



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

[Home](#) [Inspections, Compliance, Enforcement, and Criminal Investigations](#) [Enforcement Actions](#) [Warning Letters](#)

## Inspections, Compliance, Enforcement, and Criminal Investigations

Agnes E. Ubani, MD 11/21/13



Department of Health and Human Services

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

### WARNING LETTER

NOV 21, 2013

**CERTIFIED MAIL  
RETURN RECEIPT REQUESTED**

Ref: 13-HFD-45-11-02

Agnes Ubani, M.D.  
Windsor Medical Clinic  
11434 N 53<sup>rd</sup> Street  
Tampa, FL 33617-2216

Dear Dr. Ubani:

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 May 29 and June 6, 2013. Mr. Gene R. Gunn, representing the FDA, reviewed your conduct of the following clinical investigations:

- Protocol **(b)(4)**, "**(b)(4)**," of the investigational drug **(b)(4)**, performed for **(b)(4)**.
- Protocol **(b)(4)**, "**(b)(4)**," of the investigational drug **(b)(4)**, performed for **(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, Mr. Gunn presented and discussed with you Form FDA 483, Inspectional Observations. We acknowledge receipt of your June 28, 2013 written response to the Form FDA 483.

From our review of the FDA establishment inspection report, the documents submitted with that report, and your June 28, 2013 written response, 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:

**1. 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 studies are conducted in accordance with the investigational plan. The investigational plan for Protocol **(b)(4)** requires you to exclude subjects who meet the exclusion criteria and who do not meet the inclusion criteria. You failed to adhere to these requirements. Specifically:

a. Protocol **(b)(4)** requires that you exclude subjects who have a history of cancer (except for basal cell carcinoma) and/or treatment for cancer within the last five years prior to enrollment.

Subjects 58823 and 58827 were enrolled in the study with a history of cancer (prostate cancer and melanoma, respectively) within the last five years prior to enrollment.

b. Protocol **(b)(4)** requires all subjects to have "high cardiovascular risk," which is defined as at least one of the following:

- i. Confirmed history of myocardial infarction (>2 months prior to informed consent)
- ii. Evidence of multivessel coronary artery disease, in 2 or more major coronary arteries, irrespective of the revascularization status (disease affecting the left main coronary artery is considered as a 2-vessel disease)
- iii. Evidence of a single-vessel coronary artery disease with:
  - o The presence of a significant stenosis, i.e., the imaging evidence of at least 50% narrowing of the luminal diameter of one major coronary artery in subjects not subsequently successfully revascularized (measured during a coronary angiography or a multi-sliced computed tomography angiography)
  - o And at least one of the following (either 1 or 2):
    1. A positive non-invasive stress test, confirmed by either:
      - A positive exercise tolerance test in subjects without a complete left bundle branch block, Wolff Parkinson-White syndrome, or paced ventricular rhythm, or
      - A positive stress echocardiography showing regional systolic wall motion abnormalities, or
      - A positive scintigraphic test showing stress-induced ischemia, i.e., the development of transient perfusion defects during myocardial perfusion imaging
    2. Or subject discharged from hospital with a documented diagnosis of unstable angina within 12 months prior to selection
  - iv. Last episode of unstable angina >2 months prior to informed consent with confirmed evidence of coronary multivessel or single vessel disease as defined above
  - v. History of ischemic or hemorrhagic stroke (>2 months prior to informed consent)
  - vi. Presence of peripheral artery disease (symptomatic or not) documented by either: previous limb angiography, stenting or bypass surgery; or previous limb or foot amputation due to circulatory insufficiency; or angiographic evidence of significant (>50%) peripheral artery stenosis in at least one limb; or evidence from a non-invasive measurement of significant (>50% or as reported as hemodynamically significant) peripheral artery stenosis in at least one limb; or ankle brachial index of <0.9 in at least one limb

Subject 58828 was enrolled in Protocol **(b)(4)** without having high cardiovascular risk as defined above. This subject had a history of unstable angina and a positive non-invasive stress test, but did not have confirmed evidence of coronary multivessel or single vessel disease, as defined in the inclusion criteria. The subject had an approximately 20% narrowing of the lumen of a major coronary vessel (right coronary artery), but the inclusion criteria required a 50% or greater narrowing. In

addition, records indicate that the subject had a defect suggestive of myocardial ischemia rather than confirmation of a myocardial infarction. Based on inclusion criteria outlined above, this subject was ineligible and should not have been enrolled.

