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: 301-435-0668
FAX: 301-402-4256

February 8, 2001

William New
Vice President, Research Administration
Children's Hospital
300 Longwood Avenue
Boston, MA 02115

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1273

Research Article: **Ultrasonography and Limited Computed Tomography in the Diagnosis and Management of Appendicitis in Children (JAMA. 1999;282:1041-1046)**

Investigators: **Barbara M. Garcia Peña, MD, Kenneth D. Mandl, MD, MPH, Steven J. Krause, MD, Anne C. Fischer, MD, PhD, Gary R. Fleisher, MD, Dennis P. Lund, MD, George A. Taylor, MD**

Dear Dr. New:

The Office for Human Research Protections (OHRP) has reviewed your report of January 23, 2001, regarding the research described in the above referenced journal article.

Based upon its review of your July 12, 2000, and January 23, 2001 reports, OHRP makes the following determinations:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.109(a) require that the Institutional Review Board (IRB) review and approve all human subject research covered by the regulations. Furthermore, in order to approve research, the IRB must determine that all of the requirements stipulated by HHS regulations at 45 CFR 46.111 are satisfied. OHRP finds that when the Children's Hospital (CH) IRB reviewed

and approved the above referenced research, the IRB failed to obtain sufficient information from the investigators to make the determinations required under 45 CFR 46.111. In particular, the IRB failed to obtain sufficient information regarding the systematic collection of data via follow-up telephone interviews of the parents of subjects who were discharged from the emergency room to make any of the determinations required under 45 CFR 46.111.

(2) HHS regulations at 45 CFR 46.116(d) require that the IRB make and document four specific findings when approving a waiver of the requirement to obtain the informed consent of subjects (or the permission of parents of subjects who are children). OHRP finds that the CH IRB failed to make and document all of the required findings when it approved the waiver of the informed consent requirements for the above referenced research.

In your January 23, 2001 report you state that the above referenced research would have satisfied all the requirements at HHS regulations at 45 CFR 46.116(d). However, based on the information provided in your report, with respect to the requirement at 45 CFR 46.116(d)(3), it appears that it would have been practicable to obtain parental permission for at least the conduct of the follow-up research interviews and probably for the prospective collection of routine clinical data related to the emergency room evaluation. If so, the research would not have satisfied the requirements for waiver of informed consent.

(3) OHRP finds that CH has implemented a number of corrective actions that adequately address the above findings of noncompliance, as well as additional concerns raised by OHRP in its December 7, 2000 letter. In particular, OHRP notes the following:

(a) CH has expanded the resources and staff support provided to the CH IRB.

(b) CH has implemented continuous education programs for institutional officials, IRB members, investigators, and research staff.

(c) The CH IRB has implemented a requirement that revised protocols accurately reflect changes in specific aims, study design, and additional background material.

(d) CH has implemented requirements that (i) investigators provide information in protocol applications justifying waivers of the requirement for informed consent; (ii) the IRB use a form to document the findings required under HHS regulations at 45 CFR 46.116(d).

As a result of the above determinations, 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 should you have any questions.

Sincerely,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Peter Wolff, Children's Hospital
Ms. Susan Kornetsky, Children's Hospital
Dr. Barbara M. Garcia Peña, Children's Hospital
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Greg Koski, OHRP
Dr. Melody Lin, OHRP
Dr. Michael A. Carome, OHRP
Ms. Freda Yoder, OHRP
Dr. Jeffrey M. Cohen, OHRP
Mr. Barry Bowman, OHRP