DEPARTMENT OF HEALTH & HUMAN SERVICES

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December 22, 2000

Robert P. Lowman, Ph.D.
Associate Vice Provost for Research
The University of North Carolina at Chapel Hill
Office of Research Services
CB# 4100, Bynum Hall
Chapel Hill, NC 27599-4100

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1390

Research Projects: AIDS Clinical Trials Group (ACTG) Research
Principal Investigator: Dr. Charles van der Horst

Dear Dr. Lowman:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your report dated June 25, 1999 regarding possible noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR Part 46) involving AIDS Clinical Trial Group (ACTG) research at the University of North Carolina at Chapel Hill (UNC). OHRP apologizes for the delay in responding to your report.

Based upon its review of your report, OHRP finds that UNC has taken appropriate corrective actions to address the concerns of possible noncompliance raised in OHRP's May 5, 1999 letter. In particular, OHRP notes the following UNC actions:

(1) Hired a dedicated Quality Assurance Manager.

(2) Hired a regulatory coordinator to maintain all regulatory documents and coordinate all IRB activities.

(3) The adoption of Good Clinical Practices (GCP) procedures within the ACTG.

(4) Increased involvement of principal investigators in reviewing and documenting research records.

(5) Implementation of Standard Operating Procedures to monitor workload of ACTG staff.

(6) Implementation of a site management plan.

(7) Providing formal training on GCP to ACTG staff.

(8) Discontinued the practice of pre-signing prescriptions for ACTG subjects.

As a result of the above determinations, 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.

At this time, OHRP would like to provide the following additional guidance:

(1) OHRP recommends that UNC review its written IRB policies and procedures to ensure that they include operational details for each of the following:

(a) The procedures which the IRB will follow for conducting its initial and continuing review of research.

(b) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and Department or Agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

In order to assist UNC in this matter, please refer to the enclosed Guidance for Formulating Written IRB Policies and Procedures.

(2) Where HHS regulations require specific findings on the part of the IRB, such as (i) approving a procedure which alters or waives the requirements for informed consent [see 45 CFR 46.116(d)]; (ii) approving a procedure which waives the requirement for obtaining a signed consent form [see 45 CFR 46.117(c)]; (iii) approving research involving prisoners (see 45 CFR 46.305-306); or (iv) approving research involving children (see 45 CFR 46.404-407), OHRP strongly recommends that these findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding.

(3) In reviewing IRB files submitted with your report, OHRP notes that the IRB appears to approve research contingent upon substantive modifications or clarifications without requiring additional review by the convened IRB. OHRP recommends the following guidelines in such cases: (i) When the convened IRB requests substantive clarifications, protocol modifications, or informed consent document revisions, IRB approval of the proposed research must be deferred, pending subsequent review by the convened IRB of responsive material. (ii) Only when the convened IRB stipulates specific revisions requiring simple concurrence by the investigator may the IRB Chair or another IRB member designated by the Chair subsequently approve the revised research protocol on behalf of the IRB under an expedited review procedure.

(4) In conducting its review of the IRB file for study 323, OHRP notes that in a memorandum to Louise Clifford dated November 6, 1997, Claire Farel requested approval for an advertisement for ACTG 323 to be placed in local newspapers. No information is provided in either new or continuing review material regarding advertising for this study.

In conducting the initial review of proposed research, IRBs must obtain information in sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111. Materials should include the full protocol, a proposed informed consent document, any relevant grant applications, the investigator's brochure (if one exists), and any advertising intended to be seen or heard by potential subjects. Unless a primary reviewer system is used, all members should receive a copy of the complete documentation. These materials should be received by members sufficiently in advance of the meeting date to allow review of this material.

(5) HHS regulations at 45 CFR 46.115(a)(2) require that minutes of IRB meetings include a written summary of the discussion of controverted issues and their resolution. OHRP notes that the minutes of UNC IRB meetings appear to rarely include any such discussions. UNC should assess the content of its IRB minutes to ensure that summaries of controverted issues are always documented in the minutes.

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: Guidance for Formulating Written IRB Policies and Procedures

cc: Dr. Ernest N. Kraybill, IRB-01 Chair, UNC
Dr. Charles van der Horst, ACTG PI, UNC
Dr. Linda S. Adair, IRB-02 Chair, UNC
Dr. Greg E. Essick, IRB-03 Chair, UNC
Dr. Carolyn Cooper, IRB-04 Chair, UNC
Dr. David A. Eckerman, IRB-05 Chair, UNC
Dr. Mary Anne Luzar, Regulatory Affairs Branch, DAIDS, NIAID
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. John Mather, ORCA, Department of Veterans Affairs
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
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Dr. Michael A. Carome, OHRP
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Dr. Jeffrey M. Cohen, OHRP
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