DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV 7 2006

WARNING LETTER

VIA FEDERAL EXPRESS

Cathy E. Radner
Associate Corporate Counsel and
Acting IRB Chairperson
Mercy Mount Clemens Corporation
d.b.a. St. Joseph's Healthcare IRB
15855 19 Mile Road
Clinton Township, MI 48038-3504

Dear Ms. Radner:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection of your Institutional Review Board (IRB) from June 27, to July 6, 2006 by an investigator from the FDA Detroit District Office. The purpose of this inspection was to determine whether your IRB is in compliance with applicable federal regulations. IRBs that review investigations of devices must comply with applicable federal regulations of Title 21, Code of Federal Regulations (21 CFR) Part 56 – Institutional Review Boards, Part 50 – Protection of Human Subjects, and Part 812 – Investigational Device Exemptions. This letter also requests prompt corrective action to address the violations cited and discusses your August 3, 2006 written response to the noted violations.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval applications (PMA), and Premarket Notification submissions [510(k)] are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the district office revealed several violations of Title 21, Code of Federal Regulations (21 CFR) Part 56 – Institutional Review Boards. At the close of the inspection, the FDA investigator presented an inspectional observations Form FDA 483 for your review and discussed the observations listed on the form with you. The deviations noted on the Form FDA 483, your response, and our subsequent review of the inspection report are discussed below:

Failure to review all research activities 21 CFR [56.109(a)].

Pursuant to 21 CFR 56.109(a), an IRB shall review and have authority to approve, require modifications in, or disapprove research activity. You failed to adhere to the above stated regulation in that you did not review and approve research that the president of the hospital approved. The president of the hospital granted approval for the compassionate/emergency use of the [redacted] for abdominal aortic aneurysm. The approval letter states that the use of the [redacted] will be reviewed and approved by the IRB at the next scheduled meeting to take place in September. The IRB meeting minutes for 9/9/02 document that the [redacted] and [redacted] were listed as new business, however there was no vote recorded and no documentation that the study was approved by the IRB at the 9/9/02 meeting.

Your response is inadequate in that it does not address what corrective and preventive actions you have taken or plan to take to prevent this type of deviation in the future. Although you have revised your IRB policy, it does not appear to address the situation stated in observation #1. Please refer also to 21 CFR 56.112, which states that research that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB. Please provide what corrective and preventive action you propose to take to ensure that hospital officials do not grant approval of research that has not been reviewed and approved by the IRB.

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)].

Pursuant to 21 CFR 56.109(f), IRBs are responsible for conducting continuing review of research at intervals appropriate to the degree of risk, but not less than one per year. You failed to conduct continuing review of research at intervals of not less than once per year. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

A 4/10/02 letter from the IRB Chair to Dr. [redacted] states that he is granted approval of the [redacted] Clinical Study, pending review by the full IRB committee at the next meeting. The 9/9/02 meeting minutes list the [redacted] as new business, but there is no documentation of a vote taking place. In a 6/20/02 letter to Dr. [redacted] the IRB chairman again states that he granted approval of the study and the consent form, and that the approval is for one year, April 2002 – April 2003. On 2/3/03, 5/2/03, 10/3/03, 2/25/04, 4/13/04, 6/2/04, and 10/19/04 requests were made by Dr. [redacted] study coordinator for documentation of IRB renewal. On 10/10/04, the IRB chairman sent Dr. [redacted] a letter documenting that the IRB approved the protocol and consent for the period April 10, 2003, through April 10, 2004, and for the period of April 10, 2003, through April 10, 2005. Review of the meeting minutes for the years 2003 and 2004 do not document any vote regarding the [redacted].

Although your response provides documentation that was unavailable during the inspection for 483 items 3A through 3D, it does not address 483 item 3E. Please provide a response regarding your retroactive approval of Dr. [redacted]. In addition, your response is inadequate in that you do not discuss what measures you have put in place

to prevent this deviation in the future. Please provide the preventive measures that you have taken or plan to take to ensure that all appropriate documents are maintained to document your review activities.

Failure to prepare and maintain meeting minutes in sufficient detail to show actions taken by the IRB, the vote on actions, including the number of members voting for, against, and abstaining, and a written summary of the discussion of controverted issues and their resolution [21 CFR 56.115(a)(2)].

