DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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October 23, 2003

Michael J. Klag, M.D., MPH
Johns Hopkins University School of Medicine
Vice Dean for Clinical Investigation
Turner 76
720 Rutland Ave
Baltimore, MD 21205-2196

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1011

Research Publication: Wendie A. Berg, Cynthia I. Caskey, et al. Single- and Double-Lumen Silicone Breast Implant Integrity: Prospective Evaluation of MR and US Criteria. *Radiology* 1995; 197: 45-52.

Dear Dr. Klag:

The Office for Human Research Protections (OHRP) has reviewed Johns Hopkins University's (JHU's) letter dated April 22, 2003 responding to allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR Part 46) involving the above-referenced research. OHRP has determined that the corrective actions summarized below appropriately address the issues raised:

(1) OHRP finds that the JHU Institutional Review Board (IRB) failed to review and approve certain non-exempt human subjects research covered by an assurance, as required by HHS regulations at 45 CFR 46.103(b) and 46.109(a). In specific, OHRP finds that the human subjects research reported in the above-referenced publication was conducted without IRB review.

(2) OHRP finds that the investigator failed to obtain legally effective informed consent prior to initiating the above-referenced human subjects research, in contravention of HHS regulations at 45 CFR 45.116.

Corrective Actions: OHRP acknowledges that JHU concedes that the above-referenced human subjects research was conducted without appropriate IRB review and approval and without informed consent. Dr. Berg has since undergone extensive human subjects protections training and JHU now requires all JHU staff conducting human subjects

research to undergo training in the protections of human subjects, which makes it clear that all projects that involve planned prospective evaluation of clinical data must be submitted for IRB review and approval prior to conduct of the research. OHRP notes that it would probably not have been appropriate to waive informed consent for this research under HHS regulations at 45 CFR 45.116(d). OHRP recommends that the JHU IRB consider whether or not it would be appropriate to contact the subjects of this above-referenced research to more clearly explain to them that they were enrolled in a research study and the details of the research.

As a result of this determination, 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,

Kristina C. Borror, Ph.D.
Director
Division of Compliance Oversight

cc: Lewis Becker, M.D., JHM IRB #1
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