DEPARTMENT OF HEALTH & HUMAN SERVICES

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August 29, 2001

Barry M. Klein
Vice Chancellor for Research
Office of the Vice Chancellor for Research
University of California, Davis
One Shields Avenue
Davis, California 95616-8671

Re: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1325

Dear Dr. Klein:

The Office for Human Research Protections (OHRP) has reviewed your August 14, 2001 report responding to allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects that were presented in OHRP's May 29, 2001 letter.

Based upon its review of your report, OHRP finds no evidence to substantiate the allegations presented in OHRP's letter. As a result of this determination, there should be no need for further OHRP involvement in this matter. Of course, OHRP should be notified of any new information which might alter this determination.

At this time, OHRP would like to provide the following guidance regarding the University of California, Davis' (UCD's) written Institutional Review Board (IRB) policies and procedures:

(1) The IRB policies and procedures should be expanded to include additional operational details for each of the following procedures:

(a) The procedures which the IRBs follows for conducting initial and continuing review of research.

(b) The procedures which the IRB follows for determining which projects require review more often than annually.

(2) The IRB policies and procedures should specify the documents and materials that are

provided to primary reviewers and all other IRB members prior to the IRB meetings for protocols undergoing initial or continuing review.

(3) 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.

The UCD IRBs should ensure that the information being solicited by the protocol application form is in sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111. OHRP notes that limiting the description of a study to four pages may sometimes lead to insufficient information being provided to the IRBs.

(4) If the IRB uses a primary reviewer system, the primary reviewer(s) should do an in-depth review of all pertinent documentation (see (3) above). All other IRB members should at least receive and review a protocol summary (of sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111), the proposed informed consent document, and any advertising material. In addition, the complete documentation should be available to all members for review.

(5) Continuing IRB review of research must be substantive and meaningful. In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including (a) the number of subjects accrued; (b) a description of any adverse events or unanticipated problems involving risks to subjects or others and of any withdrawal of subjects from the research or complaints about the research; (c) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, reports on multi-center trials and any other relevant information, especially information about risks associated with the research; and (d) a copy of the current informed consent document. Primary reviewer systems may be employed, so long as the full IRB receives the above information. Primary reviewers should also receive a copy of the complete protocol including any modifications previously approved by the IRB. Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When conducting research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above referenced documentation.

(6) Where HHS regulations require specific findings on the part of the IRB, such as (a) approving a procedure which alters or waives the requirements for informed consent (see

45 CFR 46.116(d)); (b) approving a procedure which waives the requirement for obtaining a signed consent form [see 45 CFR 46.117(c)]; (c) approving research involving prisoners (see 45 CFR 46.305-306); or (d) approving research involving children (see 45 CFR 46.404-407), the IRB should document such findings. For research reviewed by the convened IRB, OHRP strongly recommends that all required findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding.

(7) OHRP notes that the minutes of the October 13, 2000 meeting of the Clinical Research Compliance Oversight Committee included a recommendation that all research protocols for a particular investigator be suspended. Please note that if this recommendation resulted from serious or continuing noncompliance with the HHS regulations for the protection of human subjects or lead to suspension or termination of IRB approval of research, such matters should be promptly reported to OHRP and the head of any sponsoring federal agency, in accordance with the requirements of HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5).

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,

Michael A. Carome, M.D.
Director, Division of Compliance Oversight

cc: Dr. Ahmad Hakim-Elahi, Director of Sponsored Programs, UCD
Ms. Elodia Tarango, IRB Coordinator, UCD
Dr. Neil Flynn, Chair, IRB-01, UCD
Dr. Steven Tharratt, Chair, IRB-02, UCD
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Mr. George Gasparis, OHRP
Dr. Jeffrey H. Cohen, OHRP
Dr. Kamal Mittal, OHRP
Mr. Barry Bowman, OHRP