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

Maria E. Minion, M.D.
Vice President, Medical Affairs
Children's Hospital of Orange County
455 South Main Street
Orange, CA 92868-4318

RE: Human Research Subject Protections Under Cooperative Project Assurance T-3988 and Federalwide Assurance FWA-255

Research Project: Phase I/II Trial: The Safety and Immunogenicity of Live-Attenuated Varicella Vaccine (Varivax) in HIV-Infected Children
Project Number: ACTG #265
Principal Investigator: Antonio Arrieta, M.D.

Dear Dr. Minion:

The Office for Human Research Protections (OHRP) has reviewed the Children's Hospital of Orange County's (CHOC) March 30, 2006 response to OHRP's February 17, 2006 letter expressing 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.

OHRP notes the following regarding the above-referenced research:

(1) In its letter OHRP raised a concern that there is little evidence in the documentation provided with your July 13, 2005 report that the CHOC IRB approved the research under HHS regulations at 45 CFR 46.405 during its initial review of the study. OHRP notes that your report indicates that, at the time of initial review of the study, the CHOC IRB approved the study under 45 CFR 46.405 but did not document that determination in the IRB record. In addition, prior to OHRP's inquiry, CHOC had subsequently implemented changes to its IRB procedures which include documenting the risk/benefit category in the

IRB meeting minutes.

(2) OHRP finds that the CHOC IRB failed to obtain sufficient information to make the determinations required under HHS regulations at 45 CFR 46.111(b) that additional safeguards were included in the study to protect the rights and welfare of subjects that are likely to be vulnerable to coercion or undue influence. OHRP notes that the CHOC IRB was unaware that one of the three subjects enrolled in the research was a ward of the state and had not specifically addressed additional protections regarding this subject. OHRP also notes that CHOC did not have policies and procedures in place which address participation of children who are wards of the state in research at the time the study was reviewed by the CHOC IRB.

Corrective Actions: OHRP acknowledges the following corrective actions taken by the COC IRB:

(a) The CHOC IRB has changed its procedures to include a parental acknowledgment in the parental permission document that the parents are the legal guardians of the subject and that the child is not a ward of the state.

(b) The CHOC IRB has amended its written procedures to require the recording of the relevant category of research under HHS regulations at 45 CFR 46.404-406 and required IRB findings in the minutes of the IRB meetings.

(c) The CHOC IRB has amended its written procedures to better address the IRB's consideration of the research categories under HHS regulations at 45 CFR 46.404-406.

(d) The CHOC IRB will provide education for IRB members and research staff regarding changes to the procedures for IRB review and documentation of a subject's status as a ward of the state.

OHRP finds that this response and corrective actions have adequately addressed the above determination and the additional concern raised in its February 17, 2006 letter. As a result, 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,

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

cc: Phoung Lam Dao, Research Subjects Manager, Children's Hosp Orange County
Dr. Bruce Nickerson, Chairperson, Children's Hosp Orange County IRB #1

Dr. Gabe Briones, Chairperson, Children's Hosp Orange County IRB #2
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