DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

September 26, 2011

By Overnight Delivery

Michael Dean Berger, M.D.

b(6)

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS AND OPPORTUNITY TO EXPLAIN

Dear Dr. Berger:

Between April 27, 2010 and June 10, 2010, investigators representing the Food and Drug Administration (FDA, or, the agency) conducted an inspection of the following clinical studies and met with you to review your conduct as the clinical investigator of these studies:

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You conducted these studies at Immunovative, Clinical Research, Inc. (ICRI) in Carlsbad, California.

This inspection was conducted as part of FDA's Bioresearch Monitoring Program, which includes inspections designed to monitor the conduct of research involving investigational products.

At the conclusion of the inspection, the FDA investigators presented and discussed with you the items listed on Form FDA 483, Inspectional Observations. We have reviewed the inspection report, and the documents included with that report. We have not received a written response from you to the Form FDA 483.[1]

[1] On June 21, 2010, we received a letter from the sponsor of the above-named investigations ("Sponsor") that purported to respond to the Form 483 that was issued to you. However, there was no documentation to show that you had authorized the Sponsor to respond on your behalf. Accordingly, we do not consider the Sponsor's letter to be a response to your Form 483.

Based on our evaluation of information obtained by the agency, we believe that you have repeatedly or deliberately violated regulations governing the proper conduct of clinical studies involving investigational new drugs, as set forth under *Title 21, Code of Federal Regulations* (CFR), Part 312. The regulations are available at http://www.access.gpo.gov/cgi-bin/cfrassemble.cgi?title=201021.

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 receiving investigational products as set forth under 21 CFR § 312.70.

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

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

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A. In both b(4) protocol requirements concerning b(4) b(4) were not followed. Specifically, for both studies, protocol b(4) provides that:

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FDA's inspection revealed that there was no recorded data for lesion b(4) in any of the case report forms for the b(4) subjects enrolled in b(4) or the b(4) subjects enrolled in b(4) During the inspection, you indicated that you did not use the b(4) in this study because the b(4) would have indicated that the treatment was not working.

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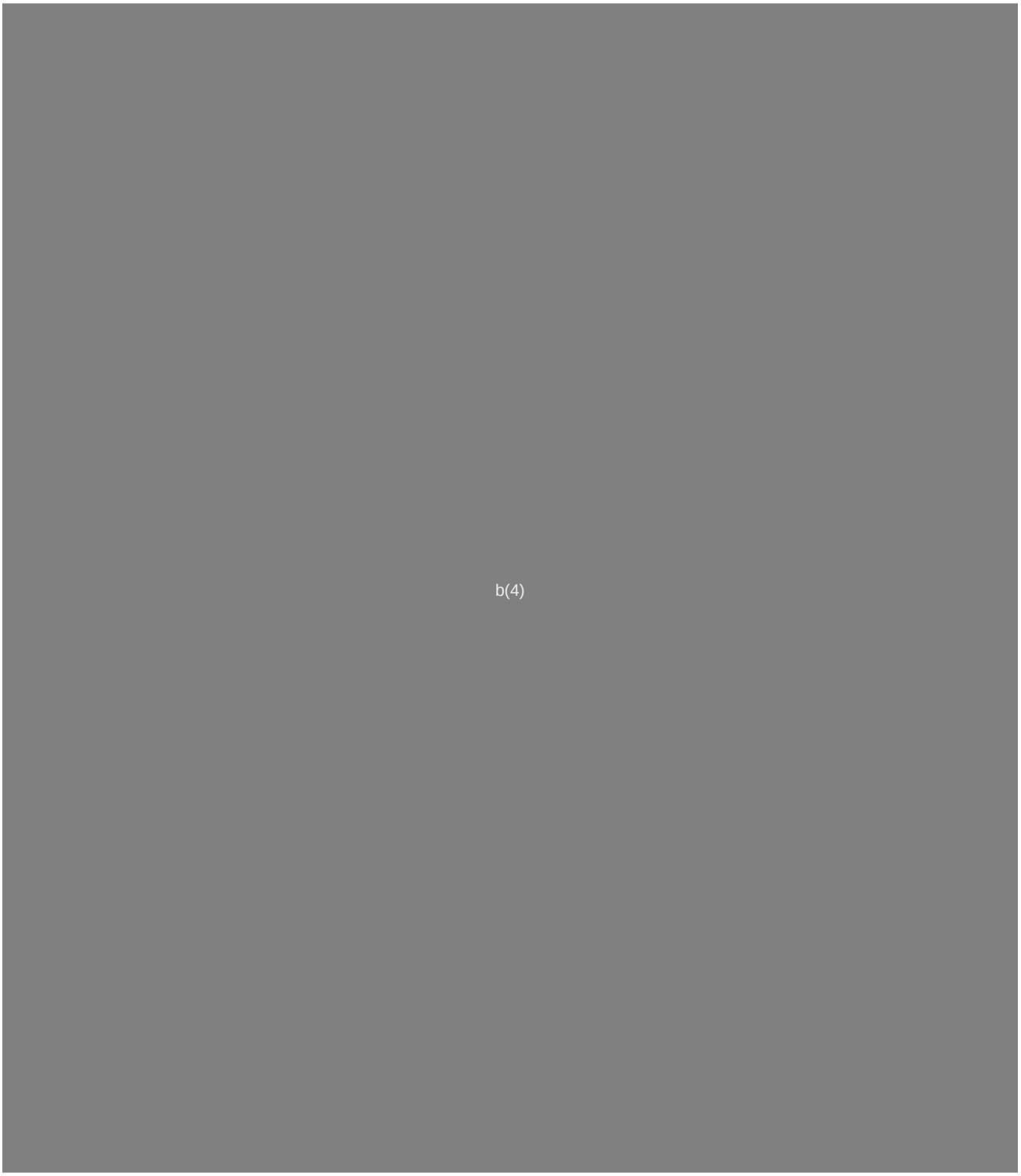
B. You failed to follow protocol requirements in b(4) concerning the dosing schedule and quantity of study drug to be administered to subjects. As documented in the table below, many subjects were dosed out of window, administered the drug by the incorrect route, and/or given numerous additional doses of the test article.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C. You failed to follow b(4) subject inclusion criteria. As shown in the table below, FDA's inspection revealed that Subject b(6) was enrolled in the study despite failing to meet the inclusion criteria in b(4) b(4)

