DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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October 20, 2003

Robert Kay, M.D.
Chief of Staff
Vice Chairman, Board of Governors
The Cleveland Clinic Foundation
9500 Euclid Avenue H18
Cleveland, OH 44195

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1388 and Federalwide Assurance FWA-5367

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. Herbert P. Wiedemann

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. Herbert P. Wiedemann

Dear Dr. Kay:

The Office for Human Research Protections (OHRP) has reviewed the August 28, 2003 report from the Cleveland Clinic Foundation (CCF) 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 CCF has implemented the required actions stipulated by OHRP's July 25, 2003 letter. In particular, OHRP acknowledges the following:

(1) The CCF 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) CCF has provided OHRP with a copy of the final version of the IRB-approved informed consent document.

(3) CCF has implemented a variety of procedures including IRB Reviewer Guidelines and Worksheet to ensure that the CCF IRBs (a) receive sufficient information to make all determinations required under HHS regulations at 45 CFR 46.111; and (b) approve an informed consent process that satisfies all requirements of HHS regulations at 45 CFR 46.116. OHRP recommends that the CCF ensure that the IRB application helps to ensure that the protocol contains sufficient information to make the determinations required under HHS regulations at 45 CFR 46.111 and that the informed consent document satisfies all requirements of HHS regulations at 45 CFR 46.116.

OHRP finds that the above corrective actions adequately address OHRP's findings and are appropriate under the CCF FWA. As a result, OHRP anticipates no need for further involvement with CCF 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. Alan Lichtin, Chair, IRB #1, CCF
Dr. Richard A. Rudick, Chair, Division of Clinical Research, CCF
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