DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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September 16, 2002

Fawwaz T. Ulaby, Ph.D.
Vice President for Research
University of Michigan Ann Arbor
4080 Fleming Building
Ann Arbor, MI 48109-1340

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1184

Research Activity: Department of Radiology Research Activities

Dear Dr. Ulaby:

The Office for Human Research Protections (OHRP) has reviewed the University of Michigan's (UM) November 15, 2001 report submitted in response to OHRP's August 21, 2001 letter regarding the above-referenced research activities.

Based on its review, OHRP makes the following determinations:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.102(d) define research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research whether or not they are conducted or supported under a program which is considered research for other purposes. In addition, HHS regulations at 45 CFR 46.109(a) stipulate that an Institutional Review Board (IRB) shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered under the regulations.

OHRP notes that the revised Department of Radiology IRB and UCUCA [University Committee on Use and Care of Animals] Policy states the following:

(a) "The Department of Radiology will follow this policy whenever research is conducted on patients using products or methods that are previously untried."

(b) "IRB approval for research is required when:

1. Using a non-FDA approved device or drug.

2. A patient will be exposed to ionizing radiation and the use of the radiation is not part of a standard clinical examination.

3. A procedure is performed or a drug is utilized in a manner, which is not well known or described in the literature, whether or not a risk is present.

4. A granting agency or company sponsors a research project and the proposal has been submitted to DRDA for approval."

OHRP finds that the Department of Radiology IRB and UCUCA Policy is not consistent with the provisions of 45 CFR 46.102(d) and 46.109(a). In specific, OHRP notes that human subject research is not necessarily limited to "products or methods that are previously untried." In addition, IRB approval would be required for any research study which meets the definition of human subject research (i) utilizing FDA-approved drugs or devices; and (ii) where a procedure is performed or drug is utilized, even if the procedure is well known in the literature.

Required Action 1: By October 15, 2002, UM must submit to OHRP a revised Department of Radiology and UCUCA Policy which adequately addresses the above finding.

(2) HHS regulations at 45 CFR 46.117(a) require that, except as provided in 45 CFR 46.117(c), informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. In addition, HHS regulations at 45 CFR 46.115(b) require that records relating to research which is conducted shall be retained for at least three years after the completion of the research. OHRP notes that your November 15, 2001 report states the following regarding protocol IRB 1998-0527:

(a) "We found evidence of missing informed consent documents, unwitnessed informed consents, and use of informed consent documents not containing an IRB approval or expiration date."

(b) "In 15 instances we were unable to locate the informed consent documents."

OHRP finds that for protocol # 1998-0527 UM failed to ensure that informed consent was

documented and that informed consent documents were retained in accordance with the requirements of HHS regulations at 45 CFR 46.117(a) and 45 CFR 46.115(b).

Required Action 2: By October 15, 2002, UM must submit to OHRP a satisfactory corrective action plan to (i) ensure that all researchers in the Department of Radiology properly obtain and document the legally effective informed consent of research subjects or their legally authorized representatives; and (ii) ensure that research documents are retained in accordance with 45 CFR 46.115(b).

(3) In its letter of August 21, 2001, OHRP raised concerns that the Chief of Radiology, who was also the chair of the IRB, may have voted on a protocol in which he had a conflicting interest during an IRB meeting in September 1999, in contravention of HHS regulations at 45 CFR 46.107(e). Your report of November 15, 2001 provided documentation that the chair of the IRB was not present for the discussion or vote on the study in question. As a result, OHRP finds that this allegation was not substantiated.

(4) In its letter of August 21, 2001, OHRP raised concerns that the Department of Radiology failed to protect the privacy of subjects and maintain the confidentiality of data relating to human subjects, as required by HHS regulations at 45 CFR 46.111(a)(7). Your November 15, 2001 report stated that after questioning a number of faculty within the Department of Radiology, there were no known breaches of confidentiality by the department. As a result, OHRP finds that this allegation was not substantiated.

OHRP has the following additional questions, concerns, and guidance:

(5) [redacted]

(6) [redacted]

Please forward your report so that OHRP receives it no later than November 1, 2002.

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

Enclosure: March 20, 2000 e-mail

cc with enclosure:

Ms. Judith A. Nowack, Assistant Vice President for Research, UM
Dr. Vernon Sondak, Chair IRB #1, UM
Dr. Robert J. Cody, Chair IRB #2, UM

cc without enclosure:

Commissioner, FDA
Dr. David Lepay, FDA
Ms. Marion Serge, FDA
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Jeffrey Cohen, OHRP
Mr. George Gasparis, OHRP
Dr. Harold Blatt, OHRP
Mr. Barry Bowman, OHRP