Inspections, Compliance, Enforcement, and Criminal Investigations

Ephraim McDowell Regional Medical Center IRB 4/26/10

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring, MD 20993

WARNING LETTER

UPS

Ref: 10-HFD-45-04-03

Ms. Vicki Darnell
President and Chief Executive Officer
Ephraim McDowell Regional Medical Center
217 S.3rd St.
Danville, KY 40422

Dear Ms. Darnell:

Between December 21, 2009 and January 6, 2010, Ms. Karen Bryerton Cooper, and Mr. Craig Rybus, representing the Food and Drug Administration (FDA), inspected the Institutional Review Board (IRB) at the Ephraim McDowell Regional Medical Center. The purpose of this inspection was to determine whether the IRB procedures for the protection of human subjects complied with Title 21 of the Code of Federal Regulations (CFR), parts 50 and 56. These regulations apply to clinical investigations of products regulated by FDA. We are aware that at the conclusion of the inspection, our investigators presented and discussed with Dr. Joan Haltom, Pharmacy Director, Ms. **(b)(6)**, Study Coordinator, and Ms. **(b)(6)**, Pharmacy Operations Clerk, a Form FDA 483, Inspectional Observations.

From our review of the establishment inspection report and the documents submitted with that report, we conclude that the IRB did not adhere to the applicable statutory requirements and FDA regulations governing the protection of human subjects. We acknowledge Dr. Thomas Baeker, IRB Chairman's written response dated February 3, 2010, to the Form FDA 483. However, because this written response was received more than fifteen business days after the Form FDA 483 was issued, the response has not been considered. We plan to evaluate Dr. Baeker's written response to the Form FDA 483 along with any other written material provided as the direct response to this letter.

We wish to emphasize the following:

1. The IRB failed to prepare and maintain written procedures for the IRB and failed to follow written procedures as required by 21 CFR 56.108(a) and (b) [21 CFR 56.115(a)(6)].

In order to fulfill the requirements of the IRB regulations, each IRB must prepare, maintain, and follow written procedures describing IRB functions and operations specified in the regulations.

Our inspection revealed that the IRB failed to prepare and maintain, and therefore did not follow, adequate written procedures for the IRB functions and operations. The IRB's Organizational Policy document, the only policy identified by the IRB staff as being in effect, and the only one examined by FDA that is signed, does not include the following:

a. Written procedures for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution [21 CFR 56.108(a)(1)]. We acknowledge some

limited references in the Organizational Policy document to certain aspects of review, such as the need for majority vote, and identification of quorum; however, this is not sufficient to address the requirements of this provision.

b. Written procedures 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 [21 CFR 56.108(a)(2)].

c. Written procedures for ensuring prompt reporting to the IRB of changes in research activities [21 CFR 56.108(a)(3)].

d. Written procedures 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 [21 CFR 56.108(a)(4)].

e. Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any unanticipated problems involving risks to human subjects or others [21 CFR 56.108(b)(1)].

f. Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB [21 CFR 56.108(b)(2)].

g. Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any suspension or termination of IRB approval [21 CFR 56.108(b)(3)].

2. The IRB failed to prepare and maintain a list of IRB members identified by name; earned degrees; representative capacity; indications of experience sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution [21 CFR 56.115(a)(5)].

As part of preparing adequate IRB records, the IRB is required to maintain a list of IRB members in accordance with the regulations.

Our inspection revealed that the IRB failed to prepare and maintain an adequate list of IRB members in compliance with the regulations. None of the IRB membership rosters reviewed by the FDA Investigators (years 2006-2007, years 2007-2008, and years 2008-2009) include each IRB member's earned degree, representative capacity, indications of experience sufficient to describe the member's chief anticipated contributions to the IRB deliberations, or any employment or other relationship between the member and the institution.

We note that this finding is a repeat issue from the previous inspection of the Ephraim McDowell Regional Medical Center IRB conducted in January 2004.

3. The IRB failed 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)].

Except when an expedited review procedure is used, the IRB may only review proposed research at convened meetings at which a majority of the IRB members (i.e., a quorum) is present, including at least one member whose primary concerns are in nonscientific areas.

