DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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February 14, 2006

Seymour Mitchell, M.S.W.
CEO
Delta Health Center
702 Martin Luther King Road, P.O. Box 900
Mound Bayou, MS 38762

RE: Human Research Subject Protections Under Federalwide Assurance FWA- 2033

Research Project: Phase III Randomized Study of Selenium and Vitamin E for the Prevention of Prostate Cancer– SELECT
Project Number: SWOG-S0000

Dear Mr. Mitchell:

The Office for Human Research Protections (OHRP) has reviewed the Delta Health Center's (DHC) December 20, 2005 report and Delta State University institutional review board's (DSU IRB's) January 16, 2006 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).

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

(1) OHRP finds that neither DHC 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 reporting its findings and actions to investigators and the institution.

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

(c) 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.

> (d) 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.
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> (e) 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.

Corrective Action: OHRP acknowledges that the DSU IRB has decided to withdraw as the IRB for DHC, agreeing to serve on a temporary basis until they are able to establish a relationship with a new IRB. OHRP also acknowledges that the DSU IRB did not send all the IRB written procedures initially, and has revised those procedures. OHRP notes that DHC plans to make arrangement with an independent IRB to review human subjects research conducted at DHC. By March 28, 2006 please provide OHRP with an update on these arrangements.

(2) HHS regulations at 45 CFR 46.103(b)(4)(iii) require the IRB to review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. OHRP finds that certain amendments to the SELECT protocol were not reviewed and approved by the DSU IRB prior to their implementation and that several subjects were enrolled in research who did not meet the eligibility criteria. For example, amendment #1 was distributed to SELECT sites in February 2002, revision #1 was distributed in January 2003, and revision #2 was distributed in October 2003, but the DSU IRB did not review these revisions and amendment until March 31, 2005. In addition, the Southwest Oncology Group (SWOG) audit indicates that 5 of 11 participants whose records were audited were not eligible to be enrolled (there was no documentation that the subjects met the eligibility criteria.)

Corrective Action: OHRP acknowledges that DHC plans to educate SELECT staff on documentation and charts will be systematically reviewed. In addition, additional staff are to be recruited.

Required Action: By March 28, 2006, please provide OHRP with a status report of the above corrective actions, and additional corrective actions to ensure that amendments are submitted to the IRB and approved prior to their implementation.

(3) OHRP finds that the DSU IRB failed to conduct continuing review at least once per year, as required by HHS regulations at 45 CFR 46.109(e).

Corrective Action: OHRP acknowledges DHC's statement that a plan is being develop to track continuing IRB reviews in the future.

Required Action: By March 28, 2006, please provide OHRP with a copy of the plan to track IRB continuing reviews.

(4) 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 found that subjects were not informed in a timely manner of new findings of selenium toxicity.

Corrective Action: OHRP acknowledges that DHC plans to contact participants to provide the additional information.

Required Action: By March 28, 2006, please provide OHRP with a copy of all IRB-approved informed consent documents for the SELECT study used by the DHC.

Please provide OHRP with corrective actions to address the above findings no later than March 28, 2006.

Please note that DHC FWA 2625 has been deactivated and FWA 2033 was renewed. DHC had been erroneously awarded two assurances and this error has now been corrected.

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: Dr. J. Reid Jones, IRB Chairperson/Academic Research Coordinator, Delta State U
Dr. Suzette Hornsby-Odoi, MD, Dir. Clin. Services, Delta Health Center
James L. Potts, M.D., Chairperson, IRB, Meharry Medical College
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