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D. The study protocol incorporates the "Chemistry, Manufacturing and Control" (CMC) document by reference. The CMC document requires final formulated doses of the study drug to be administered to subjects before expiration; i.e., b(4) As shown in the table below, study records indicate that you administered the study drug to at least b(4) subjects after the study drug had expired.

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2. You failed to obtain informed consent in accordance with the provisions of 21 CFR Part 50. [21 CFR §§ 312.60 and 50.25(a)(1)].

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You obtained consent from subjects using a consent form that contained an inaccurate description of the procedures to be followed in the study. b(4)

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b(4) This consent form did not accurately describe your study procedures related to drug dose quantity, dose schedule, route of drug administration, b(4)

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3. You failed to report promptly to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and you made changes in the research without IRB approval. [21 CFR § 312.66].

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A. b(4)

B. As documented in the table below, study records indicate that b(4) lots of the study drug that were administered to subjects were subsequently found not to be sterile under the study's sterility testing procedures. There is no documentation that you ever reported to the IRB this unanticipated problem involving risks to human subjects. Additionally, during the FDA inspection, you acknowledged that you did not inform the IRB of these sterility failures.

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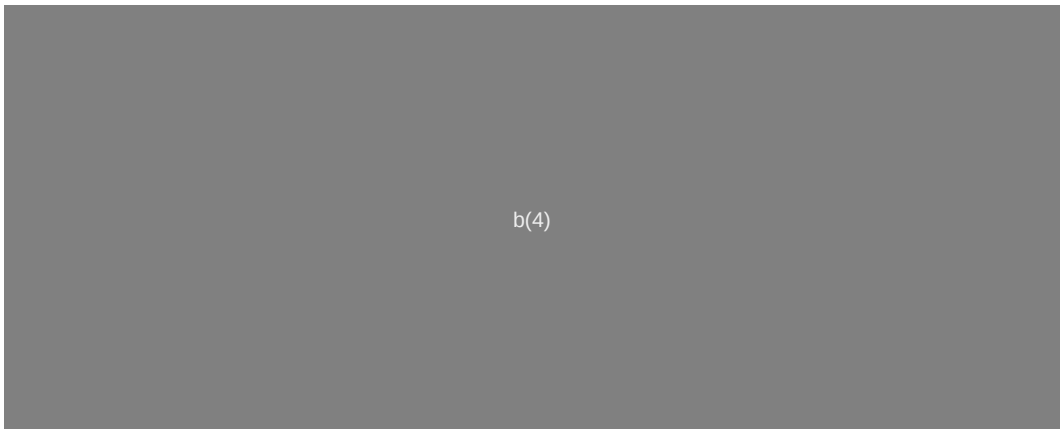
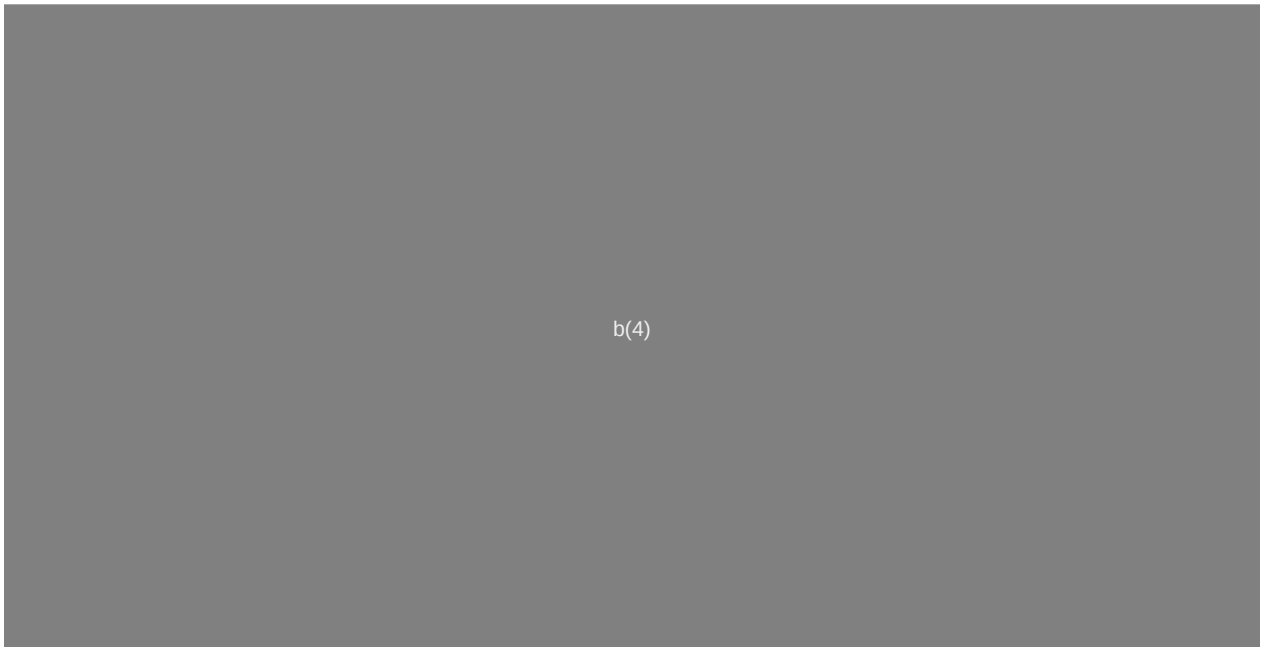
C. You failed to report promptly to the IRB unanticipated serious adverse events experienced by study subjects.



As documented in the table below, according to information obtained during the FDA inspections, you documented that several serious and unexpected adverse events (SAEs) experienced by subjects enrolled in b(4) were possibly, probably, or definitely related to the use of the study drug. However, study records indicate that you did not report these unanticipated serious adverse events to the IRB until 9/24/2010, months after they occurred.



Study records also show that at least b(4) additional subjects (Subjects b(6) b(6)) died within 30 days after the last administration of the study drug. According to the FDA inspection report, these unanticipated serious adverse events were either never reported to the IRB or not reported until on or after 9/24/2010, months after they occurred.

D. As described above in item 1.B, you did not follow the protocol's prescribed dosing schedule, dosing quantity, and/or drug administration route for subjects b(6) There is no documentation that you ever obtained IRB approval for these changes in research activity.

4. You failed to maintain adequate records of the disposition of the investigational drug, including dates, quantity, and use by subjects. [21 CFR § 312.62(a)].

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A. The drug administration record (Administration Record) for Subject b(6) does not include the drug administration date for b(4) doses administered to the subject.

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B. The Administration Record for Subject b(6) contains inaccurate dosing information. b(4)

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C. Study records for b(6) contain inaccurate drug administration information. b(4)

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5. You failed 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, including case report forms and supporting data. [21 CFR § 312.62(b)].

