DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS AND OPPORTUNITY TO EXPLAIN (NIDPOE)

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Dr. Bernard A. Corbett III, M.D.
(b) (6) [*home address*]

Dear Dr. Corbett:

Between April 30, 2012, and May 18, 2012, Ms. Esra Toussaint, representing the U.S. Food and Drug Administration (FDA), conducted an inspection to review your conduct of the following clinical investigations at Southeastern Research Associates (SRA):

- Protocol (b) (4), (b) (4) ” of the investigational drug (b) (4), performed for (b) (4); and
- Protocol (b) (4), (b) (4) ,” of the investigational drug (b) (4), performed for (b) (4).

This inspection is a part of the 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. Toussaint presented and discussed with you the items listed on Form FDA 483, Inspectional Observations. We have reviewed the inspection report and the documents submitted with that report. We note that you have not provided a written response to the Form FDA 483.

Based on our evaluation of information obtained by FDA, we believe that you have repeatedly or deliberately submitted false information to the sponsor or FDA in required reports, and repeatedly or deliberately violated regulations governing the proper conduct

of clinical studies involving investigational products, as published under Title 21, Code of Federal Regulations (CFR), part 312.

This letter provides you with written notice of the matters complained of and initiates an administrative proceeding, described below, to determine whether you should be disqualified from eligibility to receive test articles as set forth under 21 CFR 312.70, and disqualified from eligibility to conduct any clinical investigation that supports an application for a research or marketing permit for products regulated by FDA.

A listing of the violations follows. The applicable provisions of the CFR are cited for each violation.

1. **You repeatedly or deliberately submitted to the FDA or to the sponsor false information in any required report [21 CFR 312.70].**

   As a clinical investigator for Protocol (b) (4), you were required to ensure that all study records that your site submitted to the sponsor were true and accurate, including source documents and case report forms (CRFs). We have concluded that you repeatedly or deliberately submitted false information to the sponsor in the form of falsified study records. You falsified records by signing them to indicate, falsely, that you had performed study-related activities that were actually done by others while you worked elsewhere.

   During the inspection, you provided an affidavit in which you indicated that in February 2012, while you were the clinical investigator for Protocol (b) (4), you accepted a position at a facility located about 60 miles from SRA, the site where you conducted the study. In your affidavit, you indicated that you worked 12-hour shifts 20 times each month in this new position, and that the distance between your new workplace and SRA made it difficult for you to come to SRA.

   You admitted signing your name to study records for examinations that you did not perform. Specifically, you stated the following in your affidavit:

   > "I have signed patient examination records, including injection site inspections for the (b) (4) study [Protocol (b) (4)], although I did not see the patients. The patients' records that I was told to sign would be left in a folder on my desk and I would come in after hours and sign them. I cannot remember the number of records that I signed under those circumstances."

   Study records for Subject 108-010 appear to be among those that you falsified in Protocol (b) (4) by signing your name to examination records when you did not examine the subject. Based on the work schedule that you provided during the inspection, you were not present at SRA to perform the activities that your signatures suggest you performed. Instances in which you signed study records when your work schedule shows you were working elsewhere include, but are not limited to, the following:

a. Visit 10 (February 17, 2012): According to the work schedule you provided, you worked a 12-hour work shift starting at 7:00 a.m. on February 17, 2012, as an emergency doctor about 60 miles away from SRA. That same day, Subject 108-010 had assessments done for Study Visit 10 at SRA starting at approximately 7:45 a.m., and this subject was administered study drug by abdominal injection at 8:00 a.m. Based on your work schedule, you could not have been present for this study visit. However, you signed and wrote the date "17 February 2012" in three places on study records for the visit: once near the bottom of page 1, and twice on page 2. Your signatures on page 2 are next to responses regarding pre- and post-injection site inspections. Your signatures on that page give the false impression that you assessed the injection site for signs of an adverse reaction before and after dosing, when you were not available to do so. The date of your pre-injection signature was changed twice: date "05 March 2012" was crossed out and changed to "17 March 2012," and "17 March 2012" was crossed out and replaced with "17 Feb 2012."

