DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 240-453-8132
FAX: 240-453-6909
E-mail:kborror@osophs.dhhs.gov

December 13, 2005

Nathaniel Brown, M.D.
Mid-Delta Family Practice Clinic
P.O. Box 1040
403 South Davis Ave
Cleveland, MS 38732

J. Reid Jones, Ph.D.
IRB Chairperson/Academic Research Coordinator
Delta State University
P.O. Box 3115
Cleveland, MS 38733

RE: Human Research Subject Protections Under Federalwide Assurances FWA- 1198

Research Project: Phase III Randomized Study of Selenium and Vitamin E for the Prevention of Prostate Cancer– SELECT
Project Number: SWOG-S0000
Principal Investigator: **Nathaniel Brown, M.D.**

Dear Drs. Brown and Jones:

The Office for Human Research Protections (OHRP) has reviewed the Mid-Delta Family Practice Clinic's (MDFPC) and Delta State University institutional review board's (DSU IRB) September 27, 2005 report responding to allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46). OHRP notes that MDFPC has designated only the DSU IRB for review of research covered by the MDFPC FWA.

Based upon its review, OHRP makes the following determinations regarding human subjects protections at MDFPC and DSU IRB:

(1) OHRP finds that neither MDFPC nor its designated IRB, the DSU IRB, have written IRB procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5):

(a) The procedures which the IRB will follow for conducting its initial review of research.

(b) The procedures which the IRB will follow for conducting its continuing review of research.

(c) The procedures which the IRB will follow for reporting its findings and actions to investigators and the institution.

(d) The procedures which the IRB will follow for determining which projects require review more often than annually.

(e) The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

(f) The procedures which the IRB will follow for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(g) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any department or agency head, and OHRP of: (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

Required Action: By January 20, 2006, please provide OHRP with revised written IRB procedures to address this finding.

(2) HHS regulations at 45 CFR 46.116(a)(2) require that when seeking informed consent for the research, subjects be provided with an adequate description of the reasonably foreseeable risks and discomforts. OHRP finds that subjects were not informed in a timely manner of new findings of selenium toxicity. In specific, these new findings were communicated to Dr. Brown by October 2004; however, your September 14, 2005 report to OHRP indicates that this letter was not approved by the IRB until March 31, 2005 and was not distributed to subjects until after March 31, 2005.

Required Action: By January 20, 2006, please provide OHRP with a satisfactory corrective action plan to address this finding.

(3) HHS regulations at 45 CFR 46.115(a)(2) require, among other things, that minutes

of IRB meetings be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining. OHRP finds that DSU IRB minutes fail to meet these requirements. In addition, OHRP was not able to locate minutes from IRB meetings held May 3, 2001 and April 22, 2003.

Required Action: By January 20, 2005, please provide OHRP with a satisfactory corrective action plan to address this finding.

OHRP has the following additional questions and concerns:

(5) [Redacted]

(6) [Redacted]

(7)[Redacted]

(8) [Redacted]

(9)[Redacted]

Please provide OHRP with corrective actions to address the above findings and responses to above questions and concerns no later than January 20, 2005.

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

Sincerely,

Kristina C. Borror, Ph.D.
Director
Division of Compliance Oversight

cc: Commissioner, FDA
Dr. David Lepay, FDA
Dr. Lana Skirboll, Director, Office of Science Policy, NIH
Ms. Joan Mauer, CTEP, NCI, NIH
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Ms. Janet Fant, OHRP

Ms. Patricia El-Hinnawy, OHRP