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Inspections, Compliance, Enforcement, and Criminal Investigations

O'Barr, Thomas Jr., M.D. 9/30/10



Department of Health and Human Services

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

WARNING LETTER

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

Ref: 10-HFD-45-09-05

Thomas O'Barr, Jr., M.D.
1431 White Circle NW
Marietta, GA 30066

Dear Dr. O'Barr:

Between September 16 and 30, 2009, Ms. Stephanie Hubbard, representing the Food and Drug Administration (FDA), conducted an investigation and met with you to review your conduct of the following clinical investigations of the investigational drug **(b)(4)**, performed for **(b)(4)**:

Protocol **(b)(4)**, entitled **(b)(4)**"

Protocol **(b)(4)**, entitled **(b)(4)**"

This inspection is a part of the FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to help ensure that the rights, safety, and welfare of the human subjects of those studies have been protected.

From our review of the establishment inspection report, the documents submitted with that report, and your written responses to the Form FDA 483 dated October 2, 2009, we conclude that you did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations. We are aware that at the conclusion of the inspection, Ms. Hubbard presented and discussed with you Form FDA 483, Inspectional Observations. We wish to emphasize the following:

1. You failed to ensure that the investigation was conducted according to the investigational plan [21 CFR 312.60].

Protocol **(b)(4)** specified that at conclusion of the study, all primary data that are a result of the original observations and activities of the study that are necessary for the reconstruction and evaluation of any study report will be retained in a secure archive at the study site, for a period not less than two years after the last approval of a marketing application in an ICH region, and until there are no pending or contemplated marketing applications in an ICH region; or, at least two years have elapsed since the formal discontinuation of the clinical

development of the investigational product. You failed to maintain all study records as required by the study protocol.

- a. Specifically, during the inspection you were unable to provide case report forms for Protocol **(b)(4)** for any of the 20 subjects screened or 10 subjects enrolled into the study.
- b. There were no source documents found for Subject 500010 during the FDA inspection.

In your written response, you stated that in your evaluation of a subject, you would take the subject's clinical history, discuss the study with the subject, and make certain that based on the subject's clinical history, the subject was appropriate for the study. You stated that you counted on the study coordinators to make sure that the source data adequately represented and documented this information. You further stated that you clearly should have looked at the records yourself to ensure that they had been done appropriately.

Your statement that you counted on the coordinators to be sure that the source data adequately represented and documented this information is unacceptable. As the clinical investigator, it is your ultimate responsibility to ensure that the study was conducted according to the requirements set forth in the investigational plan.

2. You failed to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation [21 CFR 312.62(b)].

The following are examples of inadequate and inaccurate case histories noted for Protocol **(b)(4)**:

- a. The following was noted for Subject 500006:
 - i. The Clinically Significant Abnormal Lab Values form had a checkmark in a box that confirmed there were no clinically significant abnormal lab values identified for the Week 2 visit. However, the laboratory report for the Week 2 visit (June 29, 2005) and the Week 2 progress note had handwritten notes stating that you recommended that this subject be referred to his/her primary care physician due to the abnormally high glucose value of 156 mg/dL.

In your written response to this finding, you stated that in your review of the labs, you would sign your name indicating that you had reviewed them. If there were labs of any clinical significance, you would discuss them with the study coordinators and then with the subjects. You stated that you believed while abnormal labs were indicated, none of them are clinically significant, except patients that received specific instructions to follow up for specific values. You, however, concurred that the documentation for the lack of significance in these laboratory values was missing.
 - ii. There were two Visual Analog Scales for this subject for the Week 2 visit. We were unable to tell from the documents which Visual Analog Scale served as the accurate source record.
- b. Subject 500008's Clinically Significant Abnormal Lab Values form and the laboratory report for the Week 4 visit showed no information related to whether clinically significant abnormal labs were identified at this visit. In FDA's review of the lab report for samples collected at this visit, however, there were some test measurements that were noted on the report as being outside the reference range, including the measurements for creatine kinase, potassium, and blood monocytes.

In your written response to this finding, you stated that in your review of the labs, you would sign your name indicating that you had reviewed them. If there were labs of any clinical significance, you would discuss them with the study coordinators and then with the subjects. You stated that you believed while abnormal labs were indicated, none of them are clinically significant, except patients that received specific instructions to follow up for specific values. You, however, concurred that the documentation for the lack of significance in these laboratory values was missing.

3. You failed to maintain adequate records of the disposition of the drug, including the dates,

quantity, and use by subject [21 CFR 312.62(a)].

The following are examples noted for Protocol **(b)(4)**:

- a. Per the drug accountability log, Subject 500006 was dispensed 66 tablets of medication in Bottle A and 66 tablets in Bottle B on July 12, 2005, and none of these tablets were ever returned. However, the progress note dated July 22, 2005, states that the subject returned 48 tablets in Bottle A and 48 tablets in Bottle B.
- b. Per the drug accountability log, on July 9, 2005, Subject 500008 returned 22 tablets of medication in Bottle A and 22 tablets in Bottle B, and was also dispensed 66 new tablets in Bottle A and 66 new tablets in Bottle B. However, a Week 4 study document shows that this exchange of study drug tablets for Subject 500008 occurred on July 12, 2005.
- c. Per the drug accountability log, Subject 500013 was dispensed 66 tablets of medication in Bottle A and 66 tablets in Bottle B on June 28, 2005, and none of these tablets were ever returned. However, the progress note dated July 21, 2005, states that the subject returned 31 tablets in Bottle A and 29 tablets in Bottle B.
- d. Per the drug accountability log, Subject 500015 was dispensed 66 tablets of medication in Bottle A and 66 tablets in Bottle B on July 5, 2005 (Baseline Visit); and on July 20, 2005 (Week 2 visit), 35 tablets of medication in Bottle A and 35 tablets in Bottle B were returned. The Week 1 visit (July 12, 2005) progress note, however, shows that your site identified only 33 tablets remaining in each bottle at this visit.

In your written response, you acknowledged these findings. You stated that you did not personally review the numbers for each subject in the Drug Accountability Log reports and ensure that they corresponded to the numbers entered in the progress notes in the clinical records. You also stated that counting on the work of the coordinators, which was obviously substandard, was clearly a misjudgment on your part.

Your response that you did not review the numbers for each subject in the Drug Accountability Log reports and ensure that they corresponded to the numbers entered in the progress notes in the clinical records, is unacceptable. As the clinical investigator, it is your responsibility to ensure the maintenance of adequate records of the disposition of the drug.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study of an investigational drug. It is your responsibility to ensure adherence to each requirement of the law and relevant FDA regulations. You should address these deficiencies and establish procedures to ensure that any ongoing or future studies will be in compliance with FDA regulations.

Within fifteen (15) working 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. Failure to adequately and promptly explain the violations noted above may result in regulatory action without further notice.

If you have any questions, please contact Constance Cullity, M.D., M.P.H., at 301-796-3397; FAX 301-847-8748. Your written response and any pertinent documentation should be addressed to:

Constance Cullity (formerly Lewin), M.D., M.P.H.
Branch Chief
Good Clinical Practice Branch I
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Building 51, Room 5354
10903 New Hampshire Avenue
Silver Spring, MD 20993

Sincerely yours,
{See appended electronic signature page}
Leslie K. Ball, M.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

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/s/

LESLIE K BALL
09/30/2010

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