DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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March 18, 2002

William S. Minogue, M.D.
Interim President and Chief Executive Officer
Suburban Hospital
8600 Old Georgetown Road
Bethesda, MD 20814

RE: Human Research Subject Protections Under Cooperative Project Assurance (CPA) T-3753

Dear Dr. Minogue:

The Office for Human Research Protections (OHRP) has reviewed your December 18, 2001 letter, describing corrective actions implemented by Suburban Hospital (SH) following OHRP's on-site evaluation of human subject protection procedures at SH on September 25-26, 2001. Based upon this review, OHRP makes the following determinations relative to SH's system for protecting human research subjects.

(1) OHRP finds that the SH institutional review board's (IRB's) revised application for approval of research (10/01 version), solicits from investigators sufficient information for the IRB to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111, including that (a) the selection of subjects is equitable; (b) subjects' privacy and the confidentiality of data are adequately protected, and (c) there are additional safeguards to protect the rights and welfare of subjects who are likely to be vulnerable.

(2) OHRP finds that the SH IRB minutes submitted with SH's December 18, 2001 letter are in compliance with HHS regulatory requirements at 45 CFR 46.115(a)(2), including documentation of the number 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.

(3) OHRP finds that SH has taken initial steps to revise its written IRB policies and procedures to comply with HHS regulations at 45 CFR 46.103(b)(4) and (5), which require institutions to have written IRB policies and procedures for: (a) conducting initial and continuing review of

> research, (b) reporting findings and actions to investigators and the institution, (c) determining which projects require review more often than annually, (d) determining which projects need verification from sources other than investigators that no material changes have occurred since previous IRB review, (e) ensuring prompt reporting to the IRB of proposed changes in research activities and that such changes are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects, and (f) ensuring prompt reporting to the IRB, appropriate institutional officials, any Department or Agency head, and OHRP of (i)any unanticipated problems involving risks to subjects or others, (ii) serious or continuing noncompliance with HHS regulations at 45 CFR Part 46 or the requirements or determinations of the IRB, and (iii) any suspension or termination of IRB approval.

At this time, OHRP provides the following additional guidance to SH on the operational details that should be described in written IRB policies and procedures to comply with HHS regulations at 45 CFR 46.103(b)(4) and (5):

> (4) Written IRB policies and procedures should provide operational details for each of the written IRB procedures required under 45 CFR 46.103(b)(4) and (5). Important operational details for the above procedures should include:
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> > (a) A description of SH's primary reviewer system used for initial review, continuing review, review of protocol changes, and/or review of reports of unanticipated problems involving risks to subjects or others, or of serious or continuing noncompliance.
> >
> > (b) Lists of specific documents distributed to primary reviewers (if applicable) and to all other IRB members for initial review, continuing review, review of protocol changes, and review of reports of unanticipated problems involving risks to subjects or others or of serious or continuing noncompliance.
> >
> > (c) Details of any additional process (e.g., a subcommittee procedure) that may be used to supplement the IRB's initial review, continuing review, review of protocol changes, and/or review of reports of unanticipated problems involving risks to subjects or others or of serious or continuing noncompliance.
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> > (d) The timing of document distribution prior to IRB meetings.
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> > (e) The range of possible actions taken by the IRB for protocols undergoing initial or continuing review and protocol changes undergoing review.
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> > (f) A description of how expedited review is conducted and how expedited approval actions are communicated to all IRB members.
> >
> > (g) A description of the procedures for (a) communicating to investigators IRB action

regarding proposed research and any modifications or clarifications required by the IRB as a condition for IRB approval of proposed research; and (b) reviewing and acting upon investigators' responses.

(h) A description of which institutional office(s) and official(s) are notified of IRB findings and actions and how notification to each is accomplished.

(i) A description, if applicable, of which institutional office(s) or official(s) is responsible for further review and approval or disapproval of research that is approved by the IRB. Please note that, in accordance with HHS regulations at 45 CFR 46.112, no other institutional office or official may approve research that has not been approved by the IRB.

(j) A specific procedure for how the IRB determines which protocols require review more often than annually, including specific criteria used to make these determinations (e.g., an IRB may set a shorter approval period for high-risk protocols or protocols with a high risk:potential benefit ratio).

(k) A specific procedure for how the IRB determines which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review, including specific criteria used to make these determinations (for example, such criteria could include some or all of the following: (i) randomly selected projects; (ii) complex projects involving unusual levels or types of risk to subjects; (iii) projects conducted by investigators who previously have failed to comply with the requirements of the HHS regulations or the requirements or determinations of the IRB; and (iv) projects where concern about possible material changes occurring without IRB approval have been raised based upon information provided in continuing review reports or from other sources).

(l) A description of what steps are taken to ensure that investigators do not implement any protocol changes without prior IRB review and approval, except when necessary to eliminate apparent immediate hazards to subjects (e.g., this might be addressed through training programs and materials for investigators and in specific directives included in approval letters to investigators).

(m) A description of which office(s) or institutional official(s) is responsible for promptly reporting to the IRB, appropriate institutional officials, any supporting Agency or Department heads, and OHRP any (i) unanticipated problems involving risks to subjects or others; (ii) any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and (iii) any suspension or termination of IRB approval.

(n) A description of the required time frame for accomplishing the reporting requirements in the preceding paragraph.

(o) The range of possible actions taken by the IRB in response to reports of unanticipated problems involving risks to subjects or others or of serious or continuing noncompliance.

Presuming full implementation of the corrective actions described in SH's letters of October 26 and December 18, 2001, there should be no need for further involvement of OHRP in this matter.

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

Sincerely,

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

cc: Dr. Michael Carome, OHRP
Dr. Jeffrey Cohen, OHRP
Mr. George Gasparis, OHRP
Dr. Melody H. Lin, OHRP
Dr. Greg Koski, OHRP
Mr. Barry Bowman, OHRP
Mr. Harold Blatt, OHRP
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Warren Ashe, Howard University College of Medicine