DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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Via Federal Express

JUN - 7 1999

WARNING LETTER

Mr. Dennis Sisto
President and Chief Executive Officer
Queen of the Valley Hospital
1000 Trancas Street
Napa, California 94558

Dear Mr. Sisto:

During the period of November 17 – December 10, 1998, Ms. Darlene-Jane B. Almogela, an investigator with the Food and Drug Administration's (FDA) San Francisco District Office, visited the Queen of the Valley Hospital Institutional Reviewing Committee (IRC), an Institutional Review Board (IRB). The purpose of that inspection was to determine whether the activities and procedures of the IRB concerning the review of clinical research involving FDA-regulated products complied with applicable FDA regulations.

Our review of the inspection report and copies of your IRB's records submitted by the FDA district office revealed violations of Title 21, Code of Federal Regulations (21 CFR) Part 56 - Institutional Review Boards. These violations were listed on the Form FDA-483, "Inspectional Observations," which was presented to and discussed with Dr. Richard A. Beller, the IRB Chairperson at the conclusion of the inspection. Ms. Judith A. Hayward and Ms. Katherine Flossman were also present during this discussion. The following deviations are not intended to be an all-inclusive list of IRB deficiencies.

1. **Failure to follow written procedures for conducting initial and continuing review of research [21 CFR 56.108(a)].**

The IRB did not follow written procedures that require at least one non-scientist IRC member must be present at all convened meetings. In addition, the IRB did not follow written procedures that require materials, such as study protocols, informed consent forms, and assurance documents, be available for IRB review of a study. For example, FDA's inspection disclosed that the IRB did not have the signed "Statement of Investigator Assurances" in 20 of the 32 research studies audited. It was also determined that the IRB did not have complete copies of [redacted] study protocols necessary for review.

The IRB failed to follow its written procedure that requires determination of frequency

for continuing review and approval of studies. For example, the IRB did not specify the frequency of continuing review for the [redacted] which it initially reviewed during its October 28, 1998, meeting.

The IRB did not follow its written procedure that requires approval of the Pharmacy and Therapeutics (P&T) Committee approval prior to the IRB's review of a study. The IRB approved [redacted] on July 26, 1995. This IRB action took place before P&T Committee considered this matter in September 1995.

2. **Failure to review proposed research at convened meetings at which a majority of the members of IRB are present [21 CFR 56.108(c)].**

The written procedures require that the IRB have a majority of the members present at the meeting. The Queen of the Valley "Hospital Medical Staff Bylaws" defines a quorum as 50% percent of the members present at the meeting. The IRB conducted and approved initial and continuing review of studies without at least 50% of the members present at the January 29, 1997, April 22, 1998, July 22, 1998, and October 28, 1998, meetings.

3. **Failure to maintain adequate documentation of IRB activities and operations [21 CFR 56.115(a)(1-4)].**

Research documents and scientific evaluations for several studies that were reviewed were not retained. The IRB procedures require that all records be retained for at least three years after the completion of the study or three years after their most recent action on the study. Many of their study files did not contain the Pharmacy and Therapeutics Committee's approval letters. There were instances where study files did not contain investigational protocols. There were no final reports with the files of closed [redacted]

In addition, the IRB failed to maintain all correspondence associated with [redacted]

The IRB records are inadequate in that the records do not completely identify each IRB member, describe each member's chief anticipated contribution to the IRB deliberations (including primary reviewer), and the relationship between each member and the institution.

The IRB minutes were not written in sufficient detail to document actions taken during the meetings. For example, the IRB did not record the number of members who voted for, against, or abstained from voting on specific actions or recommendations during the 1995-1998 meetings. The minutes do not record the attendance of all members, particularly alternate members.

The IRB written procedures require that its business be conducted at a convened meeting. In special circumstances, the members may convene by telephone conferencing, provided that specific conditions are met. The IRB did not record the attendance, deliberations, and voting of the members present during the telephone conference when they approved [redacted]

4. **Failure to fulfill requirements for expedited review of research [21 CFR 56.110].**

[redacted] which was reviewed and approved in December 1997, by expedited review, did not qualify for expedited review according to the IRB's written procedures.

5. **Failure to follow procedures for ensuring prompt reporting to the appropriate institutional officials and the FDA [21 CFR 56.108(b)(3)].**

The IRB failed to follow its written procedures when it suspended [redacted] on October 24, 1997. There were no records indicating that the FDA, the hospital President, and the Chief of the Medical Staff were notified.

We acknowledge receipt of a copy of the January 25, 1999, letter from Ms. Judy Hayward, Medical Staff Coordinator, which was forwarded to our office in response to the Form FDA-483. Ms. Hayward's letter reflects an understanding of the observations FDA has made. However, this letter did not include written documentation supporting the response nor did the letter specify when the corrective actions would be taken.

As the parent institution, it is your responsibility to ensure that the Queen of the Valley Hospital IRC adheres to each requirement of the Act and regulations. Within fifteen (15) working days of receipt of this letter, please provide this office with written documentation of the specific corrective actions you have taken, or will be taking, to achieve compliance with the IRB regulations. Any comprehensive correction action plan

that you submit must include dates when the action was accomplished or will be accomplished.

Your response should also include a list of all suspended and terminated studies from 1995 to the present. In addition, you should address the training of the IRB members and clinical investigators in applicable institutional procedures and policies. We will review your response and determine whether the actions are adequate to permit the IRB to continue unrestricted activities.

If you cannot respond within 15 working days, state the reason for delay. Your failure to respond may result in further regulatory action without notice. You should direct your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch I (HFZ-311), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kevin M. Hopson. A copy of this Warning Letter has been sent to the Food and Drug Administration, San Francisco District Office, 1431 Harbor Bay Parkway, Alameda, California 94502-7070. We request that you send a copy of your response to that office.

Should you any questions concerning this matter, please contact Mr. Kevin Hopson at (301) 594-4720, extension #128.

Sincerely yours,

for Lillian J. Gill
Director
Office of Compliance
Center for Devices
and Radiological Health

cc: Richard A. Beller, M.D.
Chair, Institutional Review Committee
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