DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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January 6, 2004

Neal Nathanson, M.D.
Vice Provost for Research
University of Pennsylvania
119 College Hall
Philadelphia, PA 19104-6303

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1025 and Federalwide Assurance (FWA) 4028

Research Project: Prospective, Randomized, Multi-Center Trial of 12 ml/kg vs. 6 ml/kg Tidal Volume Positive Pressure Ventilation for Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome (ARMA Trial)
Principal Investigator: Dr. Paul Lanken

Research Project: Prospective, Randomized, Multi-Center Trial of Pulmonary Artery Catheter (PAC) vs. Central Venous Catheter (CVC) for Management of Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS) and Prospective, Randomized, Multi-Center Trial of 'Fluid Conservative' vs. 'Fluid Liberal' Management of Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS) (FACTT Trial)
Principal Investigator: Dr. Paul Lanken

Dear Dr. Nathanson:

The Office for Human Research Protections (OHRP) has reviewed the October 6 and November 21, 2003 reports from the University of Pennsylvania (U Penn) responding to determinations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects involving the above-referenced research.

Based upon its review, OHRP finds that the U Penn has implemented the required actions stipulated by OHRP's July 25, 2003 letter. In particular, OHRP acknowledges the following:

(1) The U Penn Institutional Review Board (IRB) received the additional supplemental information and the revised model informed consent document for the FACTT trial, and has subsequently re-reviewed and approved the research.

(2) U Penn has provided OHRP with a copy of the final version of the IRB-approved informed consent document.

(3) U Penn has implemented a variety of procedures including listing the criteria for IRB approval of research in the U Penn IRB Standard Operating Procedures and developing an IRB reviewer worksheet to help ensure that the U Penn IRBs receive sufficient information to make all determinations required under HHS regulations at 45 CFR 46.111. The U Penn IRB also lists the required elements of informed consent and includes an informed consent checklist in the U Penn IRB document Tips on Informed Consent and in the U Penn IRB Standard Operating Procedures to help ensure that the U Penn IRBs approve an informed consent process that satisfies all requirements of HHS regulations at 45 CFR 46.116. OHRP recommends that all of the criteria for IRB approval under HHS regulations at 45 CFR 46.111 be included in the U Penn IRB Proposal Summary instructions for investigators.

OHRP finds that the above corrective actions adequately address OHRP's findings and are appropriate under the U Penn FWA. As a result, OHRP anticipates no need for further involvement with U Penn related to this matter.

OHRP appreciates the commitment of your institution to the protection of human subjects. Do not hesitate to contact us should you have any questions.

Sincerely,

Kristina Borror, Ph.D.
Director
Division of Compliance Oversight

Michael A. Carome, M.D.
Associate Director for Regulatory Affairs
Office for Human Research Protections

cc: Dr. Mitchell Machtay, Chair, IRB #1, U Penn
Dr. James M Clark, Chair, IRB #2, U Penn
Dr. Elliot Hersh, Chair, IRB #3, U Penn
Dr. Anne A. Keane, Chair, IRB #4, U Penn
Dr. Stephen Hahn, Chair, IRB #5, U Penn
Dr. Bernard Mason, Chair, IRB #6, U Penn
Dr. Harry Chen, Chair, IRB #7, U Penn
Dr. Joseph Sherwin, Human Protections Administrator, U Penn
Dr. Paul Lanken, Principal Investigator, U Penn

Dr. B. Taylor Thompson, ARDS Network Coordinating Center Principal Investigator, Massachusetts General Hospital
Dr. Arthur Wheeler, FACTT Trial Committee Chair, Vanderbilt University
Dr. Gordon R. Bernard, Chairman, ARDS Steering Committee, Vanderbilt University
Dr. Herbert P. Wiedemann, FACTT Trial Committee Chair, Cleveland Clinic Foundation
Dr. James Kiley, Director, Division of Lung Diseases, NHLBI
Dr. Lana Skirboll, Director, Office of Science Policy, NIH
Dr. David Lepay, Director, Good Clinical Practices Program, FDA
Ms. Melinda Hill, OHRP
Ms. Patricia El-Hinnawy, OHRP