DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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April 2, 2002

Dr. K. Michael Welch
Vice Chancellor for Research
University of Kansas Medical Center
3901 Rainbow Boulevard
Kansas City, Kansas 66160-7700

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1122

Research Project: A Multicenter, Double-Blind, Placebo-Controlled Study of Estrogen Replacement Therapy in Patients with Mild to Moderate Alzheimer's Disease
Principal Investigator: Charles DeCarli, M.D.
HHS Project Number: U01-AG10483
IRB Project Number: 6523-95

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. Welch:

The Office for Human Research Protections (OHRP) has reviewed the University of Kansas Medical Center's (KUMC's) March 20, 2002 report that was submitted in response to OHRP's February 6, 2002 letter regarding the above-referenced research.

Based upon its review, OHRP makes the following determinations:

(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 6, 2002 letter, OHRP expressed concern that the KUMC's IRB may have failed to ensure that this requirement was satisfied for the above-referenced research.

OHRP finds that KUMC has adequately responded to this concern. Furthermore, OHRP acknowledges that KUMC's IRB has implemented procedures to enhance protection of 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 KUMC's IRB for the above-referenced research failed to include a description of the procedure for having the subject's caregiver fill out quality-of-life and pharmacoeconomic questionnaires related to the subject's condition and care.

Corrective Action: OHRP acknowledges that (i) the research has been completed; and (ii) KUMC's statement in its report of March 20, 2002 that the KUMC IRB requires disclosure of caregiver responsibilities in the informed consent document. OHRP finds this response to be satisfactory and appropriate under KUMC's MPA.

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

Sincerely,

Leslie K. Ball, M.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Ms. Vickie S. Eaton, Director Research Administration, KUMC
Dr. Jerry Menikoff, Chair, IRB-01, KUMC
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