DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 301-402-5567
FAX: 301-402-2071
E-mail: mcarome@osophs.dhhs.gov

November 5, 2003

R. Timothy Rice
Chief Operating Officer
Moses Cone Health System
1200 N. Elm Street
Greensboro, North Carolina 27401

Donald D. Smith, M.D.
Vice President, Medical Education
Chairman, Institutional Review Board
Moses Cone Health System
1200 N. Elm Street
Greensboro, North Carolina 27401

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 4507

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: Patrick Wright, M.D.

Dear Mr. Rice and Dr. Smith:

The Office for Human Research Protections (OHRP) has reviewed Moses Cone Health System's (MCHS) August 26 and October 20, 2003 reports responding to allegations and concerns of possible noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects involving the above-referenced research.

OHRP acknowledges the following:

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

(3) MCHS has implemented a variety of procedures including an Application for IRB Review and Approval of a Human Research Proposal to help ensure that the MCHS IRB receives sufficient information to make all determinations required under HHS regulations at 45 CFR 46.111. In addition, MCHS has developed Standards for Informed Consent Documentation for Human Research Projects to help ensure that the MCHS IRB approves an informed consent process that 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 MCHS FWA. As a result, OHRP anticipates no need for further involvement with MCHS related to this matter.

At this time, OHRP offers the following additional guidance:

(1) HHS regulations at 45 CFR 46.116(a)(8) require that informed consent include a statement that participation is voluntary, 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. The MCHS model informed consent document states "without penalty and without jeopardizing the subject's continuing medical care at this institution." OHRP notes that there could be penalties or loss of benefits other than continuing medical care at MCHS.

(2) OHRP recommends that the Application for IRB Review and Approval include information regarding provision for monitoring the data collected to ensure the safety of subjects and that the IRB written procedures explicitly outline the criteria for IRB approval required under HHS regulations at 45 CFR 46.111.

OHRP appreciates the commitment of MCHS 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. Patrick Wright, Principal Investigator, FACTT Trial, MCHS
Dr. Donald Smith, IRB Chair, MCHS
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