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John J. Lucas, Ph.D.
Vice Provost for Research
SUNY Upstate Medical University
Research Administration
750 East Adams Street
Room 1254 WH
Syracuse, NY 13210

RE: Human Research Subject Protections Under Federalwide Assurance FWA-5967

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: Coleen K. Cunningham, M.D.

Dear Dr. Lucas:

The Office for Human Research Protections (OHRP) has reviewed SUNY Upstate Medical University's (SUNYUMU) February 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.

In its February 17, 2006 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 SUNYUMU IRB documents for the above-referenced research revealed no evidence that the IRB considered and made the required findings when reviewing this research involving children.

OHRP notes that the subpart D checklist referenced in SUNYUMU's February 28, 2006 response that was purported to be used as part of the December 2002 was not identifiable as such, given that it was unsigned and it was unclear who made the handwritten marks. In addition, the form lacked any indication of the date on which the marks were made. There was no notation in the IRB minutes cross-referencing the checklist, and no version date on the checklist, so it is unclear when the checklist was used as part of an IRB review.

Corrective Actions: OHRP acknowledges the following statement in SUNYUMU's February 28, 2006 response: "The IRB meeting minutes had not specifically stated that the "Checklist for Research on Children" was reviewed; however since August 2005, it is the practice of the IRB to document this review in the IRB minutes."

OHRP notes that the copy of the checklist attached to the February 28, 2006 response (version date 2/28/06) contains a section entitled "Requirements for Children who are Wards of the State."

OHRP makes the following additional determinations:

(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 the above-referenced research, the SUNYUMU 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 SUNYUMU 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 Action: OHRP acknowledges SUNYUMU's statement that it has amended its application form to specifically ask whether wards of the state or foster children will be enrolled in the research.

(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 SUNYUMU 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 Action: OHRP acknowledges SUNYUMU's statement that it has amended its application form to specifically ask for a detailed summary of the plan to obtain 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 SUNYUMU 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 Action: OHRP acknowledges SUNYUMU's statement that it has amended its application form to specifically ask about additional safeguards that have been put into place to reduce the possibility of coercion or undue influence to participate for wards of the state or foster children.

OHRP also acknowledges SUNYUMU's statement as follows:

In addition to the above actions, we have amended the "Checklist for Research on Children" to include a section pertaining to research approved under 45 CFR 46.406 and 46.407; and, in conjunction with the Upstate Division of Pediatric Infectious Diseases, we have developed a standard operating procedure for establishing legal guardianship for pediatric subjects in order to ensure that the documentation of consent to participate in research is executed legally.

OHRP has determined that the above corrective actions adequately address the findings noted above and are appropriate under the SUNYUMU 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

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