DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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Sadis Matalon, Ph.D.
Acting Associate Provost for
Research and Scholarship
The University of Alabama at Birmingham
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1530 3rd Avenue South
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RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1149

Research Project: Study on Adolescent Substance Abuse Program
Principal Investigator: Dr. Kurt Denninghoff

Dear Dr. Matalon:

The Office for Human Research Protections (OHRP) has reviewed the University of Alabama - Birmingham's (UAB) April 7, 2003 report submitted in response to OHRP's January 30, 2003 letter regarding the human subject protections program at UAB.

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

(1) OHRP finds that the daughter of the complainant, although required to participate in a court-mandated substance abuse program administered in part by Dr. Denninghoff, was not enrolled in the above-referenced research. In particular, OHRP notes the following:

(a) Dr. Denninghoff was in charge of the READY [Realistic Education on Alcohol and Drugs for Youth] program, a collaborative effort between the UAB and the Jefferson County Family Court. The program was designed as an educational program for adolescents arrested on first-time drug or alcohol charges. The complainant's daughter was required by the Jefferson County Family Court to participate in this non-research program.

(b) Dr. Denninghoff's protocol #F001025028 was approved by the UAB institutional review board (IRB) to evaluate the recidivism rates of READY participants with those of comparable offenders.

(2) Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(b)(4)(iii) require that the IRB review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. The UAB April 7, 2003 report stated the following:

(a) "During the investigation of the complaint, the IRB became aware that the protocol did not reflect the new pool of subjects or the actual method of recruiting, and a revised protocol was requested."

(b) "This review verified the initial conclusion that the following changes had occurred but had not been clearly described to the IRB in any submissions for review:

- Addition of the 'Prevention' participants as possible study subjects.

- Change in the recruitment/enrollment process. At the PI's [principal investigator] request, the Family Court Judge agreed that the orientation of both education programs could be conducted at UAB in the PI's research office. ... This change was made to enhance recruitment by allowing the Research Coordinator to approach the adolescents in both groups about participation in the research."

(c) "Our investigation revealed that the process for participant recruitment and enrollment was different from that described in the initial protocol. The orientation to the education programs, which had been described to the IRB as being conducted within the court building, was changed."

(d) "Participants were screened and enrolled at the Bessemer Court site although that site was not mentioned in the protocol or any amendments as a site of recruitment."

OHRP finds that the following protocol changes were implemented without IRB approval:

(a) Addition of the 'Prevention' participants as possible study subjects.

(b) Screening and enrollment of subjects at the Bessemer Court site.

Corrective Action: OHRP acknowledges that the UAB IRB has conducted a complete audit of the above-referenced research and required that the principal investigator submit a revised protocol addressing these issues. In addition, the UAB IRB has suspended the above-referenced research for six months and required that the principal investigator and the research coordinator receive additional training in human subject protections.

(3) HHS regulations at 45 CFR 46.111(a)(7) require that, where appropriate, there be adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. OHRP notes that the UAB April 7, 2003 report stated "On at least one occasion, a print-out with the participation indication was transmitted to ASAP [Adolescent Substance Abuse Program]; it may have been available to court personnel. Dr. Denninghoff has acknowledged that this was inappropriate, and he has removed the information from the database immediately upon learning of its existence." OHRP finds that the principal investigator failed to ensure that the privacy of subjects was maintained by making a print-out of subjects available to court personnel.

Corrective Action: OHRP acknowledges that the principal investigator has removed any research related information from any database which will be shared with court officials.

(4) HHS regulations at 45 CFR 46.103(b) and 46.109(a) require that the IRB must review and approve all non-exempt human subject research covered by an assurance. OHRP notes the following:

(a) An October 11, 2002 memorandum from Ms. Charlotte Davis to Dr. Denninghoff stated the following:

(i) "Please note that this protocol was approved with limited modifications and the IRB has requested additional information and/or changes to the informed consent form."

(ii) "No new participants may be enrolled using any existing consent forms that you now have; however, you may continue to follow currently enrolled participants. Enrollment may continue after formal approval of the protocol and an IRB-stamped consent form has been issued by the IRB Office."

(b) The UAB April 7, 2003 report stated "Three participants were enrolled after the PI had received notification from the IRB that no new participants should be enrolled in to the study until changes in the consent form were made and an approved stamped form was returned to him." (Emphasis in original)

OHRP finds that three subjects were enrolled in the above-referenced research during a period when the IRB had required that subjects not be enrolled pending formal review and approval of a revised informed consent document.

Required Action: UAB must provide OHRP with a corrective action plan which adequately addresses the above finding. In addition, please provide OHRP with a corrective action plan to ensure that other researchers at UAB do not implement changes to research prior to IRB review and approval.

(5) In its January 30, 2003 letter, OHRP presented an allegation that the procedures for enrolling subjects failed to minimize the possibility of coercion or undue influence as required by HHS regulations at 45 CFR 46.116. OHRP finds that this allegation could not be substantiated.

OHRP has the following additional concern and guidance:

[Redacted]

(8) UAB should ensure that written IRB procedures adequately describe the operational details for each of the following procedures, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5):

(a) The procedures which the IRB will follow for determining which projects require review more often than annually.

(b) The procedures for ensuring prompt reporting to 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.

In order to assist UAB in revising its IRB procedures, please see OHRP's guidance at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/irbgd702.htm.

Please provide your corrective actions and response to the above concern to OHRP no later than August 29, 2003.

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: Ms. Sheila Moore, Director, IRB, UAB
Dr. Ferdinand Urthaler, IRB Chair, UAB
Dr. Kurt Denninghoff, UAB
Commissioner, FDA
Dr. David Lepay, FDA
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