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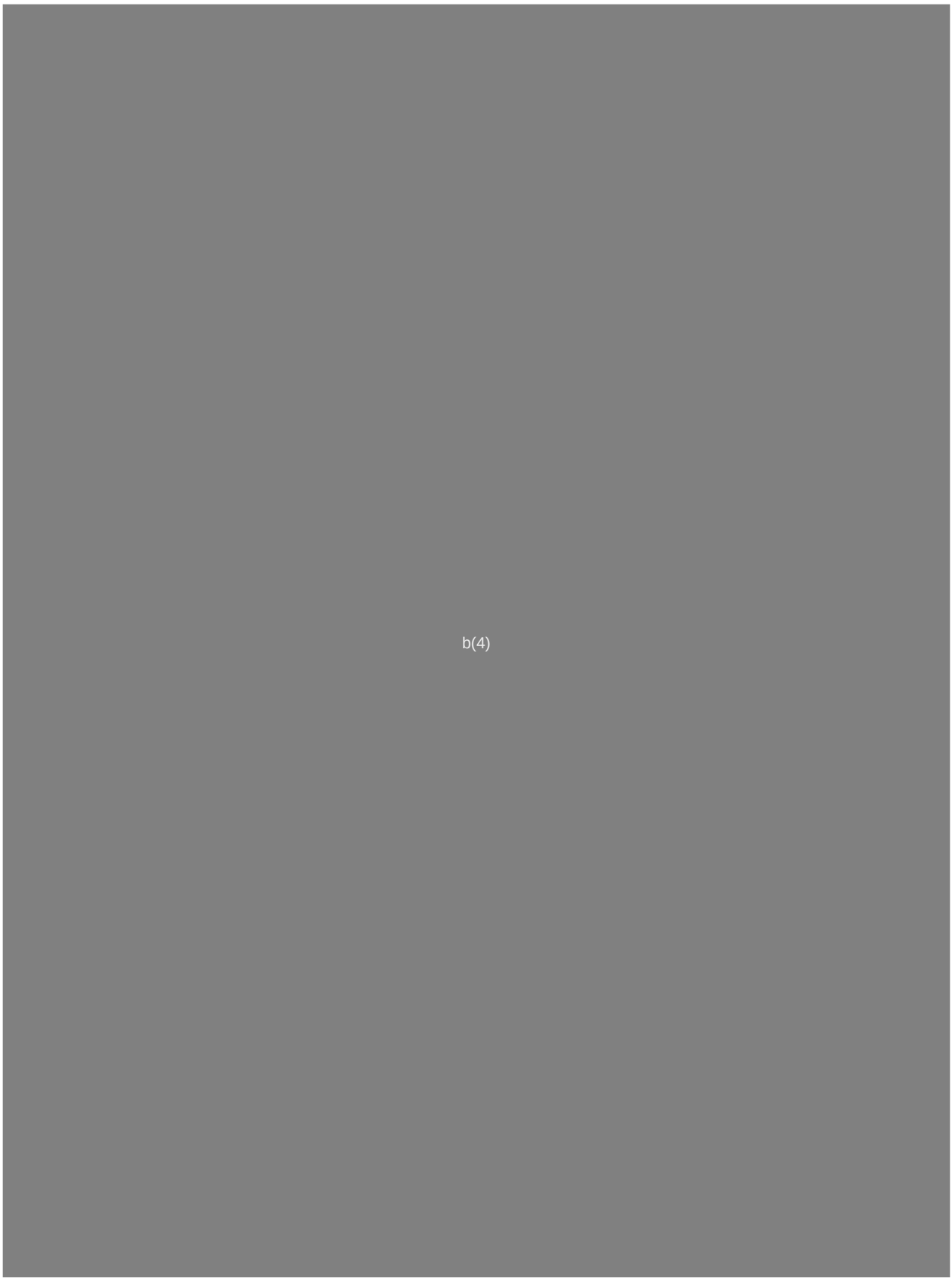
The FDA inspection revealed numerous discrepancies with regard to the dates when subjects first received the study drug (Day 0), the dates when subjects last received the study drug (test article stopped), subjects' study completion dates, and subjects' dates of death. These inconsistencies are shown in the table below. "SAE" means "serious adverse event."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This letter is not intended to contain an all-inclusive list of deficiencies with your clinical studies of investigational drugs. 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 repeatedly or deliberately failed to comply with the cited regulations. Accordingly, FDA proposes that you be disqualified as a clinical investigator. You may reply to the above stated issues, including any explanation of why you should remain eligible to receive investigational articles and 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) working days of receipt of this letter, write me to arrange a conference time or to indicate your intent to respond in writing. Your written response will need to be forwarded within thirty (30) working days of receipt of this letter. Your reply should be sent to:

Mary A. Malarkey, Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
1401 Rockville Pike, Suite 200N
Rockville, Maryland 20852-1488

Should you request an informal conference, we ask that you provide us with a full and complete explanation of the violations listed above. You should bring with you all pertinent documents. A representative of your choosing 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 thirty (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 articles. Such an agreement would terminate this disqualification proceeding. Enclosed you will find a proposed agreement between you and FDA.

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 Part 16 and 21 CFR § 312.70 (available at the internet address identified on page 1 of this letter). Before such a hearing, FDA will provide you 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. The Commissioner will determine whether or not you will remain entitled to receive

investigational articles. 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.

Sincerely yours,

for Mary A. Malarkey, Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

Enclosures: (1)