In your June 28, 2013 written response to the findings noted in Items 1.a and 1.b above, you indicate that you have established corrective action plans to prevent these violations from re-occurring. You state that subjects will be screened only after all medical records have been received and reviewed against protocol inclusion and exclusion criteria. Your response is inadequate because you have not provided details regarding how your corrective actions will be implemented. You have not provided details regarding how you will ensure that medical records are received prior to randomization, and how you will ensure that you and your staff review those records against protocol inclusion and exclusion criteria. Without these details, we are unable to determine whether your corrective actions appear sufficient to prevent similar violations from occurring in the future.

c. Protocol **(b)(4)** requires that you exclude subjects who have uncontrolled hyperglycemia with a glucose level of >240 mg/dl (>13.3 mmol/L) after an overnight fast during the placebo run-in and confirmed by a second measurement (not on the same day).

Subject 58832 was enrolled in the study, despite having uncontrolled hyperglycemia that met the conditions described above. Subject 58832 had a fasting blood glucose level of 246 mg/dl on January 23, 2012, during the placebo run-in period, followed by a reading of 261 mg/dl on January 24, 2012.

In your June 28, 2013 written response to the finding noted in Item 1.c above, you indicate that you will no longer delegate assessments that have direct or indirect bearing on subject eligibility and the subject diary reviews will be done by the investigator and not the study coordinator. Your response appears adequate to prevent similar violations from occurring in the future.

Subjects 58823, 58827, 58828 and 58832 represent 50% of the subjects who you enrolled in Protocol **(b)(4)**. Thus, one-half of the subjects you enrolled were not eligible for the study.

Enrollment of subjects who do not meet eligibility criteria jeopardizes subject safety and welfare and raises concern about the validity and integrity of the data collected at your site.

**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)].**

As a clinical investigator, you are required to prepare and 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. You have failed to maintain adequate and accurate case histories with respect to signature dates on study documents for Protocol **(b)(4)**. Specifically:

a. For Subject 58823, you received Visit 8 laboratory results on July 11, 2012. However, your signature on the laboratory report is dated June 12, 2012.

b. For Subject 58836, the Visit 4 laboratory report is dated April 21, 2012. However, your signature on the laboratory report is dated March 21, 2012.

In your June 28, 2013 written response to the finding noted in Item 2 above, you state that "Laboratory reports will be promptly revised and documented in a timely manner." Your response is inadequate because it is unclear what you intend to do with respect to revising laboratory reports.

Without details regarding your plans to revise laboratory reports, we are unable to determine whether your corrective actions appear sufficient to prevent similar violations from occurring in the future.

Your failure to maintain adequate and accurate case histories with respect to signature dates raises concerns about the validity and integrity of data captured 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 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, M.D., M.P.H.  
Branch Chief  
Good Clinical Practice Enforcement Branch  
Division of Good Clinical Practice Compliance  
Office 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}  
Thomas N. Moreno, M.S.  
Acting Director  
Office of Scientific Investigations  
Office of Compliance  
Center for Drug Evaluation and Research  
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/  
-----

THOMAS N MORENO  
11/21/2013

Page Last Updated: 01/15/2014

Note: If you need help accessing information in different file formats, see [Instructions for Downloading Viewers and Players](#).

[Accessibility](#) [Contact FDA](#) [Careers](#) [FDA Basics](#) [FOIA](#) [No Fear Act](#) [Site Map](#) [Transparency Website](#) [Policies](#)



U.S. Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993  
Ph. 1-888-INFO-FDA (1-888-463-6332)

[Email FDA](#)



[For Government](#) [For Press](#)

[Combination Products](#) [Advisory Committees](#) [Science & Research](#) [Regulatory Information](#) [Safety](#)  
[Emergency Preparedness](#) [International Programs](#) [News & Events](#) [Training and Continuing](#)  
[Education](#) [Inspections/Compliance](#) [State & Local Officials](#) [Consumers](#) [Industry](#) [Health](#)  
[Professionals](#) [FDA Archive](#)



---

### Links on this page: