DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 240-453-8141
FAX: 301-402-0527
E-mail: jgorey@osophs.dhhs.gov

February 17, 2006

Ronald R. Peterson
President
Johns Hopkins / Johns Hopkins Health System
600 North Wolfe Street
Phipps 160
Baltimore, MD 21287

RE: Human Research Subject Protections Under Multiple Project Assurance M-1011 and Federalwide Assurance FWA-6087

Research Project: Phase I Trial: Safety and Effectiveness of Four Anti-HIV Drug Combinations in HIV-Infected Children and Teens
Project Number: ACTG #377
Principal Investigator: Andrea Ruff, M.D.

Dear Mr. Peterson,

The Office for Human Research Protections (OHRP) has reviewed the Johns Hopkins Medicine's (JHM) July 13, 2005 response to OHRP's June 9, 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.

OHRP notes that your report indicated that ACTG #218, and #265 did not include wards of the state. In addition, your report indicated that #377 included two wards of the state.

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 institutional review board (IRB) for approval of research involving children. OHRP's review of JHM IRB documents for the above-referenced research revealed no evidence

that the JHM IRB considered and made the required findings when reviewing this research involving children.

(2) HHS regulations at 45 CFR 46.111 state that, in order to approve research covered by the regulations, the IRB shall determine that certain requirements are satisfied. OHRP is concerned that when reviewing this research, the CCBHS IRB failed to obtain sufficient information to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111.

(a) 45 CFR 46.111(a)(3): Selection of subjects is equitable. In making this determination, IRBs should be particularly cognizant of the special problems of research involving vulnerable populations. OHRP is concerned that JHM IRB records appear to demonstrate a failure of the IRB to obtain sufficient information regarding the selection of wards of the state and foster children as research subjects.

(b) 45 CFR 46.111(a)(4): Informed consent will be sought from each prospective subject or the subjects's legally authorized representative, in accordance with 45 CFR 46.116. In particular, OHRP is concerned that JHM IRB records appear to demonstrate a failure of the IRB to obtain sufficient information regarding the process for obtaining permission of parents or guardians for wards of the state or foster children.

(c) 45 CFR 46.111(b): When some or all of the subjects (e.g., children) are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the HHS regulations to protect the rights and welfare of these subjects. In particular, OHRP is concerned that JHM IRB records appear to demonstrate a failure of the IRB to obtain sufficient information regarding such safeguards with respect to the enrollment of wards of the state or foster children.

Corrective Actions: OHRP acknowledges that due to deficiencies previously cited in the OHRP 2001 suspension action at JHM, adequate IRB documentation was not being generated at that time. OHRP further acknowledges IRB reforms resulting from both the 2001 action and more recent application for AAHRPP accreditation. JHM IRB review forms and processes have changed extensively, with current applications addressing specific information regarding the involvement of children, and policies and procedures for the inclusion of foster children or wards of the state in accord with 45 CFR 46.409.

OHRP finds that these corrective actions adequately address the above finding and concern and are appropriate under the JHM FWA. As a result of this determination, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

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,

Julia Gorey, J.D.
Division of Compliance Oversight

cc: Dr. Howard M. Lederman, Chairperson, Johns Hopkins Univ Sch Med IRB #1
Dr. David R. Cornblath, Chairperson, Johns Hopkins Univ Sch Med IRB #2
Dr. Paul S. Lietman, Chairperson, Johns Hopkins Univ Sch Med IRB #3
Dr. Gary Briefel, Chairperson, Johns Hopkins Univ Sch Med IRB #5
Laura E. Rocco, Chairperson, Johns Hopkins Univ Sch Med IRB #7
Barbara L. Starklauf, Asst. Dean, Human Subject Research Compliance, Johns Hopkins Univ Sch Med
Michael J. Klag, MD., MPH, Vice Dean for Clinical Investigation, Johns Hopkins Univ Sch Med
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