DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

FOR US POSTAL SERVICE DELIVERY:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
National Institutes of Health (MSC 7507)
Rockville, Maryland 20892-7507

FOR HAND DELIVERY OR EXPRESS MAIL:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
Rockville, Maryland 20852

Telephone: 301-435-5649
FAX: 301-402-2071

April 13, 2001

Linda Latta, R.N., Ph.D.
Associate Administrator
Mary Bridge Children's Hospital & Health Center
317 Martin Luther King Jr. Way
P.O. Box 5299
Tacoma, WA 98415-0299

Edward I. Walkley, M.D.
Medical Director
Mary Bridge Children's Hospital and Health Center
317 Martin Luther King Jr. Way
P.O. Box 5299
Tacoma, WA 98415-0299

RE: Human Research Subject Protections Under Cooperative Project Assurance (CPA) T-4160

Research Project: CCG-1952: Randomized Comparisons of Oral Mercaptopurine vs. Oral Thioguanine and Intrathecal Methotrexate vs. Intrathecal Methotrexate/Cytarabine/Hydrocortisone for Standard Risk Acute Lymphoblastic Leukemia
Principal Investigator: Daniel J. Niebrugge, M.D.

Dear Dr. Latta and Dr. Walkley:

The Office for Human Research Protections (OHRP) has reviewed MultiCare Health System's (MultiCare's) March 22, 2001 letter, regarding the above referenced research and MultiCare's system for the protection of human subjects.

Based upon its review, OHRP has determined that MultiCare has adequately addressed the concerns raised in OHRP's letter of January 12, 2001. In particular, OHRP notes the following corrective actions taken by MultiCare:

(1) The MultiCare Institutional Review Board (IRB) has entered into a cooperative agreement with Children's Hospital and Regional Medical Center in Seattle to assist with reviews of Children's Cancer Group (CCG) protocols.

(2) MultiCare had discontinued the use of exculpatory language in its informed consent documents.

(3) MultiCare will utilize standard drug information sheets provided by the National Institutes of Health for use in cooperative research protocols.

(4) The MultiCare IRB has revised its protocol submission form to include information so as to be able to ensure that the selection of subjects is equitable and the privacy of subjects is adequately protected.

(5) MultiCare has revised its written IRB policies and procedures to address the major concerns raised by OHRP in its January 12, 2001 letter.

At this time, OHRP would like to provide the following additional guidance:

(1) The revised IRB policies and procedures provided with your letter included a description of the reporting of research misconduct to the MultiCare Health System CEO and either OHRP or FDA. Please note that research misconduct is not described in 45 CFR Part 46 and does not fall within the jurisdiction of OHRP, as defined by the Federal Government. Rather, HHS regulations at 45 CFR 46.103(a) and (b)(4) require that each institution have written policies and procedures for reporting promptly to the IRB, appropriate institutional officials, the Federal Department or Agency head, and OHRP any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with the requirements of 45 CFR Part 46 or the requirements or determinations of the IRB. The MultiCare IRB should incorporate a mechanism for reporting of unanticipated problems involving risks to subjects or others or any serious or continuing non-compliance into its written IRB policies and procedures, as required by HHS regulations at 45 CFR 46.103(b)(4). Research or scientific misconduct reporting procedures are addressed at 42 CFR Part 50, Subpart A.

(2) OHRP notes that Section 8.2 of the MultiCare IRB policies and procedures states that "A quorum, which is a majority of IRB members (more than 50%) of the membership present." This definition should be revised to indicate that a majority (more than 50%) of the membership must be present to constitute a quorum.

As a result of the above corrective actions, and on the condition that the MultiCare IRB policies and procedures are further revised in accordance with the above guidance, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must 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 research subjects. Please do not hesitate to contact me if you have any questions.

Sincerely,

Inese Z. Beitins, M.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Richard Shine, Co-Chair, IRB, MultiCare
Dr. Gordon Klatt, Co-Chair, IRB, MultiCare
Dr. Daniel J. Niebrugge, Mary Bridge Children's Hospital and Health Center
Ms. Michelle Carter, IRB Secretary, MultiCare
Ms. Joan Mauer, CTEP, NCI
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Greg Koski, OHRP
Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Jeffrey Cohen, OHRP
Ms. Helen Gordon, OHRP
Dr. Kamal Mittal, OHRP
Mr. Barry Bowman, OHRP