DEPARTMENT OF HEALTH & HUMAN SERVICES

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August 2, 2000

Joan F. Lorden, Ph.D.
Associate Provost for Research
The University of Alabama at Birmingham
1120 Administration Building
701 South 20th Street
Birmingham. AL 35294-0111

RE: Human Research Subject Protections under the University of Alabama at Birmingham(UAB) Multiple Project Assurance (MPA), M-1149

Dear Dr. Lorden:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your June 30, 2000 progress report, the revised Institutional Review Board (IRB) Policies and Procedures, and the minutes of recent IRB meetings.

OHRP has made the following determinations regarding the implementation of UAB's corrective plan:

(1) OHRP finds that the UAB has implemented an educational program for all IRB members, all IRB staff, and all research investigators about the ethical principles and regulatory requirements for the protection of human subjects.

(2) OHRP acknowledges the progress made by the IRBs in re-reviewing Federally supported research projects that were suspended.

(3) OHRP finds the UAB has significantly expanded and enhanced the staff and resources of the IRBs.

(4) OHRP acknowledges receipt of the up-dated IRB membership rosters for UAB-01 and-02. They will be placed in UAB's MPA file.

(5) Regarding the revised Policies and Procedures, OHRP has the following comments:

(a) Section b., page 7, describes the review and approval of research involving children. Children Risk Levels are mentioned, but are not further characterized. Please be reminded that HHS regulations at 45 CFR 46.404-407 require specific findings on the part of the IRB for approval of research involving children. Where HHS regulations require specific findings on the part of the IRB, such as approving research involving children, these findings should be documented by the IRB. OHRP strongly recommends that these findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding.

(b) OHRP notes the revisions made in section c, pages 7 and 8, Review and Approval of Research Involving Prisoners. OHRP recommends that the enclosed document, OPRR Guidance on Approving Research Involving Prisoners be reviewed to assist UAB in carrying out its responsibilities stipulated by HHS regulations at 45 CFR Part 46, Subpart C.

(6) Regarding the minutes of IRB meeting, OHRP has the following concerns and questions:

(a) On numerous occasions the minutes record the approval of research involving children as Children's Risk Level #2 or CRL#2. As noted above, HHS regulations at 45 CFR 46 require that when the IRB approves research involving children, it must make specific findings. OHRP is concerned that the minutes fail to document these findings.

(b) In the Conditions for Approval section of the meeting minutes for several research projects the following statement appears: "Since the protocol includes subjects 18 years of age, please add a signature line for the legally authorized representative." It is unclear from this statement whether the research does involve children. Please clarify. If the research does involve children, 45 CFR Part 46, Subpart D applies.

(c) The minutes of the March 2, 2000 IRB meeting concerning Protocol # F961227001 state the following: "The Board informed the PI that in the future this study can be reviewed through the expedited process..." Please be reminded that as research may undergo changes that may result in additional risks, a determination as to whether the expedited procedure can still be applied must be made at the time of each subsequent review. Whenever the research involves more than minimal risk, the research must be reviewed by the convened IRB.

(d) In the minutes of the March 31, 2000 IRB meeting the following statement appears under "Other Business Discussed": "Amendments which do not affect the ratio (risk/benefit) will be approved by the Chair and/or Vice-Chair and will be presented to the IRB for review at a scheduled meeting." Please note that 45 CFR 46.110 (b)(2) requires that only amendments that constitute a "minor change" in previously approved research can undergo an expedited review. Some types of change that may not affect the risk/benefit ratio may exceed the limits of "minor" change.

(e) The minutes of the March 31, 2000 IRB meeting state that Protocol #F991118003, "Syphilis Screening in Jails (STD Accelerated Prevention Campaigns Syphilis Elimination)" was reviewed. HHS regulations at 45 CFR 46.304 require modification of IRB membership for review of research involving prisoners. In specific, at least one member of the IRB shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity. When the convened IRB reviews research involving prisoners (including initial review, continuing review, review of protocol modifications, and review of unanticipated problems involving risks to subjects or others), the prisoner or prisoner representative must be present. The referenced research appears to involve prisoners. However, neither of the individuals listed in the UAB February 28, 2000 response as a prisoner representative were in attendance at the meeting. If the research was reviewed in the absence of a prisoner representative, the research should be suspended, until a properly constituted IRB reviews the research.

(f) The following suspensions of research were noted in the IRB meeting minutes:

i. March 10, 2000, Protocol # F940727021; 25 subjects were enrolled without using an approved consent form. The protocol was suspended.

ii. May 9, 2000, Protocol # F931123009; the original principal investigator was placed on a one-year suspension.

OHRP has no record of being promptly notified about either of these suspensions as required at 45 CFR 46.103(b)(5) and UAB's recently revised reporting requirements. Please explain why these were not been reported to OHRP. Also, by August 31, 2000, please provide OHRP with a full report on these matters.

(g) An apparently serious instance of noncompliance was noted in the minutes of the March 31, May 31, and June 20, 2000 IRB meetings concerning Protocol #F971118004, Principal Investigator, Dr. Edward Taub. The apparent noncompliance appears to involve enrollment of subjects "without (a) valid consent form;" enrolling subjects during the restriction of the institution's assurance; and the removal of the IRB approval stamp on a consent form. By August 31, 2000, please provide OHRP with a full report on this matter.

Your next progress report should be submitted to OHRP by October 1, 2000. The progress report should include the following: (1) a copy of the most recently revised IRB Policies and Procedures; (2) the minutes for all IRB meetings convened during August, 2000; (3) a summary of any further progress on implementation of UAB's corrective action plan; and (4) a copy of Protocol #970822004, "Cost Effective Treatment for Dually Diagnosed Homeless," Principal Investigator, Jesse B. Millaby, Ph.D.

OHRP appreciates the continued commitment of your institution to the protection of human subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Sanford Leikin, M.D.
Compliance Oversight Coordinator
Division of Human Subject Protections

Enclosure: OPRR Guidance on Approving Research Involving Prisoners

cc: Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Dr. J. Thomas Puglisi, OHRP
Mr. George Gaspariis, OHRP
Dr. Katherine Duncan, OHRP
Dr. Cliff Scharke, OHRP
Ms. Carolyn Hudley, OHRP
Ms. Sheila Moore, UAB
Dr. Ferdinand Urthaler, UAB
Commissioner, Food and Drug Administration, HF-1
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. John Mather, Department of Veterans Affairs