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Via Federal Express

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Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850WARNING LETTER

Jan Weber, M.D.  
Chairman  
Our Lady of Lourdes Medical Center  
Institutional Review Board  
1600 Haddon Avenue  
Camden, New Jersey 08103

Dear Dr. Weber:

On January 4-12, 1999, Our Lady of Lourdes Medical Center (OLLMC) Institutional Review Board (IRB) was inspected by Ms. Judith A. Jones, an investigator with the New Jersey District Office of the Food and Drug Administration (FDA). 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 OLLMC IRB records submitted by the district office revealed deviations from Title 21, Code of Federal Regulations (21 CFR) Part 56 - Institutional Review Boards and Part 50 - Protection of Human Subjects. These deviations were listed on the Form FDA-483, "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection. The description of deviations that follows is not intended to be an all-inclusive list of IRB deficiencies.

**(1) Failure to have written procedures for conducting initial and continuing review of clinical research as required by 21 CFR 56.108(a)(1) and (2).**

The IRB lacks adequate written procedures for conducting its initial review in that there is no procedure to assure that at least one member of the IRB receives and reviews the full protocol. Furthermore, protocols were not distributed sufficiently in advance of meetings to permit IRB member(s) to conduct an in-depth review.

The IRB lacks adequate written procedures for conducting its continuing review. There are no procedures for determining which projects require review more than annually. A system should be implemented and followed for determining the status of approved studies and for assuring that prompt continuing review of study progress is done within the time intervals set by the IRB at the time of initial approval.

Your IRB procedures do not include a procedure for determining "Significant Risk" (SR) versus "Non-significant Risk" (NSR) for medical device investigations. When an IRB reviews a research proposal involving a medical device, the IRB should determine whether the research proposal involves a SR device as defined under 21 CFR 812.3(m), or an NSR device. The IRB determines whether an application for Investigational Device Exemption (IDE) should be filed with FDA for review prior to the initiation of the investigation. The agency relies primarily on IRBs to review proposed research involving NSR devices regulated by FDA, because an FDA review of the research proposal is not required prior to the initiation of an NSR device investigation.

**(2) Failure to have written procedures for suspending or terminating IRB approval and notifying the investigator, the institution, and FDA of the termination as required by 21 CFR 56.113.**

Prompt continuing review of progress reports was not conducted because many reports were not submitted to the IRB in a timely manner. In cases where reports were overdue, there was no effective mechanism for securing the compliance of clinical investigators (CI) who were delinquent in submitting progress reports. When a CI fails to submit the required progress report by the due date established by the IRB, the IRB must be prepared to exercise procedures to withdraw its approval of the research if the required reports are not obtained.

**(3) Failure to maintain adequate documentation of IRB activities and operations as required by 21 CFR 56.115(a)(2), (3) and (4).**

Minutes were not in sufficient detail to document actions taken by the IRB. For example, the number of IRB members voting (specified by categories to include for, against, and abstaining) was not noted. In addition, the basis for requiring changes or disapproving research, and a written discussion of controverted issues and their resolution were not included.

Documentation was either inaccurate, or not available to substantiate attendance at IRB meetings. Our review of the meeting minutes from 1996-98 disclosed nine instances of discrepancies between the attendee sign-in sheets and the attendance reported in the minutes.

**(4) Failure to review proposed research at convened meetings at which a majority of members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas as required by 21 CFR 56.108(c).**

There were six IRB meetings convened between March 31, 1997, and November 9, 1998, at which either a nonscientific member was not present and/or a majority of the IRB members were not present.

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. These may include new IRB policies and procedures. We will review your response and determine whether the actions are adequate to permit the IRB to continue unrestricted activities.

If corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your failure to respond may result in further regulatory action without notice, including disqualification of the IRB.

Your response to this letter should be directed 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: L. Glenn Massimilla, R.Ph.. A copy of this Warning Letter has been sent to the FDA's New Jersey District Office, 10 Waterview Drive, Parsippany, New Jersey 07054. We request that a copy of your response also be sent to the New Jersey District Office.

Please direct all questions concerning this matter to Mr. Massimilla at (301) 594-4720, extension 136.

Sincerely yours,

*Charma Alkonar, RPL*

*for*

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