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

Myrna Boissen
Executive Director
San Juan City Hospital
P.O. Box 21405
San Juan, PR 00928-1405

RE: Human Research Subject Protections Under Cooperative Agreement T-3478

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 ≥1 Month Old with Asymptomatic HIV Infection
Project Number: ACTG #218
Principal Investigator: Eleanor Jiménez, M.D.

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: Eleanor Jiménez, M.D.

Dear Ms. Boissen:

The Office for Human Research Protections (OHRP) has reviewed the San Juan City Hospital's (SJCH) March 26, 2006 response to OHRP's February 17, 2006 letter raising concerns 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.

After review of your report, OHRP makes the following determinations:

(1) HHS regulations at 45 CFR 46.111(b) require that when some or all of the subjects (e.g., children) are likely to be vulnerable to coercion or undue influence, the institutional review board (IRB) must determine that additional safeguards have been included in the

study to protect the rights and welfare of these subjects. OHRP finds that SJCH IRB failed to obtain sufficient information regarding such safeguards with respect to the enrollment of wards of the state or foster children in ACTG #218. OHRP notes that although a community representative was present at the initial review of ACTG #218, no discussion regarding the enrollment of wards was noted. In addition, the information provided to OHRP with your report does not include any information related to the possible enrollment of wards or foster children. OHRP notes that your report outlines (a) a current procedure in which each subject is assigned a social worker to act as the subject's advocate; and (b) that the Department of Justice in Puerto Rico has the authority to designate a person to sign informed consent documents for foster children. However, these processes are not described in any of the documents provided with your report.

Required Action: The SJCH must provide an adequate corrective action plan to address the above determination.

(2) In its February 17, 2006 letter, OHRP raised a concern that the SJCH IRB did not have sufficient information to make the determinations required under HHS regulations at 45 CFR 46.405 during its initial review of the study. As part of your report, SJCH provided the entire IRB file for ACTG #218 which appeared to contain adequate information to make the determinations required under 45 CFR 46.405. OHRP finds that the SJCH has adequately addressed OHRP's concern.

(3) In its February 17, 2006 letter, OHRP raised a concern that the SJCH IRB inappropriately used an expedited review procedure when conducting its continuing review of ACTG #218. OHRP notes that your report stated that expedited continuing review was conducted because the no subjects were enrolled in the research and that no material changes had occurred. OHRP finds that SJCH has adequately addressed OHRP's concern.

Please provide your corrective action plan to OHRP to address item (1) above no later than July 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,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Ana Barletta, Medical Director, SJCH
Dr. Luis Medina, IRB Chair, SJCH

Commissioner, FDA
Dr. David Lepay, FDA
Dr. Sam Shekar, 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