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

Nilda Candelario
President
Universidad Central del Caribe
Hospital Univ.Ramon Ruiz Arnau
Laurel Avenue, Santa Juanita
Call Box 60-327
Bayamon, PR 00956

RE: Human Research Subject Protections Under Cooperative Agreement T-3351
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: Rosaura Aguayo, M.D.

Dear Dr. Candelario:

The Office for Human Research Protections (OHRP) has reviewed the Universidad Central del Caribe's (UCC) 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 upon its review, OHRP makes the following determinations 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 finds that when reviewing this research, the UCC IRB failed to obtain sufficient information to make the determinations required for approval of research under HHS regulations at 45 CFR 46.405-409.

(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 UCC IRB failed to obtain sufficient information to make the following determinations required for approval of research under HHS regulations at 45 CFR 46.111:

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 UCC 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 the efforts by your institution to improve human subjects protections which address these findings. A revised IRB application form requires an explanation of anticipated risks and benefits and protections that will be implemented for vulnerable groups. In order to ensure that all aspects of protocol review are discussed and documented, protocol discussion checklists include sections for subpart D of 45 CFR 46 and wards of the state. Continuing education regarding wards of the state in research is being implemented. The institution has purchased equipment to transcribe IRB meetings, avoiding previous unintelligible recordings and incomplete minutes.

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

OHRP has the following additional recommendations for revisions to the UCC IRB application:

(1) Under Subjects, OHRP recommends a question directly ask which vulnerable groups are being recruited, and response boxes should include “wards of the state”.

(2) Under Subjects, #7, note that an advocate must be appointed to represent the best interests of any ward of the state involved in research approved under HHS regulations at 45 CFR 46.406 or 46.407.

(3) Under Risks and Benefits, #2, OHRP recommends language which currently reads “(minors, fetuses in utero, prisoners....)” be amended to read “(minors including wards of the state, fetuses in utero, prisoners...).”

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. Frances Garcia, HPA and IRB Chairperson, Ramon Ruiz Arnau Univ Hosp
Dr. Sam Shekar, NIH
Dr. Anthony Fauci, NIH
Dr. Edmund C. Tramont, NIH
Ms. Donna Marchigiani, NIH
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