



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

By Certified Mail-Return Receipt Requested
And by Facsimile Transmission

CBER-09-06

Warning Letter

Se H. Choi, Pharm. D., Chair
Institutional Review Board
Provena St. Joseph Medical Center
333 N. Madison Street
Joliet, Illinois 60435

March 12, 2009

Dear Dr. Choi:

This letter describes the results of a Food and Drug Administration (FDA) inspection of the Provena St. Joseph Medical Center Institutional Review Board (IRB), which concluded on November 25, 2008. The FDA conducted an inspection of the IRB to determine if the IRB's procedures for the protection of human subjects comply with FDA regulations published in Title 21, Code of Federal Regulations (CFR), Parts 50 and 56. The inspection was conducted as part of FDA's Bioresearch Monitoring Program, which includes inspections designed to review research involving investigational products, and for the protection of human subjects.

At the end of the inspection, the FDA investigator issued and discussed with you the Form FDA 483, Inspectional Observations. From our review of the establishment inspection report, and the exhibits submitted with the report, we have determined that the IRB violated applicable regulations governing the operation and responsibilities of IRBs as published under 21 CFR 50 and 56 (available at <http://www.gpoaccess.gov/cfr/index.html>). The applicable provisions of the CFR are cited for each violation listed below. We are addressing this letter to you under 21 CFR 56.120(a) as the current IRB Chair with responsibility for ensuring that the IRB takes the actions necessary to bring the IRB into full compliance with FDA regulations. Under 21 CFR 56.120(a) we are also sending copies of this letter to the responsible head of the IRB's parent institution because under 21 CFR 56.120(c), the parent institution is presumed to be responsible for the IRB's operations.

1. **Failure to review proposed research at convened meetings at which a majority of the IRB membership are present, including at least one non-scientific member. [21 CFR § 56.108(c)].**

- a. A review of IRB meeting minutes for 2005 through 2008 revealed that the IRB consistently reviewed and approved new studies and conducted continuing review without a majority of the IRB membership present. Individuals not on the IRB membership rosters, including the IRB Chair, attended meetings and voted. Many meetings also failed to include at least one non-scientific member.

Date	No. of IRB members on roster	No. of IRB members present	Non-scientific member present
6/10/08, 4/28/08	6	1	No
12/18/07, 11/20/07	13	6	Yes
10/16/07	13	6	No
9/18/07	13	3	No
8/21/07	13	5	Yes
4/17/07	13	4	No
11/28/06	14	6	Yes
9/12/06, 3/28/06	14	5	No
7/25/06, 2/28/06	14	4	No
4/26/06	14	3	No
8/23/05	18	8	No
6/14/05	18	9	No
3/8/05	18	4	No
1/11/05	18	7	No

- b. The meeting minutes for 1/11/05 and 3/8/05 document that three and five members, respectively, voted on research studies by email. The use of email ballots to vote on issues before the IRB is not permitted because this method, in these instances, does not constitute a convened meeting.
2. **Failure to conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. [21 CFR § 56.109(f)].**
- a. The IRB approval letter dated June 6, 2006 for Protocol (b)(4) documents that this study was approved for one year. However, there is no documentation of continuing review until the June 10, 2008 IRB meeting, at which time the protocol was discussed and given approval until June 10, 2009. This protocol should have been subject to continuing review on or before June 6, 2007.
- b. Protocols (b)(4) and (b)(4) were approved during the August 21, 2007 IRB meeting. There is no documentation of continuing review of written progress reports or approval for continuation of research for either study in subsequent IRB meeting minutes. Both studies should have received continuing review on or before August 21, 2008.
3. **Failure to prepare and maintain adequate documentation of IRB activities. [21 CFR §§ 56.115(a)].**

- a. Minutes of meetings for the years 2005 through 2008 have not been prepared in sufficient detail to show actions taken by the IRB, and the vote on actions, including the number of members voting for, against and abstaining. 56.115(a)(2).
 - b. The IRB membership rosters for 2005 through 2008 do not identify members by earned degrees; representative capacity; indications of experience, such as board certifications, licenses, etc., sufficient to describe each members chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution. 56.115(a)(5).
 - c. The IRB failed to either prepare or maintain the meeting minutes for the meeting held on May 23, 2006. Minutes for July 25, 2006 state "... Further attempts will not be made to receive the minutes." 56.115(a)(2).
 - d. There are no written procedures for the following recurring IRB functions listed in the IRB's Policy Manual. 56.115(a)(6).
 - i. The reporting of the IRB's findings and actions for the initial review of research to the institution in writing.
 - ii. Determining which projects require verification from sources other than the investigator that no material changes have occurred since previous IRB review.
 - iii. Significant/non-significant risk device determination and documentation, as required by 21 CFR 812.66.
- 4. Failure of IRB members to abstain from participating in discussions and voting on projects for which the member has a conflict of interest. [21 CFR 56.107(e)].**

Meeting minutes for 7/25/06, 10/16/07 and 12/18/07 document that IRB members who were also the clinical investigator for proposed studies remained in the room during the discussion of the proposed project, and voted on his/her project.

This letter is not intended to contain an all-inclusive list of deficiencies in the operations of the IRB.

Please notify this office in writing, within fifteen (15) business days of receipt of this letter, of the actions you have taken or plan to take to bring the IRB into compliance with FDA requirements. Please include a copy of any revised documents, such as written procedures, roster, and recent meeting minutes with your response. Also, for any plans of action, please include the projected completion dates for actions to be accomplished.

Your failure to adequately respond to this letter and take appropriate corrective action may result in further administrative actions against your IRB, as authorized by 21 CFR 56.120 and 56.121. These actions could include FDA withholding approval of new studies reviewed by your IRB that are subject to Parts 50 and 56 of the FDA regulations, prohibiting the admission of new subjects to ongoing studies that are subject to 21 CFR Parts 50 and 56, terminating all ongoing studies approved by your IRB, and initiating regulatory proceedings for disqualification of your IRB.

Please send your written documentation to:

Robert L. Wesley
Division of Inspections and Surveillance (HFM-664)
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448
Telephone: (301) 827-6348

We request that you send a copy of your response to the FDA District Office listed below.

Sincerely,



Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

Cc: Scott MacIntire, District Director
Food and Drug Administration
550 West Jackson Blvd., Suite 1500
Chicago, Illinois 60661

Jeffrey Brickman
Senior VP & Regional CEO
Provena St. Joseph Medical Center
333 N. Madison Street
Joliet, Illinois 60435

Kristina Borrer, Ph.D., Director
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