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## Inspections, Compliance, Enforcement, and Criminal Investigations

### MedCentral Health System 6/22/10



Department of Health and Human Services

Public Health Service  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

#### WARNING LETTER

VIA UPS EXPRESS

**June 22, 2010**

James E. Meyer  
President  
MedCentral Health System  
335 Glessner Ave  
Mansfield, OH 44903-2269

Dear Mr. Meyer:

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 March 22, 2010 to March 31, 2010 by an investigator from the FDA Cincinnati 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 provisions of Title 21, Code of Federal Regulations (21 C.F.R.) 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 Terry Weston, M.D., IRB Chairman's written response dated April 14, 2010 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 (PMA) applications, 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 C.F.R.) Part 56 -- Institutional Review Boards and Part 812 -- Investigational Device Exemptions. At the close of the inspection, the FDA investigator presented an inspectional observations Form FDA 483 for review and discussed the observations listed on the form with Dr. Terry Weston. The deviations noted on the Form FDA 483, Dr. Terry Weston's written response, and our subsequent review of the inspection report are discussed below:

**Failure to follow written procedures governing the functions and operations of the IRB and to ensure that the IRB reviews proposed research at convened meetings at which a majority of the members are present including at least one member whose primary concerns are in nonscientific areas [21**

**CFR 56.108(a), (b), (c) and 21 CFR 812.60].**

In order to fulfill the regulatory requirements, an IRB must follow written procedures that govern certain functions and operations. You have failed to meet this standard, and, in fact, there is no evidence that your IRB has written procedures for the following:

- The IRB has no written procedures for the following:
  - o For reporting all IRB findings and actions to the investigator and the institution.
  - o For determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review.
  - o For ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.
  - o For ensuring prompt reporting to the FDA of any unanticipated problems involving risks to human subjects or others.
  - o For ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any instance of serious or continuing noncompliance with the regulations or the requirements or determination of the IRB, or of any suspension or termination of IRB approval.
- Minutes for the IRB meeting held on February 24, 2006, in which the IRB reviewed the FDA regulated study entitled "A Randomized, Controlled Trial of the Medtronic ENDEAVOR drug (ABT-578) Eluting Coronary Stent System versus the Taxus Paclitaxel-Eluting Coronary Stent System in De Novo native coronary artery lesions," indicate that the meeting was cancelled due to an inability to have a majority of IRB members present. However, per your study approval letter dated February 28, 2006, this study received IRB approval on February 24, 2006. The IRB approved this study without a convened meeting.
- The 2006 IRB roster consists of nine (9) voting members. Minutes for the IRB meeting held on November 17, 2006, identified four (4) members present during the review of this FDA regulated study entitled "A Pivotal Phase 3, Observer-Blind, Randomized Clinical Trial of the Efficacy and Safety of APF530 Compared to Aloxi for the Prevention of Acute-Onset and Delayed-Onset Chemotherapy-Induced Nausea and Vomiting Following the Administration of Either Moderately or Highly Emetogenic Chemotherapy Regimens." As a result, the IRB approved this study without a majority of IRB members present.
- The 2007 IRB roster consists of ten (10) voting members. Minutes for the IRB meeting held on November 16, 2007, identified five (5) members present, during the review of this FDA regulated study entitled, "A Phase 3, Observer-Blind, Randomized Trial of the Efficacy and Safety of APF530 Compared to Aloxi for the Prevention of Acute-Onset and Delayed-Onset Chemotherapy-Induced Nausea and Vomiting Following the Administration of Either Moderately or Highly Emetogenic Chemotherapy Regimens." As a result, the IRB approved this study without a majority of IRB members present.
- The 2005 IRB roster lists a nonscientific member. Minutes for the IRB meeting held on January 14, 2005 indicate that the IRB reviewed and approved the FDA regulated study entitled, **(b)(4)**. However, these meeting minutes also indicate that the nonscientific member was absent from this meeting. The IRB approved this study without a nonscientific member present.

In your response, you state that the IRB will only conduct meetings when there is a quorum and at least one nonscientific member present. Your response is inadequate in that it fails to provide a preventative action plan to prevent recurrence of this violation. Please provide a preventative action plan that explains how you will ensure both a quorum and at least one nonscientific member is present at future IRB meetings.

**Failure to prepare and maintain adequate documentation of IRB activities, including minutes of IRB meetings, which shall be in sufficient detail to show attendance at the meetings, actions taken by the IRB, the vote on these actions including the number of members voting for, against, and abstaining, the basis for requiring changes in or disapproving research, and a written summary of the discussion of controverted issues and their resolution [21 CFR 56.115(a)(2)].**

The following IRB activities are not documented in the meeting minutes:

- The continuing review and approval of the “(b)(4)” trial is not documented in the November 17, 2006 meeting minutes.
- For the following IRB activities, the votes are not documented in the meeting minutes:
  - o The May 14, 2004 approval of the (b)(4)
  - o The January 14, 2005 approval of the “(b)(4)” trial.
  - o The June, 26, 2009 approval of the “(b)(4)”.

In your response, you state that the IRB will record votes in future meeting minutes. Your response is inadequate in that it fails to provide a preventative action plan to prevent recurrence of this violation. Please provide a preventative action plan that explains how you will ensure meeting minutes are complete and accurate.

**Failure to adopt a method for keeping all members advised of research proposals which have been approved under an expedited review procedure [21 CFR 56.110(c)].**

Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure. You have failed to meet this requirement in the following way:

- Expedited review and approval for modification or continuing review took place on the following dates: May 5, 2005, December 19, 2005, November 30, 2007, and December 7, 2009 for the “(b)(4)” trial. However, there is no documentation to demonstrate that the IRB members were notified of these approvals.

In your response, you state that you will report expedited reviews at the next IRB meeting to keep members advised. Your response is inadequate in that it fails to provide a preventative action plan to prevent recurrence of this violation. Please provide a preventative action plan that explains the method adopted for keeping IRB members advised of research proposals which have been approved under an expedited review procedure.

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 Act and 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.

Your response should reference “CTS # EC100161” and be sent to:

Attention: Kathy Weil  
Food and Drug Administration  
Center for Devices and Radiological Health  
Office of Compliance  
Division of Bioresearch Monitoring  
10903 New Hampshire Avenue  
Building 66, Room 3500  
Silver Spring, Maryland 20993-0002.

*A copy of this letter has been sent to the FDA Cincinnati District Office, 6751 Steger Drive, Cincinnati, OH 45237-3097. Please send a copy of your response to that office.*

The Division of Bioresearch Monitoring has developed introductory training modules in FDA regulated device clinical research practices, which are available on the FDA website. The modules are for persons involved in FDA regulated device clinical research activities. These modules are located at the following website address:

<http://www.fda.gov/Training/CDRHLearn/ucm162015.htm><sup>1□</sup>

If you have any questions, please contact Kathy Weil at (301)796-6054 or [Kathy.Weil@fda.hhs.gov](mailto:Kathy.Weil@fda.hhs.gov).

Sincerely yours,

/S/

Michael E. Marcarelli, Pharm.D., M.S.

Director

Division of Bioresearch Monitoring

Office of Compliance

Center for Devices and Radiological Health

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**Links on this page:**

1. <http://www.fda.gov/Training/CDRHLearn/ucm162015.htm>