

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Gregory J. Tracey, M.D. 12/16/15



Department of Health and Human Services

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

WARNING LETTER
DEC 16, 2015

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ref.: 16-HFD-45-10-01

Gregory J. Tracey, M.D.
315 Park Avenue
Hoboken, NJ 07030

Dear Dr. Tracey:

This Warning Letter informs you of objectionable conditions observed during the U.S. Food and Drug Administration (FDA) inspection conducted at your clinical site between March 25 and April 15, 2015. Ms. Jonee J. Mearns and Ms. Byungja E. Marciante, representing FDA, reviewed your conduct of the following clinical investigations:

- Protocol **(b)(4)**, "**(b)(4)**," and
- Protocol **(b)(4)**, "**(b)(4)**."

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

At the conclusion of the inspection, Ms. Mearns and Ms. Marciante presented and discussed with you Form FDA 483, Inspectional Observations. We acknowledge receipt of your April 29, 2015, written response to the Form FDA 483.

From our review of the FDA Establishment Inspection Report, the documents submitted with that report, and your written response dated April 29, 2015, we conclude that you did not adhere to the applicable statutory requirements and FDA

regulations governing the conduct of clinical investigations. We wish to emphasize the following:

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

As a clinical investigator, you are required to ensure that your clinical investigations are conducted in accordance with the investigational plan. The investigational plan for Protocol **(b)(4)** requires that you verify that study subjects meet all eligibility criteria, and, in particular, that you not include subjects with a positive serum pregnancy test at screening or at check-in. You failed to adhere to these requirements.

Protocol **(b)(4)** specifies that subjects with a positive serum pregnancy test at screening or at check-in will not be included in the trial, and requires that you or your designee verify that subjects meet all eligibility criteria at screening and at check-in. You failed to adhere to these requirements when you enrolled into the study Subject 1214, a 22-year-old female of childbearing potential, with positive serum pregnancy tests at screening and at check-in. Specifically:

- Screening laboratory report: On December 4, 2014, Subject 1214's screening laboratory report showed clearly that the subject's serum human chorionic gonadotropin (hCG) level was 70.8 mIU/mL. That value was significantly above the reference hCG level that indicates pregnancy. You signed that laboratory report on December 4, 2015, indicating that you had reviewed the information in the report.
- Rescreening laboratory report: On December 19, 2014, Subject 1214's rescreening laboratory report showed clearly that the subject's serum hCG level was 34,833.0 mIU/mL. That value continued to be significantly above the reference hCG level that indicates pregnancy. You signed that laboratory report on December 22, 2014, indicating that you had reviewed the information in the report.
- Screening eligibility checklist: On January 2, 2015, despite these elevated serum hCG levels, you signed Subject 1214's screening eligibility checklist and indicated that Subject 1214 was eligible for study participation. That screening eligibility checklist shows the box checked "No" for whether the subject had a positive serum pregnancy test at screening or at check-in (that is, a serum hCG level above the reference level). However, your determination that Subject 1214 was eligible for study participation was contrary to the protocol, because the laboratory reports that you had signed indicated that Subject 1214 had a positive serum pregnancy test both at screening and at rescreening.
- Check-in laboratory report: On January 4, 2015, Subject 1214's check-in laboratory report showed clearly that the subject's serum hCG was 135,828.0 mIU/mL. Again, that value continued to be significantly above the reference hCG level that indicates pregnancy. You signed that laboratory report on January 5, 2015, indicating that you had reviewed the information in the report.
- Study Day 1 inclusion/exclusion summary: On January 5, 2015, you signed a

statement that you had reviewed the subject's inclusion/exclusion criteria and source documentation for the study; that you acknowledged having reviewed those records in order to determine the subject's eligibility to receive study drug; and that you had determined that the subject was eligible to receive study drug. However, as noted above, your determination that Subject 1214 was eligible to receive study drug was contrary to the protocol, because the records that you had signed indicated that Subject 1214 had a positive serum pregnancy test at screening, at rescreening, and at check-in.

As a result, on January 5, 2015 (Study Day 1), the subject received two oral **(b)(4)** doses of **(b)(4)**. On January 6 through January 8, 2015 (Study Days 2 through 4), the subject received one **(b)(4)** capsule daily.

The subject did not return to the clinic and was discontinued from the study on January 9, 2015. On January 22, 2015, the subject completed the early withdrawal/follow-up visit, and the laboratory report from that visit, which you signed, indicated that the subject's serum hCG level was 2050.0 mIU/mL.

We acknowledge your April 29, 2015, written response that serum hCG results were not flagged as being abnormal; that the subject did not report symptoms of pregnancy; and that the subject reported using condoms with spermicide and sponges. You stated that the laboratory has now agreed to flag all elevated serum hCG results, and to place elevated results in a separate column, printed in red ink.

Your response is inadequate because your corrective action plan is not sufficiently detailed. Specifically, you enrolled Subject 1214 despite the reference range for serum hCG on the laboratory reports clearly stating that any values above 5.2 mIU/mL are indicative of pregnancy, but you did not provide details regarding the laboratory's plan to use new procedures, or specifics on the steps that you and your colleagues will take to ensure the appropriate review of the laboratory's reports and the enrollment of eligible subjects. Without this information, we are unable to determine whether your corrective action plan is adequate to prevent similar violations in the future.

We emphasize our concern that you failed to fully evaluate the eligibility criteria for the study that were specifically designed to minimize foreseeable harm to enrolled subjects, and to maintain the interpretability of collected data. The enrollment of ineligible subjects raises significant concerns about the adequacy of the protection of study subjects enrolled at your site, and also raises concerns about the integrity of the data collected at your site.

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 address the violations noted above adequately and promptly may result in regulatory action without further notice. If you believe you have complied with FDA regulations, include your reasoning and any supporting information for our consideration.

If you have any questions, please contact Douglas Pham at 301-796-1955; FAX 301-847-8748. Your written response and any pertinent documentation should be addressed to:

Douglas Pham, Pharm.D., J.D.
Branch Chief (Acting)
Compliance Enforcement Branch
Division of Enforcement and Postmarketing Safety
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Building 51, Room 5348
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

Sincerely yours,

{See appended electronic signature page}

David Burrow, Pharm.D., J.D.

Director (Acting)

Office of Scientific Investigations

Office of Compliance

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DAVID C BURROW

12/16/2015

More in 2015

[\(/ICECI/EnforcementActions/WarningLetters/2015/default.htm\)](http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/default.htm)