February 21, 2002

Robert Figlin, M.D.
Medical Institutional Review Board
Office for the Protection of Research Subjects
2107 Ueberroth Building
169407

RE: IRB number 01-11-064-01: HIV Replication and Thymopoiesis in Adolescents – **PI response**

Dear Dr. Figlin:

Thank you for the Committee's December 5th, 2001 review of this study. In response to your letter of December 17th, I'd like to provide the following information.

A.

1. I would like to modify the substudy temporarily to include subjects 18 years of age or older only, and I request that the Committee reconsider the substudy in this population of adult subjects. If approved, I request an approval letter with a codicil that the study and substudy may proceed, but that the substudy is limited to subjects 18 years of age or older until the necessary approval is received from DHHS (see b below).
   a. Not applicable
   b. I request that the substudy as currently designed (to include subjects less than 18 years of age) be forwarded to the Secretary of the DHHS for review in accordance with 45 CFR 407. If approved, I request that the Committee consider the codicil described above as fulfilled, and issue a revised approval notice stating such.
2. It is expected that HIV subjects who are recruited into this study will be those who are attending the clinic for treatment for their HIV infection. Subjects will most likely have been attending clinic since birth or the time of discovery of their infection. Thus the treatment history of these subjects will indicate their method of contraction of HIV infection and its duration. The protocol summary has been revised to reflect this information; please see attached.
3. We are awaiting information on the deuterium labeled glucose and its administration. I request that the committee continue its review of the main study and consider issuing an approval for the main study with a codicil that the substudy will not be performed until this issue is resolved.
4. Subjects must allow a review of their medical records to participate in the research. The consent and assent forms have been modified to indicate that subjects will be asked to sign a separate medical records release form.
5. There will be 5-10 subjects from each of the three groups: perinatally infected, adult behavior infected, and seronegative, for a total of 15-30 subjects. This has been clarified on the revised protocol summary (section IV of the HS-1) and in the substudy consent forms, as requested.

a. In addition, the information has been added to the substudy youth assent forms, since the information is also relevant there.

6. As described in question 7 of the HS-1, subjects will be recruited through the use of flyers. These flyers were submitted with the original submission; additional copies with the IRB number added to the footer are attached for the Committee's review and approval. These flyers may be posted and/or left in waiting rooms where potentially eligible subjects may see them. In addition, flyers may be given to physicians who may see potentially eligible subjects such that the physicians can give these to subjects who may be interested. The subjects will then be instructed to contact Dr. Krogstad as directed on the flyer if they are interested in learning more about the study.
7. The compensation plan for the substudy has been modified such that subjects receive the same for day 14 and Day 28.
   a. The consent and assent forms have been modified to reflect this change.
8. In the future, samples may be sent to other researchers for viral or immunological studies that provide additional information on the same scientific questions addressed in the study. This testing may be done in response to the results obtained during the study; thus specific plans for testing have not yet been finalized.
9. Children's Hospital Los Angeles will act as a study site for this study. We have not yet received a copy of their IRB approval. We request that the Committee continue their review of this study and, once approved, issue an approval with the codicil that the Children's Hospital site will not begin the study or contact or enroll any subjects until they have received IRB approval.
10. We will forward approval from the Medical Radiation Safety Committee as soon as possible.
11. We will forward the revised 740 as soon as possible.

B.

1. The number of subjects has been added to the consents and assents.
2. The duration of the study has been added to the consents and assents.
3. The sponsor of the study, NIH, has been added to the consents and assents.
4. The types of blood tests that may be performed are described in the consents and assents.
5. The consents and assents have been modified as requested, with the following exception:
   a. The Committee's standard language regarding samples remaining at the end of the study was used in these forms. A request was made to change that standard language to indicate what types of "samples" are referred to. We request that we use the committee's standard language, without alteration, so as to be consistent with past and future consent forms that include the standard paragraph.
   b. In the substudy consent and assent forms, a requested was made in the "Purpose of the Study" section to indicate that the subjects will drink the water solution. This information is already conveyed in the "Procedures" section, and thus it is redundant in the Purpose section. We have not changed this section and ask that the committee reconsider this request.
   c. Only 6 out of the 8 consent/assent forms submitted for this study were returned with the committee's response. The main study assent for HIV infected subjects and the substudy consent for HIV subjects were not returned. Thus we do not know if additional changes were requested on those forms. We have made the changes to these forms that were requested on the other forms.

In addition, a request was made on the flyers to “mention the substudy”. The substudy is already mentioned on the flyers “You may also be asked to participate in a substudy where you would stay in the hospital overnight”. Thus be request that the Committee reconsider this request.

Thank you for your rapid attention to this response. If you require further information, please contact Alison Watts in the Office of Clinical Trials at x48713.

Sincerely,

Paul Krogstad, MD
Principal Investigator