Our inspection revealed that the IRB reviewed and approved research at meetings at which a majority of the IRB members was not present. For example:

a. Meeting minutes dated April 25, 2007 indicate that eight IRB members were present at the meeting, during which research was reviewed and approved. The IRB membership roster for the noted time period included seventeen members, meaning that at least nine members were required to be present in order to have a quorum.

b. Meeting minutes dated October 28, 2009 indicate that eight IRB members were present at the meeting, during which research was reviewed and approved. The IRB membership roster for the noted time period included seventeen members, meaning that at least nine members were required to be present in order to have a quorum.

The deficiencies found in the IRB membership rosters discussed in item #2 above, made it difficult to determine whether the required nonscientist was present at all convened IRB meetings when reviewing IRB meeting minutes.

We note that this finding is a repeat issue from the previous inspection of the Ephraim McDowell Regional Medical Center IRB conducted in January 2004.

4. The IRB failed to notify investigators and the institution in writing of its decision to approve or

disapprove proposed research activities, or of modifications required to secure IRB approval of the research activity [21 CFR 56.109(e)].

The IRB is required to notify investigators and the institution in writing of its decision to approve or disapprove proposed research, or of modifications required to secure IRB approval.

The IRB Organizational Policy document states that the minutes from the IRB will be forwarded to the Medical Executive Committee. Our inspection revealed that the IRB meeting minutes are not being forwarded to the Medical Executive Committee. There is no indication that IRB is notifying the institution in writing of its findings and actions.

This letter is not intended to be an all-inclusive list of deficiencies for the protocols reviewed and approved by the IRB. It is your responsibility to ensure that the Ephraim McDowell Regional Medical Center IRB's practices and procedures comply fully with all applicable statutes and regulations.

Within fifteen (15) business days of your receipt of this letter, you should notify this office in writing of the actions you have taken to prevent similar violations in the future. Your written response should include any documentation necessary to show that full and adequate correction will be achieved. Please include the projected completion dates for each action to be accomplished. Failure to adequately and promptly explain the violations noted above may result in regulatory action without further notice. If you believe that Dr. Baeker's written response to the Form FDA 483 dated February 3, 2010 fully explains the actions you have taken to prevent similar violations in the future, please communicate that to us in writing within fifteen (15) business days. As noted above, we plan to evaluate your written response to the Form FDA 483 along with any other written material provided as a direct response to this Warning Letter. You may reference the written response dated February 3, 2010 in your response to this letter.

We recommend that you visit the following FDA web page for information on human subject protections that may assist you in your efforts to bring the IRB into compliance with FDA regulations:

http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm□

We appreciate the cooperation shown to FDA Investigators Bryerton Cooper and Rybus during the inspection. If you have any questions, please contact Kevin Prohaska, D.O., M.P.H., at 301-796-3707; FAX 301-847-8748. Your written response and any pertinent documentation should be addressed to:

Kevin Prohaska, D.O., M.P.H.
Acting Human Subjects Protections Team Lead
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Bldg 51, Room 5356
10903 New Hampshire Avenue
Silver Spring, MD 20993

Sincerely,

/S/

Leslie K. Ball, M.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

cc: Dr. Thomas Baeker
IRB Chairman
Ephraim McDowell Regional Medical Center
217 S.3rd St.
Danville, KY 40422

Dr. Joan Haltom
Pharmacy Director
Ephraim McDowell Regional Medical Center
217 S.3rd St.

Danville, KY 40422

Ms. **(b)(6)**

Study Coordinator
Ephraim McDowell Regional Medical Center
217 S.3rd St.
Danville, KY 40422

Ms. **(b)(6)**
Pharmacy Operations Clerk
Ephraim McDowell Regional Medical Center
217 S.3rd St.
Danville, KY 40422

Dr. **(b)(6)**
Pharmacist
Ephraim McDowell Regional Medical Center
217 S.3rd St.
Danville, KY 40422

Links on this page: