DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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August 28, 2003

Raymond Menard, Ph.D.
Vice President, Administration
Center for Molecular Medicine and Immunology
520 Belleville Avenue
Belleville, New Jersey 07109-0023

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 00000800

Dear Dr. Menard:

As you know, the Office for Human Research Protections (OHRP) conducted an on-site evaluation of human subject protection procedures at Garden State Cancer Center (GSCC) on July 22-24, 2003. The evaluation, conducted by two OHRP staff with the assistance of two expert consultants, included meetings with institutional officials, the institutional review board (IRB) chair and co-chair, three scientific IRB members, and two principal investigators who submit protocols to the IRB. In addition, the evaluation involved review of IRB files for the five currently open protocols at GSCC, and the minutes of IRB meetings during 2002-2003. GSCC staff were very helpful and accommodating to OHRP during the site visit.

OHRP Findings and Concerns Relative to Systemic Protections for Human Subjects

Based on its evaluation, OHRP makes the following determinations relative to systemic protections for human subjects at Garden State Cancer Center:

(1) Under Department of Health and Human Services (HHS) regulations at 45 CFR 46.107(a), an IRB must be sufficiently qualified through the experience and expertise of its members to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, an IRB must be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. OHRP finds that GSCC IRB members lack the experience and expertise in clinical trials and human subject protection issues that is necessary for appropriate

IRB review of human subject research. OHRP further finds that the IRB Chair, co-chair and members lack a detailed understanding of the specific requirements of the HHS regulations for the protection of human subjects, 45 CFR part 46.

(2) HHS regulations at 45 CFR 46.107(e) stipulate that no IRB member may participate in the IRB's initial or continuing review of a project in which the member has a conflicting interest, except to provide information requested by the IRB. OHRP finds that research reviewed and approved by the GSCC IRB involves humanized antibodies produced by a publicly traded biotechnology company which financially supports ongoing basic research conducted at GSCC by the IRB Chair. OHRP is concerned that GSCC IRB members could potentially be influenced, or appear to be influenced, by the financial relationship between GSCC and the biotechnology company.

(3) Under HHS regulations at 45 CFR 46.111, in order to approve research, IRBs must determine that risks to subjects are minimized and are reasonable in relation to anticipated benefits, that the selection of subjects is equitable and recruitment procedures appropriate, and that privacy and confidentiality protections, and any special protections required for vulnerable populations, are in place. OHRP finds that the GSCC IRB's approval of research is not consistently based on consideration of the determinations required under HHS regulations at 45 CFR 46.111.

(a) The minutes of IRB meetings, and our discussions with IRB members, indicate that substantive review of research protocols does not take place at convened IRB meetings. OHRP finds that medical and pediatric oncologists serving as consultants to the IRB provided written or verbal comments to the IRB Chair and members, but did not attend the convened meetings at which the IRB reviewed and approved oncology trials.

(b) OHRP finds that the GSCC IRB voted at its July 2, 2003 meeting to approve a protocol funded by the National Cancer Institute entitled *Phase 1 Radioimmunotherapy Trial of 90Y-Labeled Humanized PAM4 IgG in Metastatic Pancreatic Cancer* (CMMI C-062A-92) without reviewing sufficient information to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111, including the investigator's brochure.

(4) HHS regulations at 45 CFR 46.116 require that informed consent information be in language understandable to the subject or the subject's legally authorized representative. OHRP is concerned that informed consent documents approved by the GSCC IRB frequently included complex language that would not be understandable to all subjects.

Corrective Action:

In accordance with GSCC's August 12, 2003 letter to OHRP, GSCC has undertaken the following corrective actions. GSCC is dissolving its current IRB. Review and approval of all ongoing and future protocols will be conducted by a commercial IRB unaffiliated with GSCC. In addition, the GSCC IRB has suspended all approved studies that were active and/or open to enrollment on July 24, 2003, including clinical trials and studies involving collection of tissue.

OHRP finds these corrective actions appropriate under GSCC's Federalwide Assurance. OHRP requests that GSCC provide a progress report to OHRP no later than November 15, 2003 documenting the status of these corrective actions.

OHRP appreciates Garden State Cancer Center's commitment to the protections of human subjects and is available to assist GSCC in implementing the above corrective actions.

Sincerely,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Office for Human Research Protections

cc: Dr. Rhona Stein, GSCC IRB Chair
Dr. Bernard Schwetz, OHRP
Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Yvonne Higgins, OHRP
Ms. Carol Weil, OHRP
Mr. Bob Meyer, OHRP
Ms. Shirley Hicks, OHRP
Ms. Melinda Hill, OHRP
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Dr. David Lepay, FDA
Ms. Joan Mauer, NIH