayed, however, by the level of noncompliance and the failure of oversight evident from the NIH's preliminary review of adverse event reporting in adenoviral gene therapy trial protocols. Before October 1, 1999, only 39 serious adverse events from these trials were reported to the NIH in compliance with federal regulations. Only after issuing its October 1 memorandum to all institutions conducting gene therapy trials did the NIH learn of an additional 652 unreported serious adverse events. This is failure rate of roughly 95 percent.

I ask that you comment on this failure, and provide additional information regarding its causes and any information available regarding such failures in non-adenoviral gene therapy trial protocols. I am particularly interested in whether you agree that the NIH has contributed to institutional and investigator noncompliance by raising doubts concerning the RAC's existence, by curtailing the RAC's authority over gene therapy protocols, and by the agency's failure to adequately oversee extramural compliance.

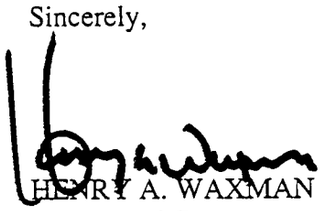
With respect to the agency's culpability, I ask that you keep me apprised of your investigation of the erroneous May 14, 1996 letter issued by the NIH Office of Recombinant DNA Activities (ORDA). Please confirm whether ORDA issued this letter without consulting or informing the RAC, and clarify which individuals authorized this letter and the May 1996 memorandum "sent to all investigators involved in clinical gene transfer research." I would also appreciate learning whether the RAC continued its review and approval of protocols between May 1996 and October 31, 1997, when the RAC's authority was ultimately abridged.

I am also disappointed that the NIH has failed to implement the database of human gene therapy trial protocols. The database was announced by the NIH in 1996, and was intended to ensure protocols and adverse events alike would be subject to public scrutiny. Given the many questions raised by recent deaths and the increased emphasis upon secrecy in this area, the NIH could greatly enhance public confidence by committing to improving disclosure and public knowledge of this important field of research. I ask that you commit to a definitive timetable to implement the database by the end of 2000. Failing that, I would appreciate learning what milestones will be met and what staff and budget the NIH will commit in "Phase I" of the database's implementation this year.

I hope you agree that the NIH must remedy the apparent problems in its oversight of this important field of research. As an essential step in resolving these problems, I ask that the NIH commit to enhancing the staffing and resources available for the analysis and reporting of adverse event reports. I would also appreciate being informed of the progress of the Director's Advisory Committee and the RAC in finalizing the adverse event reporting revisions to the NIH Guidelines. Finally, I ask that you comment on whether the public interest would be best served by transferring the RAC and the Office of Biotechnology Activities from NIH to the Office of the Secretary, as was recently done with the Office for Protection from Research Risks (OPRR).

I appreciate your attention to these matters and request a response by Friday, January 21, 2000. If you have any questions, please contact Paul Kim of my staff at (202) 225-3976.

Sincerely,



HENRY A. WAXMAN
Member of Congress