b. Visit 11 (February 23, 2012): According to the work schedule you provided, you were working about 60 miles away from SRA until 7:00 a.m. on February 23, 2012. That same day, Subject 108-010 had assessments done for Study Visit 11 at SRA starting at approximately 7:35 a.m. Based on your work schedule, you could not have been present for this study visit. However, you signed and wrote the date "23 February 2012" in three places on study records for the visit: once near the bottom of page 1, and twice on page 2. (The date for the second of your two signatures on page 2 appears to have been written over to reflect a February 23, 2012 date.) Your signatures on page 2 are next to responses regarding pre- and post-injection site inspections. Your signatures on that page give the false impression that you assessed the injection site for signs of an adverse reaction before and after dosing, when you were not available to do so.

c. Visit 13 (March 8, 2012): According to the work schedule you provided, you started working a 12-hour shift at 7:00 a.m. on March 8, 2012, about 60 miles away from SRA. That same day, Subject 108-010 had several assessments done for Study Visit 13 at SRA starting at 7:55 a.m., and this subject was administered study drug by abdominal injection at 8:05 a.m. Based on your work schedule, you could not have been present for this study visit. However, you wrote your initials and the date "08 March 2012" in two places on page 2 of study records for this visit, next to responses regarding the pre- and post-injection site inspections. Those entries give the false impression that you conducted the pre- and post-injection site inspections, when you were not available to do so.

d. Visit 18 (March 15, 2012): According to the work schedule you provided, you started working a 12-hour shift at 7:00 a.m. on March 15, 2012, about 60 miles away from SRA. That same day, Subject 108-010 had several assessments done for Study Visit 18 at SRA starting at approximately 8:00 a.m. Based on your work schedule, you could not have been present for this study visit. However, you signed the signature line on page 1 of study records for the visit, directly underneath physical exam findings, and recorded the date of "15 March 2012" next to your signature. That entry gives the false impression that you conducted the

physical exam, when you were not available to do so. You also wrote your initials and the date "15 March 2012" on page 2 of study records for this visit.

e. Week 20 Follow-up Visit (March 29, 2012): According to the work schedule you provided, you were working a 12-hour shift until 7:00 a.m. on March 29, 2012, about 60 miles away from SRA. That same day, Subject 108-010 had assessments done for the Week 20 Follow-up Visit starting at approximately 7:30 a.m. Based on your work schedule, you could not have been present for this study visit. However, you wrote your initials and the date "29 March 2012" next to a response regarding injection site inspection. That entry gives the false impression that you inspected the injection site, when you were not available to do so.

As the clinical investigator, you are responsible for ensuring that the data collected from study subjects are accurate and can be relied upon in any analyses of the study endpoints. When you signed the Statement of the Investigator, Form FDA 1572, you agreed to provide accurate information to the sponsor and to ensure that you will comply with FDA regulations related to the conduct of the clinical investigations of the investigational drugs; and you agreed to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations in meeting their commitments. Furthermore, your signature constitutes both your affirmation that you are qualified to conduct the clinical investigation, and your written commitment to abide by FDA regulations in the conduct of the clinical investigations. The falsification of records significantly compromises the study integrity, as well as the reliability and validity of the data.

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

As a clinical investigator, you were required to ensure that your clinical studies were conducted in accordance with the investigational plan. The investigational plan for Protocol (b) (4) required that you enroll subjects whose body mass index fell within a certain range, and that you perform study-related procedures as specified in the protocol. You failed to adhere to these requirements. Specifically:

a. Protocol (b) (4) required enrolled subjects to have a body mass index of 27 to 45 kg/m . Subject 108-009 was enrolled in the study with a body mass index of 55.4 kg/m^2.

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.

b. Protocol (b) (4) did not allow disclosure of any information regarding treatment assignment to study personnel responsible for appraisal or care of subjects unless a subject became seriously ill or pregnant, and knowledge of the administered study drug would affect treatment options. On December 15, 2011, a study staff member (ES) responsible for appraisal or care of subjects contacted

the interactive voice response system for Protocol [redacted] and obtained the randomized treatment assignment, including the study drug dose, for Subject 108-010. In addition, you did not follow the protocol requirements to consult with the [redacted] medical monitor prior to unblinding, nor did you promptly notify the sponsor.

Allowing a treatment assignment to be disclosed to a study staff member who is not permitted to have that information also raises concerns about the validity and integrity of the data collected at your site, because study staff members were not blinded to the subject's treatment arm.

