Supplementary Online Content


**eAppendix.** Two Examples of FDA Redactions

**eReferences.** References 76 through 184 from the main article

This supplementary material has been provided by the authors to give readers additional information about their work.
NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS AND OPPORTUNITY TO EXPLAIN (NIDPOE)
JAN 27, 2012

CERTIFIED MAIL
RETURN RECEIPT REQUESTED
Elmore Alexander, D.O.
(b)(6)

Dear Dr. Alexander:

Between November 13, 2009, and October 20, 2010, Ms. Stephanie Hubbard and Mr. LaReese Thomas, representing the U.S. Food and Drug Administration (FDA), conducted an investigation to review your conduct of the following clinical investigations of the investigational drug \( (b)(4) \), performed for \( (b)(4) \):

- Protocol \( (b)(4) \)
- Protocol \( (b)(4) \)
- Protocol \( (b)(4) \)

This inspection is 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 the human subjects of those studies have been protected.

At the conclusion of the inspection, Ms. Hubbard and Ms. Thomas attempted multiple times to present you with a Form FDA 483, Inspectional Observations. However, you refused to review the Form FDA 483 with FDA investigators. Consequently, and because your medical office had closed during the course of the inspection, the FDA investigators left a copy of the Form FDA 483 at your residence, and observed that you retrieved it.

We have reviewed the inspection report and the documents submitted with that report. We note that you did not provide a written response to the Form FDA 483. 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 (copy enclosed).

This letter provides you with written notice of the matters under complaint 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 the violations follows. The applicable provisions of the CFR are cited for each violation.

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

Based on the information obtained during the course of the inspection, the FDA has determined that you submitted falsified subject records for three subjects enrolled in your clinical trials. The FDA inspection revealed that all of the subjects you enrolled in Protocol \( (b)(4) \) and Protocol \( (b)(4) \) were, in fact, study coordinators whom you enrolled under fictitious names.

a. Protocol \( (b)(4) \): You enrolled your study coordinator \( (b)(6) \) into the study as Subject 1012 under a fictitious name (DCJ). In addition, you signed study records that showed the fictitious name for this subject.
(b)(6) completed the following study related documents for himself/herself while falsely claiming to be subject DCJ:

- Patient medical history questionnaire for the December 3, 2008, visit date.
- Inclusion/exclusion form on December 3, 2008.
- Screening records for Visit 1 on December 3, 2008. On the same date, you signed the physical examination portion of these records as the physician completing the examination.
- Informed consent document (ICD) showing falsified subject DCJ's signature on December 22, 2008. (This date was later crossed out and changed to January 23, 2009, and was initialed on February 3, 2009.) You also signed this subject's ICD on February 3, 2009.
- Study records for Visit 3 on December 23, 2008. In addition, you signed the Investigator Symptom Assessment for this visit on the same date.

Furthermore, study records note that you signed an informed consent document executed by falsified subject DCJ; you conducted physical examinations for subject DCJ at both the screening visit on December 3, 2008, and Visit 3 on December 23, 2008; and you signed a laboratory report for laboratory samples drawn from subject DCJ on January 23, 2009. These records indicate that you were aware that you enrolled your study coordinator into Study (b)(4) under a fictitious name.

b. Protocol (b)(4): You enrolled your study coordinator ((b)(6)), who was also the Chief Executive Officer of the Site Management Organization (SMO), Clinical Trial Providers Inc., into the study as Subject 1011 under a fictitious name (MD). You and (b)(6) also signed study records that showed the fictitious name for this subject. Specifically:

- ICD (August 13, 2008, version) showing falsified subject MD's signature on November 26 and December 10, 2008. You also signed these ICDs on November 26 and December 10, 2008.
- ICD (October 30, 2008, version) showing falsified subject MD's signature on January 13, 2009. Your study coordinator (b)(6) signed as the person obtaining consent on the ICD for subject MD on this date
- Screening records for Visit 1 on November 26, 2008. You completed and signed a physical examination form for subject MD at the screening visit on November 26, 2008. Your study coordinator (b)(6) also completed and signed screening records for Visit 1 on this date.
- Screening records for Visit 2 on December 10, 2008 (later crossed out and changed to December 9, 2008). Your study coordinator (b)(6) completed and signed these study records on December 16, 2008
- Visit 3 study records dated December 10, 2008. Your study coordinator (b)(6) completed and signed these study records on December 10, 2008, and you signed the Investigator Symptom Assessment section of these records on the same date.
- Visit 4 EGD report dated January 13, 2009. The signature at the bottom of this endoscopy report was not his/her true signature.
- Visit 4 EGD CRF (visit date January 13, 2009). Your study coordinator (b)(6) completed and signed the Visit 4 EGD CRF for subject MD on January 13, 2009.