You failed to adhere to the above regulation in that you did not prepare and maintain meeting minutes in sufficient detail to show actions taken by the IRB, the vote on actions, including the number of members voting for, against, and abstaining, and a written summary of the discussion of controverted issues and their resolution. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

A review of minutes for IRB meetings conducted in 2001, 2002, 2003, 2004, 2005, and 2006 demonstrated the lack of required documentation regarding voting actions and summary discussion held. In addition, in many instances the IRB did not document the name of the clinical investigator and/or the title of the clinical trial under discussion.

a. On 4/22/04, [redacted] was approved by the IRB to serve as a principle investigator, however, the name of the study in which he was to serve as the principle investigator was not documented in the IRB meeting minutes. Dr. [redacted] was involved in both the [redacted] study and the [redacted] Clinical Study. In addition, there is no documentation regarding the number of members voting for, against, and abstaining on this decision.

b. The 6/30/05 meeting minutes list annual reports received for the [redacted] study, the [redacted] study, and the [redacted] study. The IRB approved these annual reports and changed the frequency of review for the [redacted] study, however the minutes for these meetings do not include the discussion or voting actions, including the number of members voting for, against, and abstaining.

c. The IRB meeting minutes for 9/9/02 include an evaluation of the [redacted] for the [redacted] The minutes do not include any documentation on voting actions. The [redacted] involved in this study is considered a significant risk device.

d. The IRB meeting minutes of 11/13/03 reflect discussion of the compassionate use request for [redacted] by Dr. [redacted]. The recommendation was voted upon and the recommendation failed, however, the minutes do not state the name of the study, or the number of members voting for, against, and abstaining on this decision.

Your response includes a revised IRB policy which describes recordkeeping procedures that should help you in the documentation of activities in the meeting minutes. Your response is adequate to address this concern.

Failure to prepare and maintain copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects [21 CFR 56.115(a)(1)].

Pursuant to 21 CFR 56.115(a)(1), IRBs are responsible for preparing and maintaining copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, and progress reports submitted by investigators. Examples of your failure to adhere to the above stated regulations include but are not limited to the following:

The IRB recommended approval of Dr. [redacted]'s participation in the [redacted] Study on 4/2/02. This letter, the protocol, and the informed consent form were not maintained by the IRB, but were faxed to the IRB on 7/4/06 & 7/6/06, during the FDA inspection.

Your response is inadequate in that it does not appear to address this deviation. Please provide what measures you have taken or plan to take to correct deficiencies in preparing and maintaining copies of all research proposals, informed consent forms, progress reports and other documents as required.

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

Pursuant to 21 CFR 56.108(c), a majority of IRB members, including at least one member whose primary concerns are in the nonscientific area, is needed to review proposed research at convened meetings. You failed to adhere to the above stated regulation in that you failed to review proposed research at convened meetings at which a majority of the members of the IRB are present. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

The IRB membership list for 2006 consists of ten members. During the meeting that occurred on 4/27/06, the IRB approved the continuation of Dr. [redacted]'s participation in the [redacted] Clinical Study, however, the minutes of the meeting document that only five members of the IRB were present.

Regarding Form FDA 483 observation #7, your written response states that you have revised your IRB policy. We acknowledge that the section regarding IRB membership, operation and duties describes membership, quorum, and responsibilities. Adhering to this policy should help you in adhering to the regulations.

Your revised policy should also help you ensure that the IRB follows written procedures for conducting initial review of research as noted in Form FDA 483 observation #2.

Your written response also states that you have revised your IRB policies and written procedures for compassionate use, humanitarian use device/humanitarian device exemption approval, and significant and non significant device determination procedures noted in Form FDA 483 observation #5.

We acknowledge that you are in the process of updating/and creating a data log of all ongoing research for use as a tool in monitoring research and which will enable you to verify what research is open, due dates of progress reports, renewal dates, and closure date. We also acknowledge that the need for training has been discussed. However, your response is inadequate in that it does not specifically address timelines for implementation of your corrective actions and training, nor does it address what measures you are taking to monitor the effect of your corrective actions to ensure that they are effective in preventing similar violations in the future.

The violations described above are not intended to be an all inclusive list of problems that may exist at the IRB. The IRB is responsible for ensuring compliance with the Federal Food, Drug, and Cosmetic Act and all applicable regulations.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the additional actions you have taken or will take to correct these violations and prevent the recurrence of similar violations. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. Send your response to: Attention: Doreen Kezer, Chief, Special Investigations Branch, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-311, Rockville, Maryland 20850.

A copy of this letter has been sent to the Detroit District Office, 300 River Place, Suite 5900, Detroit, MI, 48207. Please send a copy of your response to that office.

If you have any questions, please contact Doreen Kezer at (240) 276-0125 or via e-mail at doreen.kezer@fda.hhs.gov .

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and Radiological Health