DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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July 31, 2002

Alvin W. Kwiram, Ph.D.
Vice Provost for Research
Office of the Provost
Box 351237
University of Washington
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Seattle, Washington 98195

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

Research Project: A Multicenter, Double-Blind, Placebo-Controlled Study of Estrogen Replacement Therapy in Patients with Mild to Moderate Alzheimer's Disease
Principal Investigator: Murray A. Raskind, M.D.
HHS Project Number: U01-AG10483

Research Publication: Estrogen Replacement Therapy for Treatment of Mild to Moderate Alzheimer Disease: A Randomized Controlled Trial (Mulnard, et al. JAMA. 2000;283:1007-1015)

Dear Dr. Kwiram:

The Office for Human Research Protections (OHRP) has reviewed the University of Washington's (UW's) June 26, 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 determinations regarding the above-referenced research:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.111(b) stipulate that in order to approve research, the Institutional Review Board (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 responded to this concern. Furthermore, OHRP acknowledges that the UW IRBs have implemented procedures to ensure consideration of additional safeguards for subjects who may be vulnerable as a result of impaired mental capacity.

(2) HHS regulations at 45 CFR 46.116(a)(1) require that when seeking informed consent, each subject be provided with, among other things, a description of the procedures to be followed and identification of any procedures which are experimental. OHRP finds that the informed consent documents approved by the UW IRB failed to include an adequate description of the procedure for performing the lumbar punctures.

(3) HHS regulations at 45 CFR 46.116(a)(2) require that when seeking informed consent, each subject be provided with a description of any reasonably foreseeable risks or discomforts to the subject. OHRP finds that the informed consent documents approved by the UW IRB failed to adequately describe the risk of the lumbar puncture procedures.

Corrective actions: OHRP acknowledges that (i) the research has been completed; (ii) none of the subjects enrolled at UW underwent the lumbar puncture procedures; and (iii) UW will reiterate to its IRB members the importance of including in informed consent documents an adequate description of all procedures that subjects will undergo and the reasonably foreseeable risks of these procedures. OHRP finds this corrective action to be satisfactory and appropriate under the UW MPA.

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

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 commitment of UW to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Michael A. Carome, M.D.
Director, Division of Compliance Oversight

cc: Ms. Helen McGough, Manager, Human Subjects Division, UW
Dr. Zane A. Brown, Chairperson, IRB-01, UW
Dr. Alan J. Wilensky, Chairperson, IRB-02, UW
Dr. Patricia Kuszler, Chairperson, IRB-03, UW
Dr. Sharon Durfy, Chairperson, IRB-04, UW
Dr. Murray A. Raskind, UW
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Dr. David Lepay, FDA
Dr. Greg Koski, OHRP
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Mr. George Gasparis, OHRP
Dr. Kamal Mittal, OHRP
Mr. Barry Bowman, OHRP