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 17, 2003

Joseph Moerschbaecher, Ph.D.
Vice Chancellor for Academic Affairs
Louisiana State University Health Sciences Center
433 Bolivar Street, Suite 824
New Orleans, LA 70112-2223

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 2762

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. Bennett DeBoisblanc

Dear Dr. Moerschbaecher:

The Office for Human Research Protections (OHRP) has reviewed Louisiana State University Health Science Center's (LSU) April 9 and October 29, 2003 reports 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 LSU has implemented the required actions stipulated by OHRP's July 25, 2003 letter. In particular, OHRP acknowledges the following:

(1) The LSU 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) LSU has provided OHRP with a copy of the final version of the IRB-approved

informed consent document.

(3) LSU has implemented a variety of procedures including a reviewer checklist to ensure that the protocol contains sufficient information to make the determinations required under HHS regulations at 45 CFR 46.111 and that the informed consent document satisfies all requirements of HHS regulations at 45 CFR 46.116. The LSU IRB utilizes a primary reviewer system, and in some cases a secondary reviewer, to help ensure that the IRB receives sufficient information. LSU has also developed clinical research protocol summary instructions and informed consent document instructions for investigators soliciting the information required for IRB approval of the research and legally-effective informed consent.

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

At this time, OHRP provides the following additional guidance:

(4) OHRP notes that, while the LSU IRB checklists and instructions include prompts for mention of confidentiality protections in the informed consent document, they do not include prompts for the inclusion of a description of these protections in the protocol. OHRP recommends the addition of such prompts.

(5) Page 3 of LSU's April 9, 2003 report indicates that if the IRB feels that additional information is required to make a final determination whether a study should be approved, the IRB requests additional information from the investigator. This is typically done as "Approval with Changes." The information required by the IRB is then reviewed by the IRB chair or his designee among the members of the IRB.

OHRP recommends the following guidelines in such cases: (a) When the convened IRB requests substantive clarifications or modifications regarding the protocol or informed consent documents that are directly relevant to the determinations required by the IRB under HHS regulations at 45 CFR 46.111, IRB approval of the proposed research should be **deferred**, pending subsequent review by the convened IRB of responsive material. (b) Only when the convened IRB stipulates specific revisions requiring simple concurrence by the investigator may the IRB Chair or another IRB member designated by the Chair subsequently approve the revised research protocol on behalf of the IRB under an expedited review procedure.

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: Ms. Charlene Valvoord, Senior IRB Coordinator, LSU
Dr. Kenneth Kratz, Chair, IRB, LSU
Dr. Bennett DeBoisblanc, Principal Investigator, FACTT trial, LSU
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