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 13, 2004

Edgar Thorsland, Jr
Medical Center Director
Veterans Affairs Medical Center (151)
1055 Clermont St.
Denver, CO 80220

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1494 and Federalwide Assurance FWA-1681

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 Mr. Thorsland:

The Office for Human Research Protections (OHRP) has reviewed the October 7, 2003 and January 28, 2004 reports from the Denver Veterans Affairs Medical Center (Denver VA) 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 Denver VA 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) The Denver VA has provided OHRP with a copy of the final version of the IRB-approved informed consent document.

(3) UCSHC and the Denver VA have 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 Denver VA FWA. As a result, OHRP anticipates no need for further involvement with the Denver VA 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. Boris Draznin, Denver VA
Dr. Edward Abraham, Principal Investigator, Denver VA
Dr. David Weber, Acting Chief Officer, Office of Research Oversight, Dept of Veterans

Affairs
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
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