**DEPARTMENT OF HEALTH & HUMAN SERVICES**

**Office of the Secretary**
**Office of Public Health and Science**

**Office for Human Research Protections**
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November 10, 2003

Richard H. Dean, M.D.
President and Chief Executive Officer
Wake Forest University School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157

**RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1161 and Federalwide Assurance (FWA) 1435**

**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: R. Duncan Hite, M.D.**

Dear Dr. Dean:

The Office for Human Research Protections (OHRP) has reviewed Wake Forest University School of Medicine's (WFU) August 27 and October 27, 2003 reports responding to OHRP's July 25, 2003 letter regarding 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 WFU has implemented the required actions stipulated by OHRP's July 25, 2003 letter. In particular, OHRP acknowledges the following:

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

(3) WFU has revised the Protocol Application and Reviewer Comment Sheet to specifically address the required IRB determinations for approval of research at HHS regulations at 45 CFR 46.111 and the requirements for informed consent under HHS regulations at 45 CFR 46.116. In addition, information stressing the importance of these elements was included in the monthly newsletter published by the WFU Office of Research. The importance of assuring that sufficient information is received and considered by the WFU IRB was stressed at the IRB Members Update Program in August of 2003, and IRB members have been provided with the series of articles published in the New England Journal of Medicine related to this matter.

OHRP finds that the above corrective actions adequately address the findings and are appropriate under the WFU FWA. As a result, OHRP anticipates no need for further involvement with WFU regarding this matter.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please 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. Wesley G. Byerly, Director, IRB, WFU
Dr. Richard Weinberg, Chair, IRB #1, WFU
Dr. Ronald Smith, Chair, IRB #2 and #4, WFU
Dr. Robert DuRant, Chair, IRB #3, WFU
Dr. R. Duncan Hite, Principal Investigator, FACTT trial, WFU
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