DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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November 29, 2001

Gerald T. Nepom, M.D., Ph.D.
Director
Virginia Mason Research Center
1201 Ninth Avenue
Seattle, Washington 98101-2795

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1040

Dear Dr. Nepom:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed the Virginia Mason Research Center (VMRC) report dated March 10, 2000 regarding noncompliance with the Department of Health and Human Services (DHHS) regulations for protection of human subjects (45 CFR Part 46) involving human subjects research conducted by the VMRC. OHRP apologizes for the delay in its response.

OHRP has reviewed your March 10, 2000 report, as well as copies of follow-up correspondence between the Food and Drug Administration (FDA) and the VMRC in response to FDA's Warning Letter dated September 23, 1999. OHRP finds that the following corrective actions taken by VMRC adequately address the concerns raised in OHRP's letter of December 16, 1999:

(1) VMRC now requires that a two person subcommittee prospectively review the progress

report and the complete study file of each ongoing study submitted for continued Institutional Review Board (IRB) approval. The subcommittee will then report its findings and recommendations for each study to the IRB at the next scheduled IRB meeting. The

IRB will discuss and vote on each study as to whether to continue approval for a defined interval, not to exceed one year.

(2) VMRC has revised its IRB Policies and Procedures to address:

(a) the procedures the IRB will follow when conducting expedited review;

(b) the current list of categories of research that may be reviewed by the IRB through an expedited review procedure; and

(c) the inclusion of names and phone numbers of individuals who can be contacted for information regarding the IRB review process in an informational document included in all IRB review applications.

(3) VMRC has implemented a program to educate IRB members, investigators and research staff on an ongoing basis about the ethical principles and regulatory requirements for the protection of human subjects.

(4) VMRC has established a Clinical Research Steering Committee to develop and implement institution-wide efforts to educate and train investigators.

(5) The IRB minutes now include all the information stipulated at 45 CFR 46.115(a)(2).

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 regarding the VMRC Policies and Procedures:

(1) The last sentence in section III. B. Quorum on page three states: “IRB members must

abstain from voting and absent themselves from deliberations if they have a conflicting interest in the study being reviewed, but may provide information requested by the IRB and, if present, be counted towards the required quorum [emphasis added]. OHRP strongly recommends that IRB members absent themselves from the meeting room when the IRB votes on research in which they have a conflicting interest, and such should be noted in the IRB meeting minutes.

(2) HHS regulations at 45 CFR 46.103(f) require that an institution with an approved assurance shall certify that each *application* for research has been reviewed and approved by the IRB. OHRP recommends that Section III. D. Materials on page three be revised to state that unless a primary reviewer system is used, all members should receive a copy of any Grant Application in the materials distributed to IRB members prior to the next scheduled IRB meeting.

(3) In order to comprehensively state the requirements at 45 CFR 117(b)(2), OHRP recommends that section VII. E. Verbal Consent on page seven be revised by stating that the witness, in addition to signing the short form, shall also sign a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the subject's representative, in addition to the copy of the short form.

(4) OHRP notes that alternates have been assigned for two regular IRB members and the IRB plans to list an additional two alternates in order to assure that a majority of members are present at convened IRB meetings. OHRP notes, however, that the IRB minutes for November 18, 1999, December 16, 1999 and February 17, 2000 lists the attendance of both the primary IRB member Ken Devaney, and his formally designated alternate, Kathy Kaye. Further, the recorded voting tally shows that both Mr. Devaney and Ms. Kaye voted and were counted as part of the quorum at such IRB meetings. OHRP advises that an alternate IRB member should only vote and be counted as part of the quorum when substituting for a primary member who is unable to be present at a convened IRB meeting. OHRP acknowledges that subsequent IRB meetings have been conducted with an appropriate quorum.

(5) OHRP recommends that 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.

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,

Robert J. Meyer
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Steven C. Springmeyer, VMRC
Dr. James E. Bredfeldt, VMRC
Mr. Ken J. Devaney, Administrative Director, VMRC
Ms. Sonja De Moya, IRB Administrator, VMRC
Commissioner, FDA
Dr. David A. Lepay, FDA
Dr. James F. McCormack, FDA
Ms. Elaine Knowles Cole, FDA
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