DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1100 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 301-402-3006
FAX: 301-402-2071
E-mail: rmeyer@osophs.dhhs.gov

September 3, 2003

Jay H. Stein, M.D.
Senior Vice President and Provost for Health Affairs
University of Rochester
601 Elmwood Avenue
Rochester, New York 14642

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1357

Research Project: Adolescents Use of Complementary and Alternative Medicine
Principal Investigator: Jonathan D. Klein, M.D.
HHS Project Number: R21AT000407

Dear Dr. Stein:

The Office for Human Research Protections (OHRP) has reviewed the University of Rochester's (UR) report of August 13, 2002 that was submitted in response to OHRP's July 2, 2002 letter to UR regarding allegations of possible noncompliance with the Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR part 46).

Based upon its review, OHRP makes the following determinations:

(1) HHS regulations at 45 CFR 46.111(a)(7) require that, in order to approve research covered by the regulations, the institutional review board (IRB) shall determine that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. It was alleged that the primary investigator failed to protect the privacy and maintain the confidentiality of data for a subject in the above-referenced study. OHRP was unable to resolve conflicting information regarding

noncompliance with the requirements of HHS regulations at 45 CFR 46.111(a)(7). As a result, OHRP was unable to make a finding regarding this allegation.

Corrective action: OHRP acknowledges that the UR has taken several actions to ensure compliance with the provisions to protect the privacy of subjects and to maintain the confidentiality of data. OHRP acknowledges that the UR IRB has reminded Dr. Klein that discussions potentially relating to a research subject should occur in a private setting and has directed Dr. Klein to implement a training session for his staff on the proper procedures to safeguard subject privacy.

(2) 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. Based on a review of documentation contained in UR's August 13, 2002 report, OHRP notes the following:

(a) The April 4, 2002 memorandum from the UR IRB Executive Director to Dr. Klein regarding the above-referenced study stated the following:

> "Eligibility of subjects: The study is approved for subjects aged 17 [*sic*] to 19. The subject in question has turned 20 one month before the session, thus making her ineligible. The session moderator was aware of this fact at the beginning of the session. Also, the Board [IRB] notes that the session moderator stated that subjects known to the staff should not participate. Despite these two facts, the subject was allowed to participate, thus violating the protocol eligibility criteria as approved by the Board..."

(b) The May 10, 2002 final audit report regarding a review of the above-referenced study conducted in accordance with the Standard Operating Procedure QA-003-03, "Quality Assurance Program for Good Clinical Practices" indicated that two subjects were enrolled who were above the inclusion criteria age limit.

Based on (a) and (b) above, OHRP finds that changes to eligibility criteria were made in the above-referenced study prior to IRB review and approval, in contravention of the requirements of HHS regulations at 45 CFR 46.103(b)(4)(iii).

Corrective action: OHRP acknowledges that UR has taken several corrective actions to address the above finding of noncompliance. The UR IRB has reminded Dr. Klein about his responsibilities for ensuring compliance with all IRB-approved study procedures and

that changes to study procedures must be approved by the UR IRB before such changes are implemented. The UR IRB has also directed Dr. Klein to conduct a specific training session for his research staff on the importance of adhering to the procedures and conditions specified in the IRB-approved protocol. OHRP acknowledges that this training is in addition to UR's routine training for investigators and research staff about the ethical principles and regulatory requirements for the protection of human subjects. OHRP finds that these corrective actions are satisfactory and appropriate under the UR MPA. OHRP strongly recommends that UR remind all of its research staff that changes to IRB-approved protocols may not be implemented prior to IRB review and approval of such changes.

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.

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

Sincerely,

Robert J. Meyer
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Gary L. Chadwick, IRB Executive Director, UR
Dr. Robert E. Dicenzo, Chair, IRB #1, #1P, UR
Dr. Scott Kim, Chair, IRB #2, #2P, UR
Dr. Jeanne T. Grace, Chair, IRB #3, #3P, UR
Dr. John E. Loughner, Chair, IRB #4, #4P, UR
Commissioner, FDA
Dr. David A. Lepay, FDA
Dr. Bernard A. Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael A. Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Shirley Hicks, OHRP

Ms. Yvonne Higgins, OHRP
Ms. Melinda Hill, OHRP
Ms. Patricia El-Hinnawy, OHRP