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: 301-402-5567
FAX: 301-402-2071
E-mail: mc2a@nih.gov

January 25, 2001

Peggy N. Troy
President
Cook Children's Medical Center
801 Seventh Avenue
Fort Worth, Texas 76104-2796

Larry Tubb
Chair, Institutional Review Board
Cook Children's Medical Center
801 Seventh Avenue
Fort Worth, Texas 76104-2796

**RE: Human Research Protections Under Cooperative Project Assurance (CPA) T-3987**

Dear Ms. Troy and Mr. Tubb:

The Office for Human Research Protections (OHRP) has reviewed your January 21, 2001 report and the revised written policies and procedures of the Cook Children's Medical Center (CCMC) Institutional Review Board (IRB) that were submitted in response to the concerns and questions raised by OHRP in its September 5, 2000 letter.

Based upon its review, OHRP has determined that CCMC has adequately addressed the major concerns raised by OHRP in its September 5, 2000 letter. As a result, 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.

At this time, OHRP provides the following additional guidance:

(1) The written IRB policies and procedures should be expanded to include additional operational details for the following activities, in accordance with Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(b)(4) and (5):

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

(b) 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 previous IRB review.

(c) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, the head of any supporting HHS Agency, and 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.

(2) IRBs must determine which protocols require continuing review more often than annually, as appropriate to the degree of risk [see 45 CFR 46.103(b)(4) and 46.109(e)]. OHRP recommends that the minutes of IRB meetings clearly reflect these determinations regarding risk and approval period (review interval).

(3) When the convened IRB reviews protocol amendments that involve more than a minor change to the research, copies of the proposed amendments should be provided to all IRB members prior to IRB meeting.

(4) Regarding the CCMC IRB review of adverse events, OHRP strongly recommends that copies of adverse event reports be reviewed by at least one physician member of the IRB.

(5) HHS regulations at 45 CFR 46.404-407 require specific findings on the part of the IRB for approval of research involving children. OHRP strongly recommends that these required findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding, for all HHS-supported protocols being conducted by CCMC.

OHRP appreciates the commitment of your institution to the protection of human research subjects. Please contact me if you have any questions regarding this matter.

Sincerely,

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

cc: Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Ms. Joan Mauer, CTEP, NCI

Dr. Gregory Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. Jeffery Cohen, OHRP
Dr. Clifford C. Scharke, OHRP
Ms. Helen Gordon, OHRP
Mr. Barry Bowman, OHRP