DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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February 17, 2006

Mary Ellen Sheridan, Ph.D.
Associate Vice President for Research
University of Chicago
970 E. 58th Street
Chicago, IL 60637

RE: Human Research Subject Protections Under Multiple Project Assurance M-1264 and Federalwide Assurance FWA-5565

Research Project: Phase I Safety Trial: A Placebo-Controlled, Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of Recombinant Envelope Proteins of HIV-1 gp160 and gp120 in Children ≥1Month Old with Asymptomatic HIV Infection
Project Number: ACTG #218
Principal Investigator: Daniel Johnson, M.D.

Research Project: Phase I/II Study: Ritonavir Therapy in HIV-I Infected Infants and Children
Project Number: ACTG #345
Principal Investigator: Daniel Johnson, M.D.

Research Project: Pram 2 – A Phase I/II Randomized Multicenter Protocol Comparing Four Antiretroviral Regimens Containing Combinations of Protease Inhibitors, NRTIs and NNRTI
Project Number: ACTG #377
Principal Investigator: Daniel Johnson, M.D.

Dear Dr. Sheridan:

The Office for Human Research Protections (OHRP) has reviewed the University of Chicago's (UC) August 3, 2005 response to OHRP's June 22, 2005 letter regarding indications of possible noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46) involving the above-referenced research.

Based upon its review, OHRP makes the following determination regarding the above-referenced research:

(1) HHS regulations at 45 CFR 46.404-409 require specific findings on the part of the IRB for approval of research involving children. OHRP's review of UC institutional review board (IRB) documents for the above-referenced research revealed no evidence that the IRB considered and made the required findings when reviewing this research involving children.

OHRP acknowledges the following statement included in UC's August 3, 2005 letter: "The minutes of the IRB meetings for the cited protocols do not reflect the Subpart D category under which these protocols were reviewed."

Corrective Action: OHRP acknowledges the following statement in UC's August 3, 2005 letter:

> In 2002, the IRB implemented a revised procedure and submission form (IRB Supplemental Form C) to assist the IRB in their review of research involving children and to aid in the determination of the appropriate Subpart D category. Supplemental Form C requests that the investigator specify the category of research involving children proposed. The IRB Committee then discusses and makes a determination as to whether or not the IRB agrees with this determination.

OHRP acknowledges that Supplemental Form C includes the following questions:

- Will this protocol involve children who are wards of the State as potential subjects?
- Is this research greater than minimal risk with no prospect of direct benefit to subjects?
- Please describe your plan to appoint an advocate for potential subjects who are wards of the State.
- Please provide a description of how the assent of the child would be obtained and documented.
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Required Action: By March 31, 2006, please provide a satisfactory corrective action plan to specifically address the above finding. OHRP requests that you send a copy of the revised procedure for review of research involving children referenced above, the current version of the IRB application, as well as recent IRB minutes that demonstrate the use of IRB Supplemental Form C.

In addition, OHRP has the following concerns:

(2) [Redacted]

[Redacted]

Please forward your response to the above finding and concerns so that OHRP receives it no later than March 31, 2006.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Karena Cooper, J.D., M.S.W.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Jonathan Moss, Chairperson, IRBs #1A, and #4-01, Cmte. C, Univ. of Chicago
Dr. Tina L. Rzepnicki, Chairperson, IRB #2, Univ. of Chicago
Dr. Bennett Bertenthal, Chairperson, IRB #3, Univ. of Chicago
Commissioner, FDA

Dr. David Lepay, FDA
Dr. Lana Skirboll, NIH
Dr. Anthony Fauci, NIH
Dr. Edmund C. Tramont, NIH
Ms. Donna Marchigiani, NIH
Dr. Robinsue Frohboese, OCR
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Janet Fant, OHRP