DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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October 21, 2002

Robert Kay, M.D.
Chief of Staff
Vice Chairman, Board of Governors
The Cleveland Clinic Foundation
9500 Euclid Avenue H18
Cleveland, OH 44195

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1388

Research Project: Ovarian Cancer Trials

Dear Dr. Kay:

The Office for Human Research Protections (OHRP) has reviewed the Cleveland Clinic Foundation's (CCF's) January 10, 2003 letter 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.

(1) It was alleged that there was a failure, over a period of several years, to report unanticipated problems involving risks to subjects or others, as required by HHS regulations at 45 CFR 46.103(b)(5). In specific, it was alleged that an audit of the above-referenced trials uncovered adverse events that were not reported to the IRB, sponsors, or to OHRP.

OHRP finds that the above allegation cannot be substantiated. OHRP acknowledges CCF's statement that the serious adverse events (SAEs) that occurred in the above-referenced research projects were due to underlying disease, were judged to be anticipated, and therefore did not need to be reported to the CCF Institutional Review Board (IRB) or to OHRP.

(2) OHRP finds that informed consent was obtained and documented from some subjects

in the above-referenced trials using incomplete, expired informed consent documents, in contravention of HHS regulations at 45 CFR 46.117(a).

Corrective Action: OHRP acknowledges that the CCF has taken numerous steps to enhance operating procedures and to improve performance of Cancer Center clinical trials in accordance with Federal regulations. These steps include: (i) use of standard operating procedures including Clinical Trial AE/SAE Management, Clinical Trial SAE Reporting, Obtaining Informed Consent, and Procedures for Informed Consent Revisions Processing; (ii) the CCF has revised its informed consent document approval stamp to include the expiration date for the approval period; (iii) all researchers must undergo training in good clinical practices and human subject protections; (iv) the Department of Experimental Therapeutics maintains a SAE tracking log to assure timely and accurate submission of SAEs to the IRB and regulatory agencies; (v) and the Gynecology Oncology program has a study coordinator who assures timely submission of AEs and tracks informed consent of all subjects.

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.

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.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Richard A. Rudick, Chair, Division of Clinical Research, CCF
Dr. Alan Lichtin, Chair, IRB, CCF
Dr. David LePay, FDA
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Dr. Bernard Schwetz, OHRP
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