DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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February 17, 2006

Donald E. Wilson, M.D., M.A.C.P.
Vice President of Medical Affairs
Univ. of Maryland Baltimore School of Medicine
655 West Baltimore Street
Baltimore, MD 21201

RE: Human Research Subject Protections Under Federalwide Assurance FWA-7145

Research Project: Phase I Study: A Double-Blind Placebo-Controlled Trial of the Safety and Immunogenicity of a Seven Valent Pneumococcal Conjugate Vaccine in Presumed-HIV-Infected Infants (ACTG #292)
Project Number: IRB #1297046
Principal Investigator: Peter Vink, M.D.

Dear Dr. Wilson:

The Office for Human Research Protections (OHRP) has reviewed the University of Maryland Baltimore School of Medicine's (UMD-Balt) July 19, 2005 response to OHRP's June 9, 2005 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 determination of noncompliance regarding the above-referenced research:

(1) HHS regulations at 45 CFR 46.404-409 require specific findings by the institutional review board (IRB) for approval of research involving children. OHRP finds no evidence that the UMD-Balt IRB considered or made the required findings in its initial review and its July 7, 1995 approval of the research, including approval of the research under one of the permissible research categories set forth at 45 CFR 46.404-407.

OHRP acknowledges that as part of the IRB's continuing review of the research on June 26, 1998 and May 28, 1999, the IRB documented that the research posed no greater than minimal risk to children, under 45 CFR 46.404. OHRP notes that the basis for the IRB's risk designation is not documented. OHRP further notes that the study was closed to enrollment when the IRB designated the research minimal risk, and questions whether

the IRB intended that designation to apply solely to data evaluation and/or long-term follow-up of subjects, rather than to the entire research study.

Corrective Action: OHRP notes that the UMD-Balt IRB file for ACTG #292 contains a checklist of protections for children in research, apparently used at the 1998 and 1999 continuing review of the protocol. OHRP notes that the checklist does not include any consideration of how the IRB would fulfill the requirements of HHS regulations at 45 CFR 46.409.

Required Action: By March 31, 2006, UMD-Balt must provide a corrective action plan to indicate how it has addressed the above findings to date, and how it will address those portions of the above findings not previously addressed.

OHRP has the following concern regarding the above-referenced research:

(2) [Redacted]

Please respond to the above required action and concern. In your response, please describe how the IRB made the determinations required under 45 CFR 46.111 for the above-referenced research. If you identify additional noncompliance in preparing your response to OHRP's concern, please provide a description of any corrective actions that have been or will be taken to address the noncompliance.

Please forward your response so that OHRP receives it no later than March 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,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Robert Edelman, Chairperson, U Md. Balt. Sch of Med IRBs #1 - #6
Dr. David Lepay, FDA
Dr. Lana Skirboll, NIH
Dr. Anthony Fauci, NIH
Dr. Edmund C. Tramont, NIH
Ms. Donna Marchigiani, NIH
Dr. Robinsue Frohboese, OCR
Dr. Bernard Schwetz, OHRP
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Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Dr. Kristina Borror, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Janet Fant, OHRP