DEPARTMENT OF HEALTH & HUMAN SERVICES

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Norman H. Altman, V.M.D.
Vice Provost for Research
Office of Research
University of Miami
1600 N.W. 10th Avenue, RMSB 1128A
Miami, Florida 33101

RE: Human Research Protections Under Multiple Project Assurance (MPA) #1196 Research Projects:(1) Women's Health Initiative Clinical Trial and Observational Study (WHI); (2)Pediatric Oncology Group(POG) protocols

Dear Dr. Altman:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your reports dated November 17, 1998 and July 28, 1999 concerning the referenced research projects, the minutes of the University of Miami Institutional Review Board (IRB) conducted from January through December 1999, and the April 8, 1999 revised IRB Policies and Procedures.

OHRP has made the following determinations concerning the WHI protocol:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46. 46.103 (b)(5) requires that institutions have written procedures for ensuring prompt reporting to appropriate institutional officials, and the Department or Agency head of any unanticipated problems involving risks to subjects or others, or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB.

The OHRP finds that unanticipated problems involving risks to subjects or others were not reported by the principal investigator to appropriate institutional officials, the IRB, and the OHRP as required by HHS regulations at 45 CFR 46.103(b)(5).

Corrective Actions: The University of Miami has revised its Policies and Procedures and its Guidelines for Investigators to include detailed information concerning the requirements and procedures for notifying the IRB of unanticipated problems or events involving risks to subjects or others, or any serious or continuing noncompliance with this policy, or the requirements or determinations of the IRB. Furthermore, OHRP acknowledges that the principal investigator on the WHI was replaced.

(2) HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted at intervals appropriate to the degree of risk and not less than once per year. The regulations make no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval. If the IRB does not re-approve the research by the specified expiration date, subject accrual should be suspended pending re-approval of the research by the IRB. (Enrollment of new subjects cannot ordinarily occur after the expiration of IRB approval. Continuation of research interventions or interactions in already enrolled subjects should only continue when the IRB finds that it is in the best interests of individual subjects to do so. OPRR and IRBs must address on a case-by-case basis those rare instances where failure to enroll would seriously jeopardize the safety or well-being of an individual **prospective** subject.)

OPRR found instances in which extensions beyond the expiration date were granted.

Corrective Action: The University of Miami has revised its Policies and Procedures to include actions to be taken when the approval period has expired.

OHRP has made the following determinations concerning the POG research:

(3) HHS regulations at 45 CFR 46.110(b)(2) permit use of expedited procedures for review of minor changes to previously approved research. OHRP is aware that there are possible inconsistencies between POG's policy and HHS regulations. OHRP acknowledges that the University of Miami has instituted a policy in which all POG amendments go to the full IRB for review.

(4) As stated above, HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted at intervals appropriate to the degree of risk and not less than once per year.

OHRP found numerous instances in which extensions were granted beyond the expiration date.

Corrective Action: As stated above regarding the WHI protocol, the University of Miami has revised its Policies and Procedures to include actions to be taken when the approval period has expired.

The corrective actions described above appropriately address the issues raised by OHRP concerning the research referenced above. As a result there should be no need for further involvement of OHRP in these matters. Of course, OHRP should be notified should new information be identified which might alter this determination.

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

Sincerely,

Sanford Leikin, M.D.
Compliance Oversight Coordinator
Division of Human Subject Protections

cc: Dr. J. Thomas Puglisi, OHRP
Dr. Melody Lin, OHRP
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