3. 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. Protocol [redacted] required that subjects have a body mass index of 27 to 45 kg/m^2 in order to be eligible for enrollment into the study. You have failed to maintain adequate and accurate case histories that allow for an accurate calculation of body mass index. Specifically:

Calculations of body mass index require body weight as a component of the calculation. Subject 108-009 had recorded weight discrepancies as follows:

Visit Date	Initial Recorded Weight	Recorded Weight Changed 01/26/2012
11/28/2011	175.6 kg/386.3 lbs.	152 kg/334.4 lbs.
12/05/2011	177.7 kg/390.9 lbs.	154.1 kg/339 lbs.
12/12/2011	172.4 kg/379.3 lbs.	150.1 kg/330.2 lbs.
12/19/2011	171.7 kg/377.7 lbs.	149.2 kg/328.2 lbs.
12/27/2011	175.3 kg/385.7 lbs.	153.2 kg/337 lbs.
01/03/2012	173.3 kg/381.3 lbs.	151.1 kg/332.4 lbs.
01/09/2012	171.0 kg/376.2 lbs.	149.2 kg/328.2 lbs.
01/16/2012	169.5 kg/ 372.9 lbs.	148.5 kg/326.7 lbs.
01/23/2012	170.4 kg/374.9 lbs.	148.4 kg/326.5 lbs.

You have not documented why these weights were changed in the study records. Your failure to maintain adequate and accurate case histories, including the failure to maintain accurate weight measurements on Subject 108-009, compromises 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 studies of investigational products. It is your responsibility to ensure adherence to each requirement of the law and relevant regulations.

On the basis of the above-listed violations, FDA asserts that you have failed to protect the rights, safety, and welfare of subjects under your care; repeatedly or deliberately submitted false information to the sponsor; and repeatedly or deliberately failed to comply with the cited regulations, thereby placing unnecessary risks to human subjects and jeopardizing the integrity of data, and the FDA proposes that you be disqualified as a clinical investigator. You may reply to the above-stated findings, including an explanation of why you should not be disqualified as a clinical investigator, in a written response or at an informal conference in my office. This procedure is provided for by regulation 21 CFR 312.70.

Within fifteen (15) days of receipt of this letter, write me at the address below or call me at 301-796-3865 to arrange a conference time or to indicate your intent to respond in writing.

Should you choose to respond in writing, your written response should be forwarded within thirty (30) days of receipt of this letter.

Your reply should be sent to:

Sean Y. Kassim, Ph.D.
Acting Director
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Building 51, Room 5346
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Should you request an informal conference, we ask that you provide us with a full and complete explanation of the above-listed violations. You should bring with you all pertinent documents, and a representative of your choice may accompany you. Although the conference is informal, a transcript of the conference will be prepared. If you choose to proceed in this manner, we plan to hold such a conference within 30 days of your request.

At any time during this administrative process, you may enter into a consent agreement with FDA regarding your future use of investigational products. Such an agreement would terminate this disqualification proceeding. Enclosed you will find a proposed agreement between you and FDA.

The FDA's Center for Drug Evaluation and Research (the Center) will carefully consider any oral or written response. If your explanation is accepted by the Center, the disqualification process will be terminated. If your written or oral responses to our

allegations are unsatisfactory, or we cannot come to terms on a consent agreement, or you do not respond to this notice, you will be offered a regulatory hearing before FDA, pursuant to 21 CFR 16 and 21 CFR 312.70 (enclosed). Before such a hearing, FDA will provide you with notice of the matters to be considered, including a comprehensive statement of the basis for the decision or action taken or proposed, and a general summary of the information that will be presented by FDA in support of the decision or action. A presiding officer who has not participated in this matter will conduct the hearing. After such hearing, the Commissioner will determine whether you will remain entitled to receive test articles and to conduct any clinical investigation that supports an application for a research or marketing permit for products regulated by FDA. You should be aware that neither entry into a consent agreement nor pursuit of a hearing precludes the possibility of a corollary judicial proceeding or administrative remedy concerning these violations.

To enter into the enclosed consent agreement with FDA, thereby terminating this disqualification process, you must:

(1) Initial and date each page of this Agreement;
(2) Sign and date the last page of this Agreement; and
(3) Return this Agreement initialed, signed, and dated to the signer below.

A copy of the fully executed Agreement will be mailed to you.

Sincerely yours,

{See appended electronic signature page}

Sean Y. Kassim, Ph.D.
Acting Director
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

Enclosures:
#1 - Consent Agreement
#2 - 21 CFR 16
#3 - 21 CFR 312.70

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

/s/

SEAN Y KASSIM
07/16/2014