DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Bethesda MD 20892

November 5, 1999

Dear Gene Therapy IND Sponsor/Principal Investigator:

As you are aware, the Food and Drug Administration (FDA) and the National Institutes of Health (NIH) have been working together to optimize and streamline federal regulation and oversight of human gene transfer research. FDA and NIH each make unique and complementary contributions to the scientific evaluation of safety and potential efficacy of human gene therapy trials. FDA has statutory authority to permit an Investigational New Drug (IND) to go into effect or, if necessary, to place an IND on clinical hold, in order to ensure the safety of human subjects. The NIH is responsible for convening the Recombinant DNA Advisory Committee (RAC) which conducts public scientific and ethical review and discussion of novel applications of human gene transfer, as well as important public policy issues.

This letter outlines an established process for submission of a gene therapy IND and any subsequent adverse event reports to the Center for Biologics Evaluation and Research (CBER), FDA, and how that process relates to the submission of gene therapy protocols and adverse event reports to the NIH Office of Recombinant DNA Activities (ORDA), as required by the *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)*. The submission process was initially established in 1994 through a cooperative effort between FDA and NIH.

- The documentation required in Appendix M-I of the current *NIH Guidelines* (http://www.nih.gov/od/orda/toc.htm) should be submitted to NIH/ORDA prior to the submission of an IND to FDA. This will help to ensure that novel issues will be identified and discussed publicly in a timely manner.

- FDA will notify NIH/ORDA of the receipt of a gene therapy IND to assist NIH/ORDA in monitoring investigator compliance with the *NIH Guidelines*.

- In accordance with the FDA regulations found at US Code of Federal Regulations, Title 21, part 312.32 "IND Safety Reports" and *NIH Guidelines, Appendix M-VII-C "Adverse Event Reporting,"* investigators/sponsors are expected to report all serious adverse events to both the FDA and NIH.

- 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*.

- Within 15 working days after receipt by NIH/ORDA of a complete submission, the RAC will determine whether a protocol is novel and, therefore, requires public RAC review.

NIH/ORDA will notify FDA within one working day of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. The FDA will request that the sponsor delay initiation of, or suspend an ongoing protocol until the RAC has determined whether the protocol requires public review.

- If the RAC decides that full public review is warranted, the FDA will request, at the completion of its IND review (within 30 days of receipt of the IND or when the IND is allowed to proceed by FDA), that sponsors delay initiation of the protocol until after completion of the RAC review process.

These policies and procedures will enable investigators and sponsors to initiate important research in a timely fashion under FDA regulations and, at the same time, ensure that novel gene transfer experiments benefit from full public review by the RAC.

Sincerely,

Kathryn C. Zoon, Ph.D.
Director
Center for Biologics Evaluation and Research