DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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July 1, 2003

Dr. Clayton D. Mote
President
University of Maryland
1101 Main Administration Building
College Park,MD 20742-5025

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1362
Research Project: Treatment of Childhood Social Phobia
Principal Investigators: Deborah C. Beidel and Samuel M. Turner
Grant Number: 2RO1MH053703-05A2

Dear Dr. Mote:

The Office for Human Research Protections (OHRP) has reviewed your May 24, 2002 report responding to OHRP's April 22, 2000 letter expressing concern about possible noncompliance by University of Maryland (UM) investigators with Department of Health and Human Services (HHS) regulations for the protection of human subjects, 45 CFR part 46. We apologize for the delay in OHRP's response.

Based upon its review, OHRP makes the following determinations regarding the above-referenced research:

HHS regulations at 45 CFR 46.116(a) set forth the basic elements of informed consent that shall be provided to each subject whose participation in research is sought. Under 45 CFR 46.116(a)(1), these elements include, among other things: (1) the expected duration of the subject's participation, and (2) a description of the procedures to be followed.

(a) OHRP finds that the informed consent form for the above study did not include the anticipated duration of diagnostic assessments to be conducted before treatment and at three interval periods after treatment.

(b) OHRP also finds that the informed consent form confounded the concepts of treatment and experimental intervention in a manner that was potentially misleading. The description of procedures states that child subjects "will be assigned randomly to one of three groups", and that "one group" will receive social effectiveness therapy. It subsequently states that the "second treatment" is fluoxetine and the "third treatment" is a placebo. This description fails to clarify that the fluoxetine, placebo, and social therapy groups represent separate and independent experimental arms of the trial.

(c) OHRP further finds that the informed consent form did not include or describe the EKG procedure (and any expenses associated with the procedure) that was a required part of the study. OHRP acknowledges that the consent form has already been amended to include EKG in the description of procedures.

Required Action: The investigators for the above-referenced research must prepare, and the UM institutional review board (IRB) must renew and approve, a revised informed consent document. The revised document must address the following:

(a) clarify in the informed consent form that subjects are randomized to one of three separate and independent study arms: (i) social effectiveness therapy, (ii) fluoxetine, or (iii) placebo;

(b) amend the procedures section of the informed consent form to include the anticipated duration of physical assessments;

Furthermore, the IRB must approve a procedure for seeking informed consent from all currently enrolled subjects using the revised version of the consent form containing required modifications (a) and (b) above.

Please submit the revised informed consent document to OHRP by July 30, 2003.

At this time, OHRP provides the following guidance to UM:

(1) Under HHS regulations at 45 CFR 46.111, when an IRB reviews protocol applications, it must receive sufficient information to make the determinations required for approval of research, including whether risks to subjects are minimized and whether risks to subjects are reasonable in relation to anticipated benefits, if any, to the subjects, and the importance of the knowledge that may reasonably be expected to result. OHRP notes that operational details such as changes in travel time required of subjects, or proposed additional meetings with investigators, may affect the level of risk and discomfort involved in research and should therefore be brought to the attention of the IRB.

(2) HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5) require that institutions have written IRB procedures for each of the following:

> (1) The procedures which the IRB will follow for conducting its initial review of research.
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> (2) The procedures which the IRB will follow for conducting its continuing review of research.
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> (3) The procedures which the IRB will follow for reporting its findings and actions to investigators and the institution.
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> (4) The procedures which the IRB will follow for determining which projects require review more often than annually.
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> (5) The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.
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> (6) The procedures which the IRB will follow for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.
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> (7) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any Department or Agency head, and OHRP of: (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

The document provided to OHRP describing the UM IRB's policies and procedures (approved by the Board of Regents April 25, 1991) lacks operational details regarding the required written IRB procedures under 45 CFR 46.103(a) and 46.103(b)(4) and (5). OHRP recommends that the UM IRB's written policies and procedures provide a step-by-step description with key operational details for each of these procedures. For guidance, see OHRP's July 11, 2002 Guidance on Written IRB Procedures, http://ohrp.osophs.dhhs.gov/humansubjects/guidance/irbgd702.htm.

OHRP appreciates your continued commitment to the protection of human research subjects. Feel free to call me if you have any questions.

Sincerely,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Division of Human Subject Protections

cc: Dr. Bernard Schwetz, OHRP
Ms. Melinda Hill, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Pat El-Hinnawy, OHRP
Ms. Shirley Hicks, OHRP
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Mr. Harold Blatt, OHRP
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