DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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November 22, 2006

Patrice M. DiMario, M.S., R.N.
Sr. Vice President, Patient Support Services
Women & Infants Hospital of Rhode Island
101 Dudley Street
Providence, R.I. 02905

RE: Human Research Subject Protections Under Federalwide Assurance FWA-56

Research Project: A Phase III Randomized Trial of Paclitaxel and Carboplatin vs. Triplet or Sequential Doublet Combinations in Patients with Epithelial Ovarian or Primary Peritoneal Carcinoma
Principal Investigator: Paul A. DiSilvestro, M.D.
Project Number: GOG Protocol 182

Dear Ms. DiMario:

The Office of Human Research Protections (OHRP) has reviewed Women & Infants Hospital of Rhode Island's (WIH) October 18, 2006 letter responding to OHRP's September 25, 2006 letter concerning the above-referenced research study.

In addition to its September 25, 2006 findings, OHRP makes the following determinations regarding allegations of noncompliance by WIH with Department of Health and Human Services (HHS) regulations protecting human research subjects (45 CFR part 46).

(1) HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5) require that institutions have written institutional review board (IRB) procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, 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. OHRP found that a randomization error by WIH investigators in the above research represented an unanticipated problem involving risk to the subject. OHRP also found that the investigators failed to report this unanticipated problem to the WIH IRB.

Corrective Action: WIH has expanded its reporting policy to include the requirement to

report problems which place subjects or others at risk of serious harm. The amended policy includes a form to be used when reporting problems. The form and policy were distributed to all current investigators and research coordinators at WIH and is accessible on the hospital's intranet.

(2) HHS regulations at 45 CFR 46.116 require investigators to seek consent for research participation under circumstances that provide prospective subjects with sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. In its September 25, 2006 letter, OHRP expressed concern regarding allegations that the principal investigator discussed enrollment in the above research with a surgical patient and subsequent research subject in a manner that did not afford the subject sufficient opportunity to consider whether or not to participate, or minimize the possibility of undue influence, in violation of 45 CFR 46.116.

Regarding the subject referenced in OHRP's September 25, 2006 letter, WIH stated the following its October 18, 2006 letter: (a) The subject had surgery on June 21, 2004 at WIH and (b) the subject signed a consent form to participate in the above research on July 1, 2004, the third day after her discharge from WIH and ten days post surgery.

Based on this response to OHRP's expressed concern, OHRP does not find evidence sufficient to support the above allegations.

OHRP finds that the corrective action detailed above adequately addresses the related determination in paragraph (1) and is appropriate under WIH's FWA. As a result, there should be no need for further OHRP involvement in this matter, unless WIH uncovers additional facts indicating possible noncompliance with the HHS regulations.

OHRP appreciates the continued commitment of WIH to the protection of human research subjects. Feel free to contact me should you have any questions.

Sincerely,

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

cc: Ms. Barbara J. Riter, Research Administrator, Women & Infants Hospital
Dr. Paul A. DiSilvestro, IRB Chair/Gynecologic Oncologist, Women & Infants Hospital
Commissioner, FDA
RADM Linda Tollefson, FDA
Dr. Sam Shekar, Director, OEP/OER, NIH
Dr. Andrew C. von Eschenbach, Director, NCI, NIH
Ms. Joan Mauer, NCI, NIH
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP

Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Dr. Kristina Borror, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Carla Brown, OHRP