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: 301-435-8072
FAX: 301-402-2071
E-mail:kborror@osophs.dhhs.gov

November 3, 2003

Donald E. Wilson M.D., M.A.
Dean, School of Medicine
University of Maryland at Baltimore
655 West Baltimore Street
Baltimore, MD 21201-1559

Dr. Dennis H. Smith
Director, Veterans Affairs Maryland Health Care System
Veterans Affairs Medical Center
10 North Greene Street
Baltimore, MD 21201

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1174 and Federalwide Assurance (FWA) 1483

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: Henry Silverman, M.D.

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: Henry Silverman, M.D.

Dear Drs. Wilson and Smith:

The Office for Human Research Protections (OHRP) has reviewed the University of Maryland, Baltimore's (UM) and Baltimore Veterans Affairs Medical Center's (VA) September 3, 2003

letters and October 28, 2003 email responding to determinations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects involved in the above-referenced research.

OHRP acknowledges the following:

> (1) The UM 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.
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> (2) UM and the Baltimore VA have provided OHRP with a copy of the final version of the IRB-approved informed consent document.
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> (3) UM has implemented a variety of procedures including a web-based system for research protocol creation to help ensure that the UM IRBs receive sufficient information to make all determinations required under HHS regulations at 45 CFR 46.111. The UM IRB also lists the required elements of informed consent in the UM IRB Policies and Procedures Manual and has developed a sample informed consent document to help ensure that the UM IRBs approve an informed consent process that satisfies all requirements of HHS regulations at 45 CFR 46.116. OHRP recommends that the criteria for IRB approval under HHS regulations at 45 CFR 46.111 be included in the UM IRB Policies and Procedures Manual or as a checklist for IRB members.

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

OHRP appreciates the commitment of UM and the Baltimore VA 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. Anne N. Hirshfield, HPA, UM
Dr. Robert Edelman, Chair, IRB, UM
Dr. Henry Silverman, Principal Investigator, ARMA and FACTT trials, UM
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
Ms. Patricia El-Hinnawy, OHRP