DEPARTMENT OF HEALTH & HUMAN SERVICES

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October 23, 2000

James A. Lane
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1800 Harrison Street, 16th Floor
Oakland, California 94612

and

Nancy R. King
Administrative Director
Kaiser Foundation Research Institute
1800 Harrison Street, 16th Floor
Oakland, California 94612

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1312

Dear Mr. Lane and Ms. King:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your letters dated April 15, 1999 and May 28,1999, regarding the policies and procedures of the Kaiser Foundation Research Institute (KFRI) Institutional Review Boards (IRBs). OHRP apologizes for the delay in responding to your letters.

OHRP has determined that the corrective actions summarized below appropriately address the issues raised in OHRP's February 3, 1999 letter:

(1) Regarding the minutes of IRB meetings:

(a) KFRI has expanded the content of the minutes of IRB meetings in a manner that satisfies the requirements of HHS regulations at 45 CFR 46.115(a)(2).

(b) With respect to documentation of approval of protocols involving pregnant women and children as subjects, the response of KFRI agreeing to document the IRB's determinations required by HHS regulations at 45 CFR Part 46, Subpart B and Subpart D, respectively, is adequate.

(c) The new language used for documenting specific findings for (i) approving a procedure which alters or waives the requirement of informed consent, and (ii) approves a procedure which waives the requirement for obtaining a signed consent form satisfies the requirements of HHS regulations at 45 CFR 46.116(d) and 46.117(c), respectively.

(d) Changes made to the minutes of IRB meetings and outlined in the new IRB Policies and Procedures that describe the "primary reviewer" and "presenter" for protocols reviewed at IRB meetings clarify the roles of these individuals. The KFRI also has adequately outlined its procedure for handling situations where an IRB member has a conflicting interest in protocols being presented to the IRB.

(2) KFRI has revised its IRB Policies and Procedures to include an adequate description of most major IRB procedures, as required by HHS regulations at 45 CFR 46.103(b)(4) and (5). Please see additional OHRP guidance below regarding the requirements for reporting to OHRP and any supporting Federal department of agency head.

(3) KFRI has reported that the IRB will no longer conduct meetings via telephone conference except to address emergency situations. Please note that since OPRR's letter of February 3, 1999, OHRP has changed its policy regarding the convening of IRB meetings by telephone conference. OHRP now permits such a procedure provided that all IRB members receive appropriate protocol materials in advance of the meeting.

(4) KFRI has included revised informed consent guidelines which include language requiring the disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject, as required by HHS regulations at 45 CFR 46.116(a)(4).

(5) OHRP acknowledges the activities taken by KFRI to ensure that the local research context is appropriately addressed for its Mid-Atlantic and Rocky Mountain regions. OHRP encourages KFRI to continue with its plans to establish an IRB for its Mid-Atlantic region and to continue dialogs with researchers and program leaders especially in areas outside the Northern California area.

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) 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. OHRP strongly recommends that all required findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding.

(2) The IRB Policies and Procedures should be revised to indicate that at least one IRB member, serving as primary reviewer, receives and reviews a copy of complete Federal grant applications, if applicable, in order to satisfy the requirements of HHS regulations at 45 CFR 46.103(f). Furthermore, please note that at least one IRB member, serving as primary reviewer, should receive and review of the Investigator's Brochure for any protocol testing an investigational product.

(3) Section VIII 1(f) of the revised Policies and Procedures require that the IRB be satisfied that "Appropriate additional safeguards have been included in the study to protect the rights and welfare of subjects who are members of a vulnerable group." Since this document may be utilized by individuals unfamiliar with federal guidelines, OHRP recommends that the term "vulnerable group" be defined to include children, pregnant women, fetuses and prisoners.

(4) Please note that the any instances of the following events must be promptly reported to OHRP and any sponsoring Federal department or agency head, as required by HHS regulations at 45 CFR 46.103(b)(5) and the KFRI MPA:

(a) Any unanticipated problems involving risks to subjects or others.

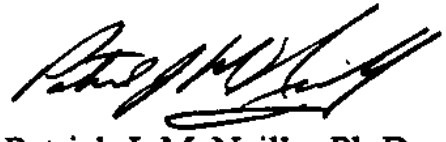
(b) Any serious or continuing noncompliance with the requirements of 45 CFR Part 46, or the requirements or determinations of the IRB.

(c) Any suspension or termination of IRB approval of research.

These events are not to be selectively reported at the discretion of KFRI. The KFRI IRB Policies and Procedures should be amended accordingly.

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
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cc: Dr. Edmund Van Brunt, Kaiser Northern California IRB Chair
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