DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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June 19, 2006

Myron Rosenthal, Ph.D.
Vice Provost for Human Subjects Research
University of Miami
1500 N.W. 12th Avenue JMT/East
Suite 1002
Coral Gables, FL 33124

RE: Human Research Subject Protections Under Multiple Project Assurance M-1196 and Federalwide Assurance FWA-2247

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: Gwendolyn Scott, M.D.

Dear Dr. Rosenthal:

The Office for Human Research Protections (OHRP) has reviewed the University of Miami's (UM) March 28, 2006 response to OHRP's February 17, 2006 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 on its review, OHRP makes the following determinations:

HHS regulations at 45 CFR 46.111 state that, in order to approve research covered by the regulations, the institutional review board (IRB) shall determine that certain requirements are satisfied. OHRP finds that when reviewing this research, the UM IRB failed to obtain sufficient information to make the following determinations required for approval of research under HHS regulations at 45 CFR 46.111:

(1) 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. In particular, OHRP finds that UM IRB records for the above-referenced research demonstrate a failure

of the IRB to obtain sufficient information regarding the selection of wards of the state and foster children as research subjects.

Corrective Actions: OHRP acknowledges the following statements in UM's March 28, 2006 letter:

> It is current practice for each element under 45 CFR 46.111 to be individually considered and specifically documented in the minutes for each new protocol and continuing review. Our current IRB reviewer checklists ask primary and secondary reviewers to note if wards of the state (which include foster children) will be included in the study population. The checklist also requires primary and secondary reviewers to determine if the selection of subjects is equitable. Reviewers read through each item listed on the checklist during their presentation at the IRB meeting. Our minute-takers record the discussion on each of these items and ensure this is documented in the minutes.
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> Therefore, our corrective actions to ensure regulatory compliance and adequate documentation of the required elements under 45 CFR 46.111 in the minutes are:
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> 1. Requiring IRB members to specifically note if wards of the state will be included as research subjects;
> 2. Requiring IRB members to specifically discuss the selection of subjects and consider if selection is equitable; and
> 3. In the near future, we will specifically ask investigators to indicate if wards of the state will be included as research subjects in our new protocol form.

(2) 45 CFR 46.111(a)(4): Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with 45 CFR 46.116. In particular, OHRP finds that UM IRB records for the above-referenced research 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.

Corrective Actions: OHRP acknowledges UM's statements that it will require IRB members to specifically note if the process for obtaining informed consent is appropriate in accordance with 45 CFR 46.116 and specifically ask investigators to provide a detailed description of the process for obtaining informed consent.

(3) 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 study to protect the rights and welfare of these subjects. In particular, OHRP finds that UM IRB records for the above-

referenced research 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 UM's statements that it will require IRB members to specifically discuss additional safeguards necessary to protect vulnerable populations, such as wards of the state or foster children, per the checklist and will ask investigators to provide a detailed description of additional safeguards to protect the rights and welfare of vulnerable subjects in the current UM protocol form.

OHRP notes that in addition to the specific corrective actions above, UM states that it has provided education to IRB members on the necessity of individually addressing and documenting all of the elements under 45 CFR 46.111 when approving new research and the continuation of research.

OHRP also notes that UM states that it has undertaken an extensive restructuring of its Human Subject Research Office, its IRB panels and its policies and procedures. UM states that it is attempting to foster a "culture of compliance" through educational efforts and more effective partnerships between the IRB and university and the investigators.

OHRP has determined that the above corrective actions adequately address the findings noted above and are appropriate under the UM Assurance. As a result, 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,

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

cc: Dr. Steven G. Ullmann, Vice Provost for Faculty Affairs, U. Miami
Dr. Thomas Sick, Chairperson, U. Miami Med. Sci. IRB #1
Dr. Stephen Sapp, Chairperson, U. Miami Soc. & Behav. Sci. Cmte.
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