DEPARTMENT OF HEALTH & HUMAN SERVICES

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James McGahee
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RE: Human Research Subject Protections Under Cooperative Project Assurance (CPA) T-4142 – Southwest Oncology Group Clinical Trials

Dear Mr. Sauls and Mr. McGahee:

The Office for Human Research Protections (OHRP) has reviewed South Georgia Medical Center's (SGMC's) July 26, 2000 corrective action plan (CAP) to address deficiencies and concerns cited in OHRP's June 13, 2000 letter. OHRP finds that SGMC's revised practices and policies as outlined in the CAP adequately respond to the issues OHRP raised, as follows:

(1) OHRP found that based upon SGMC's IRB minutes and description of continuing review procedures, continuing review of human subject research by the SGMC IRB was not substantive and meaningful. SGMC's description in its July 26, 2000 report of its revised continuing review practices indicates that SGMC is providing all members prior to IRB meetings with sufficient information to make the determinations required for continuing review. In addition, the IRB minutes sent with SGMC's report appropriately document separate deliberations, actions and votes for each protocol undergoing continuing review by the convened IRB, in accordance with OHRP guidance.

(2) OHRP found in its June 13, 2000 letter that the IRB failed to conduct continuing review of the SWOG 9343 protocol at least annually as required by 45 CFR 46.109(e). OHRP finds that SGMC has subsequently implemented an administrative procedure to

ensure that continuing review of research occurs prior to a protocol's specified expiration date.

(3) HHS regulations at 45 CFR 46.103(b)(4)(iii) require the IRB to conduct prior review and approval of changes proposed in research studies before expiration of the approval period, except when such changes are necessary to eliminate apparent immediate hazards to subjects. OHRP expressed concern that (i) protocol amendments for certain Southwest Oncology Group (SWOG) Clinical Trials were implemented by investigators before they were submitted to the IRB for review, and that (ii) protocol amendments were presented at IRB meetings without prior distribution to IRB members. OHRP acknowledges that SGMC IRB members now receive all proposed changes in approved research two weeks in advance of the IRB meeting. However, OHRP remains concerned that SGMC appears not to have addressed the problem of investigators initiating protocol amendments without prior IRB review and approval.

Recommended Action: OHRP strongly recommends that SGMC educate investigators that HHS regulations at 45 CFR 46.103(b)(4)(iii) require IRB approval of all amendments before their implementation, including amendments developed by SWOG, except for amendments necessary to eliminate apparent immediate hazards to subjects.

(4) OHRP found that the minutes of SGMC IRB meetings did not reflect systematic consideration of the determinations required under HHS regulations at 45 CFR 46.111, including equitable selection of subjects and subject recruitment, privacy and confidentiality protections, and special protections required for vulnerable populations. OHRP further found that the minutes did not separately document, for each individual protocol undergoing review, IRB deliberations, actions, and votes, as required by HHS regulations at 45 CFR 46.115(a)(2).

OHRP finds that minutes of the SGMC IRB submitted with its report reflect consideration of protocols individually, and document actions taken by the IRB, votes on these actions (including the numbers of members voting for, against, and abstaining); the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. In addition, minutes indicate that the IRB makes the determinations required under 45 CFR 46.111 before approving research projects.

(5) OHRP found that SGMC did not have written IRB policies and procedures that adequately described the activities outlined in 45 CFR 46.103(b)(4) and (5).

SGMC submitted with its report revised Policies and Procedures which included the review and reporting procedures required at 45 CFR 46.103(b)(4) and (5). SGMC indicated that the policy was scheduled for presentation to the IRB. Presuming ultimate approval by the IRB and SGMC, OHRP finds that SGMC now has written policies and procedures that incorporate the requirements of 45 CFR 46.103(b)(4) and (5).

(6) OHRP strongly recommended that SGMC develop and distribute a handbook of IRB guidelines for research investigators. OHRP finds that SGMC's revised IRB Policies and Procedures provide important and adequate guidance to investigators.

As a result of the above findings and corrective actions, there should be no need for further involvement of OHRP in this matter. Of course, OHRP should be notified immediately of any new developments that might alter the above determination.

Upon review of SGMC's IRB Policies and Procdures, OHRP adds the following guidance:

(7) SGMC's policies appears to conflate the concepts of minimal risk and exempt research. The section on research exempt from IRB review (page 4 of Policies and Procedures) lists as exempt

> "Research in which the risks of harm reasonably anticipated are not greater than those ordinarily encountered in daily life or during the performance of routine procedures in education or practices in psychology or medicine."

This description pertains to the definition of minimal risk at 45 CFR 46.102(I), but does not constitute a standard for exemption from IRB review.

OHRP appreciates SGMC's continued commitment to the protection of human research subjects.

Sincerely,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Division of Human Subject Protections

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