DEPARTMENT OF HEALTH & HUMAN SERVICES

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January 31, 2001

Mr. Mark S. Weiner
Administrator
St. Luke's Medical Center
2900 West Oklahoma Avenue
P.O. Box 2901
Milwaukee, WI 53201-2901

RE: Human Research Subject Protections Under the Cooperative Project Assurance (CPA) # T-3533

Research Project A: STLMC-BRM-9401, Phase II study of auto-lymphocyte therapy for non-metastatic renal cell carcinoma

Research Project B: STLMC-BRMC-9503, Phase II study of activated T-cells and low dose interleukin-2 combined with autologous peripheral blood stem cell transplantation in women with stage IIIB or metastatic adenocarcinoma of the breast

Dear Mr. Wiener:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your July 13, 2000 report regarding the above referenced research projects that was submitted in response to OPRR's May 23, 2000 letter. OHRP has also reviewed Dr. John Hansen's September 27 and November 28, 2000 follow-up letters regarding this matter.

OHRP acknowledges that the above referenced research projects were not supported or conducted by the Department of Health and Human Services (HHS). As a result, OHRP has determined that it does not have jurisdiction to investigate the allegations related to the above reference research and is closing its compliance oversight investigation of this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

At this time OHRP provides the following additional guidance:

(1) The St. Luke's Medical Center written Institutional Review Board (IRB) policies and procedures should be expanded to provide additional operational details for each of the following activities, in accordance with HHS regulations at 45 CFR 46.103(b)(4) and (5):

(a) The procedures which the IRB follows for conducting its continuing review of research.

(b) The procedures which the IRB follows for reporting its findings and actions regarding initial and continuing review to the institution.

(c) The procedures which the IRB follows for determining which projects require review more often than annually.

(d) The procedures which the IRB follows for determining which projects need verification from sources other than the investigators that no material changes have occurred since the previous IRB review.

(e) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, the head of any supporting Federal Department or Agency, and, if appropriate, OHRP of each of the following events:

(i) Any unanticipated problems involving risks to subjects or others.

(ii) Any serious or continuing noncompliance with the requirements of 45 CFR Part 46, or the requirements or determinations of the IRB.

(iii) Any suspension or termination of IRB approval of research.

(2) Continuing IRB review of research must be substantive and meaningful. In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including (a) the number of subjects accrued; (b) a description of any adverse events or unanticipated problems involving risks to subjects or others and of any withdrawal of subjects from the research or complaints about the research; (c) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, reports on multi-center trials and any other relevant information, especially information about risks associated with the research; and (d) a copy of the current informed consent document. Primary reviewer systems may be employed, so long as the full IRB receives the above information. Primary reviewers should also receive a copy of the complete protocol including any

modifications previously approved by the IRB. Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When conducting research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above referenced documentation.

(3) Where HHS regulations require specific findings on the part of the IRB, such as (a) approving a procedure which alters or waives the requirements for informed consent [see 45 CFR 46.116(d)]; (b) approving a procedure which waives the requirement for obtaining a signed consent form [see 45 CFR 46.117(c)]; (c) approving research involving prisoners (see 45 CFR 46.305-306); or (d) approving research involving children (see 45 CFR 46.404-407), the IRB should document such findings. OHRP strongly recommends that all required findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding.

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

Sincerely,

Michael A. Carome, M.D.
Director, Division of Compliance Oversight

cc: Dr. Robert F. Taylor, Chair, IRB, SLMC
Dr. John P. Hanson, Jr., M.D., SLMC
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. Jeffrey Cohen, OHRP
Ms. Roslyn Edson, OHRP
Ms. Helen Gordon, OHRP
Mr. Barry Bowman, OHRP