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

Manoj K. Patel, M.D.
7117 Brockton Avenue
Riverside, California 92506

Dear Dr. Patel:

Between November 2 and November 23, 2010, and between April 4 and May 3, 2011, Mr. Comyar Shoghi, representing the U.S. Food and Drug Administration (FDA), conducted an inspection to review your conduct of the following clinical investigation of the investigational drug (b) (4), performed for (b) (4)

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 conducted between November 2 and November 23, 2010, Mr. Shoghi presented and discussed with you the items listed on Form FDA 483, Inspectional Observations. We acknowledge receipt of your November 30, 2010, written response to the Form FDA 483.

We have reviewed the FDA establishment inspection reports, the documents submitted with the reports, and your November 30, 2010, 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 the Agency, 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 312.70 (copy enclosed).

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(a)].**

   As a clinical investigator for Protocol , you were required to submit certain reports to the sponsor, including case report forms (CRFs) and the SF-36 Health Status Questionnaires. We have concluded that you repeatedly or deliberately submitted false information to the sponsor on such forms.

   Specifically, you submitted the following falsified records to the sponsor for Subject 001, your study coordinator ( ), whom you enrolled in the study (in violation of the investigational plan's restrictions against enrolling people directly involved in the study) under a fictitious name (DB):

   - The Visit-1 Screening CRF, dated June 21, 2007, which includes the study subject's medical history, physical examination, American College of Rheumatology (ACR) Classification of Global Functional Status, and vital signs
   - The Visit-2 Baseline (Pre-Dose-morning) CRF, dated July 2, 2007
   - The Visit-2 Baseline (Post-Dose) CRF, dated July 2, 2007
   - The Visit-2 (Baseline) SF-36 Health Status Questionnaire, dated July 2, 2007
   - The Visit-3 CRF, dated July 18, 2007
   - The Visit-4 CRF, dated August 13, 2007
   - The Visit-5 SF-36 Health Status Questionnaire, dated October 1, 2007
   - The Visit-5 CRF, dated October 1, 2007
   - The Week-20 Phone Call 1 CRF, dated November 19, 2007
   - The Visit-7 SF-36 Health Status Questionnaire, dated December 28, 2007
   - The Visit-7 CRF, dated and signed by you on December 28, 2007
   - The Week-33 Phone Call 2 CRF, dated February 18, 2008
   - The Visit-8 CRF, dated March 31, 2008
   - The Week-46 Phone Call 3 CRF, dated May 18, 2008
   - The Visit-9 End-of-Treatment CRF, and SF-36 Health Status Questionnaire, both dated July 3, 2008, when you were not in the United States

- The Visit-10 Follow-up CRF, dated July 10, 2008, when you were not in the United States
- The Study Completion CRF, dated July 3, 2008, when you were not in the United States, and signed by you on October 2, 2008

Your signatures on the Study Completion CRF and Investigational Review Board (IRB) correspondence indicate that you knew, or should have known, that these records contain false information, including a fictitious name and initials in place of the true name and initials of your study coordinator. You signed the Study Completion CRF on October 2, 2008, under the Investigator's Statement that reads, "I have reviewed the case report forms, and have found all data pertaining to this subject to be complete, accurate, and a true reflection of the subject's record." In addition, your written communication (dated November 17, 2008) to the Chairperson of your IRB states, "I alone was involved in the care of subject # 001 from the beginning to the completion of the study... I was under the impression given to me by this subject (who was also the study coordinator) that I had managed her case appropriately and according to protocol."

In your November 30, 2010, written response to the Form FDA 483, you indicated that your study coordinator's use of a fictitious name while in the study "was communicated [to you] through the monitor and was concluded to be a deviation and was addressed appropriately." In addition, your response states that the IRB also notified you of this "misinformation and forgery." Lastly, your written response indicates that you have undertaken "the necessary housekeeping with good clinical practice, procedural re-training with standard operating procedures and proper documentations [*sic*] …."

Your written response is inadequate. You failed to explain why you allowed your study coordinator to enroll in the study using a fictitious name, and you failed to explain why you signed the Investigator's Statement attesting to the accuracy of CRF data that you knew or should have known were inaccurate with respect to subject identity. You also failed to provide evidence that your study coordinator's use of a fictitious name was "addressed appropriately," as you state in your written response. Lastly, you have failed to describe or include any documentation of "the necessary housekeeping with good clinical practice, procedural re-training with standard operating procedures and proper documentations [*sic*]" that you identified in your response.

