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

James H. Shore, M.D.
Chancellor

Dr. John R. Sladek, Jr.
Vice Chancellor for Research
University of Colorado Health Sciences Center
4200 East 9th Avenue, A095
Denver, CO 80262

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1494 and Federalwide Assurance 5070

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. Edward Abraham

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. Edward Abraham

Dear Drs. Shore and Sladek:

The Office for Human Research Protections (OHRP) has reviewed the October 6 and December 4, 2003 reports from the University of Colorado Health Sciences Center (UCHSC) 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 UCHSC has implemented the required actions stipulated by OHRP's July 25, 2003 letter. In particular, OHRP acknowledges the following:

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

(3) UCHSC has implemented a variety of procedures including IRB Instructions for Clinical Investigators and the IRB Primary Reviewer Protocol Checklist to help ensure that the UCHSC IRBs receive sufficient information to make all determinations required under HHS regulations at 45 CFR 46.111. The UCHSC also lists the required elements of informed consent in the IRB Instructions for Clinical Investigators and in the IRB Primary Reviewer Protocol Checklist to help ensure that the UCHSC IRBs approve an informed consent process that satisfies all requirements of HHS regulations at 45 CFR 46.116. OHRP recommends that the IRB Instructions for Clinical Investigators and the IRB Primary Reviewer Protocol Checklist include the requirement that the informed consent document include a statement that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled (there could be penalties or loss of benefits other than medical care to which the subject is entitled).

OHRP finds that the above corrective actions adequately address OHRP's findings and are appropriate under the UCHSC FWA. As a result, OHRP anticipates no need for further involvement with UCHSC 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. Ken Easterday, Chair, COMIRB Panel A, UCHSC
Dr. Norman Stoller, Chair, COMIRB Panel B,UCHSC
Dr. Adam Rosenberg, Chair, COMIRB Panel C, UCHSC
Dr. William Jacobs, Chair, COMIRB Panels 1-8,UCHSC
Ms. Lisa Jensen, Director, COMIRB, UCHSC
Dr. Edward Abraham, Principal Investigator, UCHSC
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