U.S. FOOD & DRUG ADMINISTRATION

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

VIA UNITED PARCEL SERVICE

James W. Baker, M.D.
9495 SW Locust Street, Suite E
Portland, Oregon 97223

Dear Dr. Baker:

Between May 15 and June 19, 2017, Dr. Sherri N. Rohlf, representing the U.S. Food and Drug Administration (FDA), conducted an inspection to review 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 was conducted as a part of 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 human subjects have been protected.

At the conclusion of the inspection, Dr. Rohlf presented and discussed with you the items listed on Form FDA 483, Inspectional Observations. In addition, amendments to the Form FDA 483 were sent to you on July 20, 2017, and September 20, 2017. We acknowledge receipt of your July 10, 2017, written response to the original Form FDA 483 dated June 19, 2017.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903
www.fda.gov

We have reviewed the inspection report, the documents submitted with that report, and your July 10, 2017, written response to the Form FDA 483. We do not find your response to be acceptable in addressing the matters under complaint, which are described below.

Based on our evaluation of information obtained by FDA, we believe that you have repeatedly or deliberately submitted false information to the sponsor in required reports.

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 FDA-regulated products, including drugs, biologics, devices, new animal drugs, food, including dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, and tobacco products.

The violations and applicable CFR provisions are as follows:

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

As a clinical investigator for Protocols (b) (4) and (b) (4), you were required to perform physical examinations under Protocol (b) (4) and an oropharyngeal examination under Protocol (b) (4) at certain time points.

FDA has concluded that you submitted false information to the sponsor in required reports by signing forms stating that you performed physical and oropharyngeal examinations on subjects when you did not perform such examinations. Specifically:

1. Protocol (b) (4) required that physical examinations be conducted for each subject at Screening, Day 8, and on Day 90. The protocol further required that all data collected from subject evaluations, including the Screening, Day 8, and Day 90 physical examinations, be recorded on the appropriate Case Report Form (CRF) or electronic diary page. The protocol required that the clinical investigator guarantee that regulatory authorities, the institutional review board/independent ethics committee (IRB/IEC), and the sponsor would have direct access to all source documents, CRFs, and other study documentation.

    a. For Subject 001 in Protocol (b) (4) you signed and dated study records to falsely state that you performed the subject's Day 8 physical examination on August 22, 2013. You included data from these falsified documents in the CRFs submitted to the sponsor. However, you did not perform the Day 8 physical examination for this subject. In fact, you did not see the subject on that date at all because you were out-of-state at a wedding in Pennsylvania.

b. For Subject 003 in Protocol (b) (4):

   i. You signed and dated study records to falsely state that you performed the subject's Day 8 physical examination on October 20, 2013. You included data from these falsified documents in the CRFs submitted to the sponsor. However, you did not perform or see the subject for the Day 8 physical examination because you were out-of-state attending a medical meeting in Las Vegas, Nevada, on October 20, 2013.

   ii. You signed and dated study records to falsely state that you performed the subject's Day 90 physical examination on January 22, 2014. You included data from these falsified documents in the CRFs submitted to the sponsor. However, you did not perform the Day 90 physical examination because you were out-of-state attending a medical meeting in Hawaii on January 22, 2014.

c. For Subject 004 in Protocol (b) (4), you signed and dated study records to falsely state that you performed the subject's Screening physical examination on August 4, 2013. You included data from these falsified documents in the CRFs submitted to the sponsor. However, you did not perform the physical examination or see the subject on that date because you were out-of-state attending a medical meeting in New York City.

d. For Subject 005 in Protocol (b) (4), you signed and dated study records to falsely state that you performed the subject's Screening physical examination on August 4, 2013. You included data from these falsified documents in the CRFs submitted to the sponsor. However, you did not perform the physical examination or see the subject on that date because you were out-of-state attending a medical meeting in New York City.

2. Protocol (b) (4) required that an oropharyngeal examination for each subject be conducted at Visit 1. The protocol required that all subject data have supportive original source documentation. Data for the study, including records of oropharyngeal examinations, was required to be collected using specifically designed CRFs that would be captured in a clinical data management system available to the sponsor. Further, the protocol required that medical experts, study monitors, auditors, IEC/IRB, and health authority inspectors or their agents be given direct access to source data and documentation for source data verification.

   For Subject 003 in Protocol (b) (4), you signed and dated study records to falsely state that you performed the subject's Visit 1 oropharyngeal examination on October 9, 2015. You also signed the following statement and dated it October 9, 2015: "I verify that I have reviewed all source and study procedures for this subject and visit in its entirety and verify this with my signature below." You included data from these falsified documents in the CRFs submitted to the sponsor. However, you did not perform the oropharyngeal examination or see the subject on that date because you were out-of-state attending a medical meeting in San Juan, Puerto Rico.

In your July 10, 2017, written response to the Form FDA 483, you explained that in September 2016, your site was trained on and implemented new standard operating procedures (SOPs) for tracking institutional review board (IRB) approvals and documenting clinical investigator

availability for medical patients and research subjects. You indicated that because this 2017 inspection focused on studies conducted during the same timeframe as studies reviewed in the 2016 inspection, the inspection findings do not reflect the new processes you implemented.

You also acknowledged that you should not have signed and dated the documents when you were not present in the clinic. At the time, however, you assumed that you thought you missed signing some documents and therefore, backdated them without confirming if you were in the office, were present for the study visit, and performed the examination. You admitted you should have signed and dated the documents in real-time with a note explaining the late date and signature, and you have instructed Study Coordinators to bring a missed visit signature to your attention immediately so you can sign and date in real-time with an explanation, if applicable.

We acknowledge that you implemented the corrective actions described above. However, your response is inadequate because implementation of new SOPs does not negate your repeated submission of falsified study records to the sponsor. You failed to ensure that physical and oropharyngeal examination records for the studies cited above were true and accurate, and this significantly compromises the reliability and validity of the data from these studies. These source documents served as the basis for the data recorded in the electronic case report forms that were submitted to the sponsor's electronic database. As a result, you repeatedly submitted false information to the sponsor or FDA in the form of falsified records of physical and oropharyngeal examinations that were required to be made available to FDA and/or the sponsor.

As the clinical investigator, you are responsible for ensuring that the study is conducted properly and in compliance with FDA regulations in order to protect the rights, safety, and welfare of study subjects and to ensure the integrity of study data. Additionally, when you signed the Statement of the Investigator, Form FDA 1572, you agreed to comply with FDA regulations related to the conduct of the clinical investigations of the investigational drugs. The use of false information significantly compromises the study integrity, as well as the reliability and validity of the data.

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.

Based on the violations stated above, FDA asserts that you have repeatedly or deliberately submitted false information to the sponsor, which placed unnecessary risks to human subjects and jeopardized the integrity of data. Therefore, 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, either 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) working days of your receipt of this letter, write to me at the address below or call me at 301-796-5632 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 your receipt of this letter.

Your reply should be sent to:

David C. Burrow, Pharm.D., J.D.
Acting Director
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, MD 20993-0002

Should you request an informal conference, we ask that you provide us with a full and complete explanation of the violations stated above. 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 (copy enclosed) and 21 CFR 312.70. 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}

David C. Burrow, Pharm.D., J.D.
Acting Director
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
U.S. 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/

DAVID C BURROW
03/23/2018