DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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June 19, 2006

Robert A. Saporito, D.D.S.
Executive Sr. Vice President, Academic Affairs
University of Medicine and Dentistry of New Jersey
65 Bergen Street, SSB 1441
Newark, NJ 07107

RE: Human Research Subject Protections Under Federalwide Assurance FWA-1861

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: Sunandra Gaur, M.D.

Dear Dr. Saporito:

The Office for Human Research Protections (OHRP) has reviewed the University of Medicine and Dentistry of New Jersey's (UMDNJ) May 5, 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.

In its February 17 letter, OHRP made 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 the UMDNJ IRB documents for the above-referenced research revealed no evidence that the UMDNJ IRB considered and made the required findings when reviewing this research involving children.
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> **Corrective Action:** The August 29, 2005 response to OHRP acknowledged that appropriate determinations required under HHS regulations at 45 CFR part 46, subpart D, were not made by the IRB for this research. OHRP acknowledges that the UMDNJ instituted in 2001 a Human Subjects Protection Program for education and training of all individuals involved in the conduct of research with human subjects. The IRB

infrastructure was reorganized, with the creation of a Human Subjects Protection Program. New documentation standards were put into place, with required documentation of determinations required under HHS regulations at 45 CFR part 46, subpart D, for every study involving children since 2002. Systematic improvements have continued beyond regulatory requirements, including implementation of best practice standards.

UMDNJ's August 29, 2005 response to OHRP specified that actions taken after June 2005 included adding additional quarterly investigator training outlining specific requirements for research involving children, including enrollment of wards of the state, consistent with the requirements of HHS regulations at 45 CFR 46.409. All IRB members were provided with OHRP guidance on subpart D of 45 CFR part 46, with special emphasis on investigators enrolling wards of the state and the additional determinations required. Language was added to approval notices to alert investigators enrolling pediatric subjects that wards require additional protections.

Based upon its review of your May 5, 2006 response, OHRP makes the following additional determination:

(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 finds that when reviewing this research, the UMDNJ IRB failed to obtain sufficient information to make the following 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. In particular, OHRP finds that UMDNJ 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 subject's legally authorized representative, in accordance with 45 CFR 46.116. In particular, OHRP finds that UMDNJ 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 study to protect the rights and welfare of these subjects. In particular, OHRP finds that UMDNJ 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: IRB applications have been revised to inform the IRB during the initial review process of the intent to enroll a foster child or ward of the state; IRB applications also now require a description of the assent process that will be used. IRB approval notices include instructions to the principal investigator that he or she must notify the IRB in advance of any intent to enroll a ward of the state and must arrange for a child advocate in this event. An IRB reviewer checklist has been added to assure that each study involving child participants has been reviewed appropriately under 45 CFR 46 subpart D, and campus-wide educational sessions have been instituted and contain topics related to vulnerable populations and consent processes.

OHRP finds that these corrective actions adequately address the stated finding and are appropriate under the UMDNJ assurance. As a result of this determination, there should be no need for further involvement of OHRP in this matter.

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
Division of Compliance Oversight

cc: Ms. Barbara J. LoDico, HPA, UMDNJ
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