DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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June 28, 2006

William F. Owen, Jr., M.D.
Chancellor
The University of Tennessee Health Science Center
62 South Dunlop Street
Memphis, TN 38163

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1056 and Federalwide Assurance (FWA) 2301

Research Project: A Clinical Trial of Two Medications on Smoking Cessation ("STAR Study")
Principal Investigator: Karen C. Johnson, M.D., M.P.H.
HHS Grant Number: R01 HL066025

Dear Dr. Owen:

The Office for Human Research Protections (OHRP) has reviewed the University of Tennessee's (UT) June 9, 2006 letter responding to OHRP's May 17, 2006 letter concerning the above-referenced UT research project (hereinafter referenced as "STAR Study").

In addition to OHRP's findings in its May 17, 2006 letter, OHRP makes the following determinations regarding allegations of noncompliance in the STAR study with Department of Health and Human Services (HHS) regulations protecting human research subjects (45 CFR part 46).

(1) HHS regulations at 45 CFR 46.116(a)(1) require that informed consent documents contain a description of any procedures to be followed, and identification of any procedures which are experimental, in a language understandable to all subjects. OHRP found that STAR consent documents did not describe all medical or research procedures in a manner that would be understandable to the target STAR population of young, low income smokers.

Corrective Action: OHRP acknowledges that following receipt of OHRP's May 17, 2006 letter, UT made several modifications to the STAR consent form. Specifically, the form now (a) defines "Zyban", "NRT" (nicotine replacement therapy), and "blood repository"; (b) notifies subjects about contact and investigative procedures researchers employ to track

down subjects who fail to attend follow-up clinic visits; and (c) informs subjects that if they withdraw from the study, any data collected up until the time of withdrawal will remain part of the study.

(2) HHS regulations at 45 CFR 46.116(a)(7) require that the following information be provided to subjects in the informed consent process:

> An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

OHRP found that the STAR informed consent document provided incorrect information concerning the individual to contact for after-hours questions or in the event that subjects experience any injury as a result of the study.

Corrective Action: OHRP acknowledges that UT modified the STAR consent form to clarify that the telephone number for the primary STAR investigator, when called after business hours, connects to an answering service which will direct calls to a nurse or other physician designated to take the evening/weekend call.

(3) In its May 17, 2006 letter, OHRP expressed concern that changes in approved protocol activities were implemented by STAR investigators without IRB review and approval, in violation of HHS regulations at 45 CFR 46.103(b)(4)(iii). Specifically,

> (a) OHRP received allegations that the investigative team may not have included a sufficient number of appropriately trained personnel at all times to meet the following project staffing needs set forth in the protocol:
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> > Every detail of all of the study visits will be planned and staff roles clearly delineated. . . . Sufficient time will be spent with each potential participant to instruct them about the study and what will be expected of them (page 13 of 17).
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> (b) OHRP received allegations that subjects with a history of drug abuse, eating disorders (anorexia or bulimia), and eczematous dermatitis may have been inappropriately enrolled in the study despite exclusion criteria prohibiting enrollment of such subjects.
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> (c) OHRP received allegations that STAR investigators may have told study personnel to ignore subject requests to withdraw from the research and to continue contacting subjects who verbally expressed the desire to withdraw, in violation of informed consent provisions permitting subjects to withdraw at any time without penalty or denial of benefit.

Based upon UT's responses to OHRP's expressed concerns, OHRP does not find evidence sufficient to support the allegations raised in (3)(a)-(c).

OHRP finds that the corrective actions detailed above adequately address related determinations and are appropriate under UT's FWA. As a result, there should be no need for further OHRP involvement, unless UT uncovers additional facts indicating possible noncompliance with the HHS regulations.

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

Sincerely,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

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