As the clinical investigator, you are responsible for ensuring that the data collected from study subjects are accurate and reliable. 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 your affirmation that you are qualified to conduct the clinical investigation, and also constitutes your written commitment to abide by FDA regulations in the conduct of the clinical investigations. The use of false information 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 are required to ensure that your clinical studies are conducted in accordance with the investigational plan. The investigational plan requires that you exclude from enrollment any person with direct involvement with the study conduct at your site. You failed to adhere to this requirement. Specifically, as discussed in Item 1 above, you enrolled your study coordinator ( ) into the study as Subject 001.

We recognize that the Form FDA 483 issued to you does not list this violation, so that your written response did not directly address this violation.

Your enrollment of study staff when the protocol prohibits such enrollment undermines confidence in the integrity of the data that you generated in this study.

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. Case histories include the informed consent documents and any source document worksheets. You have failed to maintain adequate and accurate case histories with respect to these records. Specifically:

a. On June 21, 2007, Subject 001, who is also your study coordinator ( ), signed the informed consent document using a fictitious name (DB). The consent document contains your purported signature, also dated June 21, 2007.

In your November 30, 2010, written response to the Form FDA 483, you indicated that your study coordinator's use of a fictitious name while in the study "was communicated [to you] through the monitor and was concluded to be a deviation and was addressed appropriately." In addition, your response states that the IRB also notified you of this "misinformation and forgery." Lastly, your written response indicates that you have undertaken "the necessary housekeeping with good clinical practice, procedural re-training with standard operating procedures and proper documentations [*sic*] …."

Your written response is inadequate. You failed to explain why you allowed your study coordinator to sign the consent document using a fictitious name, and you failed to provide evidence that your study coordinator's use of a fictitious name was "addressed appropriately," as you state in your written response. In addition, you have failed to describe or include any documentation of "the necessary housekeeping with good clinical practice, procedural re-training with standard operating procedures and proper documentations [*sic*]" that you identified in your response.

b. For Subject 001, who is also your study coordinator ([redacted]), two records bearing your purported signatures were dated when you were not in the United States. The Visit-9 Source Document Worksheet, dated July 3, 2008, bears your signature, also dated July 3, 2008, under the physical examination findings, giving the impression that you conducted the physical examination on that date. In addition, a laboratory report with a collection date of July 3, 2008, contains your signature dated July 23, 2008. However, airline records indicate that you left the United States on June 25, 2008, and did not return until July 31, 2008. In addition, during the November 2010 inspection, you indicated that you were not in the United States during the month of July 2008.

During the November 2010 inspection, you stated that you did not make your sub-investigator responsible for the study and did not authorize the study coordinator to see any patients. You also stated that you believe that Subject 001, your study coordinator, conducted the Visit-9 physical examination on herself, and that this coordinator signed your name to this document. You also indicated that you terminated the employment of your study coordinator when you became aware that the coordinator signed your name to this record.

In your November 30, 2010, written response, you indicated that the IRB notified you of this "misinformation and forgery" which came "as a shock and shook me up completely. This all transpired when I was out of the country …."

Your response is inadequate because it does not describe corrective actions taken to prevent similar violations in the future.

With respect to your signature on the laboratory report, you did not address this finding in your November 30, 2010, written response. However, we recognize that the Form FDA 483 issued to you does not list this violation.

c. On July 19, 2007, your Site Director (VB) signed the consent document using a fictitious name (SY). The consent document contains your purported signature, also dated July 19, 2007.

During the November 2010 inspection, you indicated that you were aware that your Site Director used a different name on the consent document. In your November 30, 2010, written response to the Form FDA 483, you indicated that your Site Director's use of a fictitious name while in the study "was communicated through the monitor and was concluded to be a deviation and was addressed appropriately." In your November 30, 2010, written response, you also indicated that a related Form FDA 483 item (Observation 3) "… included misinformation and forgery" which came "as a shock and shook me up completely." In addition, your written response indicates that you have undertaken "the necessary housekeeping with good clinical practice, procedural re-training with standard operating procedures and proper documentations [*sic*] …."

Your written and verbal responses are inadequate because they failed to explain why you allowed your Site Director to sign the consent document using a fictitious name,

and you failed to provide evidence that your Site Director's use of a fictitious name was "addressed appropriately," as you state in your written response. In addition, you have failed to describe or include any documentation of "the necessary housekeeping with good clinical practice, procedural re-training with standard operating procedures and proper documentations [*sic*]" that you identified in your response.

Failure to maintain adequate and accurate case histories compromises the interpretation and validity of the investigational endpoints and further undermines confidence in the integrity of the data that you generated in this study.

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, which placed unnecessary risks to human subjects and jeopardized 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, 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) days of your receipt of this letter, write 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 (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}

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
04/30/2014