DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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March 21, 2003

Craig J. Hogan, Ph.D.
Vice Provost for Research
Office of the Provost
Box 351202
University of Washington
G80 Gerberding Hall
Seattle, WA 98195

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1183

Research Publication: Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Respiratory Distress Syndrome. (N Engl J Med 2000; 342:1301-8)
Project Title: Prospective, Randomized, Multicenter Trial of 12 mL/jg vs. 6mL/kg TidalVolume Positive Pressure Ventilation and Ketoconazole vs. Placebo for Treatment of Acute Respiratory Distress Syndrome
Principal Investigator: Dr. Leonard D. Hudson
HHS Project Number: N01-HR46055

Dear Dr. Hogan:

The Office for Human Research Protections (OHRP) has reviewed the University of Washington's (UW) August 13, 2002 report that was submitted in response to OHRP's February 4, 2002 letter regarding the above-referenced research.

Based upon its review, OHRP makes the following additional determinations regarding the above-referenced research:

(1) OHRP finds that UW has taken appropriate corrective actions to address the findings of noncompliance in OHRP's February 4, 2002 letter and are appropriate under the UW MPA. In particular, OHRP acknowledges that UW implemented improved training for institutional review board (IRB) members, staff and investigators including (i) orientations for new IRB members regarding human subjects protections and relevant regulations; (ii) tutorials for investigators on the human subjects research review process; (iii) institution of the CITI web-based tutorial for all faculty, staff, and students; and (iv) continued training sessions on the ethical conduct of research for faculty, staff, and students.

(2) Department of Health and Human Services (HHS) regulations at 45 CFR 46.111(b) stipulate that in order to approve research, the IRB shall determine that when some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of the subjects. In its February 4, 2002 letter, OHRP expressed concern that the UW IRB may have failed to ensure that this requirement was satisfied for the above-referenced research.

OHRP finds that UW has adequately addressed this concern. Furthermore, OHRP acknowledges that UW has a policy to ensure that additional safeguards are included in research involving subjects who may be vulnerable to coercion or undue influence.

(3) OHRP finds that UW has adequately addressed the additional concerns raised in OHRP's February 4, 2002 letter.

At this time OHRP would like to provide the following additional guidance:

HHS regulations at 45 CFR 46.107(c) require that an IRB shall include at least one member whose primary concerns are in nonscientific areas. Furthermore, HHS regulations at 45 CFR 46.108(b) require that except when an expedited review process is used, an IRB will review proposed research at convened meetings at which a majority of members are present, including at least one member whose primary concerns are in nonscientific areas. UW's August 13, 2002 report stated "... we have taken steps to make sure that a person who does not have experience conducting medical research, and does not hold a tertiary degree is always present at a meeting at which IRB votes and actions take place." OHRP notes that the requirements of the regulations are specific with regard to inclusion of a member **whose primary concerns are in nonscientific areas** as part of the IRB. UW's description of members (i.e., a person who does not have experience conducting medical research, and does not hold a tertiary degree) may not meet the requirements set forth under the HHS regulations. OHRP recommends that UW ensure that the composition of each of its IRBs meet the requirements of HHS regulations at 45 CFR 46.107(c).

As a result of the above determinations, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Ms. Helen McGough, Director, Humans Subjects Division, UW
Dr. Zane Brown, Chair Human Subjects Committee A, UW
Dr. Alen Wilenski, Chair Human Subjects Committee B, UW
Dr. Patricia Kuszler, Chair Human Subjects Committee C, UW
Dr. Rebekah Rein, Chair Human Subjects Committee D, UW
Dr. Nancy Robinson, Chair Human Subjects Committee G, UW
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