As noted above, in addition to enrolling your study coordinator under a fictitious name, you signed study records that showed the fictitious name for this subject. These records indicate that you should have been aware that you enrolled your study coordinator, (b)(6), into Study (b)(4) under a fictitious name.

c. Protocol (b)(4): You enrolled your study coordinator ((b)(6)) into the study as Subject 1012 under a fictitious name (DCJ). You also signed study records that showed the fictitious name for this subject. Furthermore, your study coordinator, (b)(6), completed these study-related documents for himself/herself while falsely claiming to be subject DCJ:

- ICD dated January 23, 2009. Your study coordinator (b)(6) completed and signed her/his own informed consent document under the false identity of DCJ, originally on December 22, 2008. On February 3, 2009, your study coordinator, using the initials DCJ, crossed out the original date and changed it to January 23, 2009.
• Inclusion/exclusion criteria form on January 23, 2009. Your study coordinator (b)(6) completed and signed this study record on June 8, 2009, using his/her true identity as the person completing the form but using the false identity of DCJ as the subject.
• Visit 1 study records for January 23, 2009, visit date. You signed the Investigator Symptom Assessment study record for this visit, originally on December 23, 2009, then crossed out that date and changed it to January 23, 2009. You initialed this change on February 5, 2009.
• Visit 4 study records on February 26, 2009.

As noted above, in addition to enrolling your study coordinator into Study (b)(4) under a fictitious name, you signed study records that showed the fictitious name for this subject. These records indicate that you should have known that you enrolled your study coordinator into Study (b)(4) under a fictitious name.

As the clinical investigator, it was your ultimate responsibility to ensure that these studies were conducted properly and that subjects’ true identities were used on study records.

d. The signature of your subinvestigator, (b)(6), was falsified on the following documents:
• Financial disclosure form, signed and dated April 20, 2009.
• Endoscopy report dated January 13, 2009, for Subject 1011 in Study (b)(4).
• Memo dated February 4, 2009, which was attached to the November 21, 2008, endoscopy report for Subject 1004 in Protocol (b)(4).

As the clinical investigator, it is your responsibility to ensure that the data collected from study subjects are accurate and can be relied upon in all analyses of the study endpoints. As all of the collected data were based on falsified subjects, none of the data collected in support of the referenced studies are considered reliable. When you signed the Statement of Investigator, Form FDA 1572, you agreed to provide accurate information to the sponsor, and to assure that you will comply with FDA regulations related to the conduct of the clinical investigations of the investigational drugs. You also agreed to ensure that all associates, colleagues, and employees assisting in the conduct of the studies would be informed of 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 use of fictitious information significantly compromises the integrity of your studies, as well as the reliability and validity of the data.

2. **You failed to personally conduct or supervise the clinical investigations [21 CFR 312.60].**

When you signed the Statement of Investigator (Form FDA 1572) for the above referenced clinical trials, you agreed to take on the responsibilities of a clinical investigator at your site. Your general responsibilities as a clinical investigator include ensuring that the clinical trials are conducted according to the signed investigator statement, the investigational plan, and applicable regulations; protecting the rights, safety, and welfare of subjects under your care; and ensuring control of drugs under investigation [21 CFR 312.60]. By signing the Form FDA 1572, you specifically agreed to personally conduct the clinical trials or to supervise those aspects of the trials that you did not personally conduct. While you may delegate certain study tasks to individuals qualified to perform them, as a clinical investigator you may not delegate your general responsibilities. Our investigation indicates that your supervision of personnel to whom you delegated study tasks was not adequate to ensure that the clinical trials were conducted according to the signed investigator statement, the investigational plan, and applicable regulations, and in a manner that protects the rights, safety, and welfare of human subjects.

Specifically, you failed to adequately supervise the study coordinators to whom you delegated tasks. Your failure to adequately supervise the conduct of the studies referenced above led to many of the violations noted in this letter. These violations include, for example, the fabrication of records by your study coordinators; their enrollment under fictitious names in Protocols (b)(4) (Protocol (b)(4)) and (b)(4) (Protocol (b)(4)); and falsified signatures. Had you provided adequate oversight, you would have been able to prevent many of these violations from occurring.

As the clinical investigator, it was your ultimate responsibility to ensure that the studies were conducted properly and in compliance with FDA regulations, in order to protect the rights, safety, and welfare of study subjects and ensure the integrity of the study data. Your lack of supervision and oversight of the clinical studies raises significant concerns about the protection of study subjects enrolled into the studies, and the integrity of the data from your site.

3. **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 investigations are conducted according to the signed investigator statement, the investigational plan, and applicable regulations. You failed to conduct Protocols (b)(4) and (b)(4) according to the investigational plans. Examples of this failure include, but are not limited to, the following:
a. A sponsor newsletter, dated July 2008, prohibited the enrollment of “site staff associates” in your studies at the sites where the staff were employed. The purpose of this requirement was to avoid the introduction of bias into the study data. You violated this requirement by enrolling your study coordinators into the studies at your site. Specifically, you enrolled (b)(6) into Protocol (b)(4) in November 2008; you enrolled (b)(6) into Protocol (b)(4) in December 2008; and you enrolled (b)(6) into Protocol (b)(4) in January 2009, all of which were after the publication date of the sponsor newsletter. By enrolling your study coordinators into your studies, you introduced bias and compromised the study data.

b. Exclusion criteria for Protocol (b)(4) (version of March 24, 2008, exclusion criterion 7) and Protocol (b)(4) (version of February 11, 2008, exclusion criterion 3), require that subjects with current (b)(4) be excluded from enrollment into the study. Contrary to these exclusion criteria, you enrolled Subject 1012/DCJ (your study coordinator, (b)(6), using a fictitious identity) into Studies (b)(4) and (b)(4) despite two screening endoscopic evaluations on December 22, 2008, and January 22, 2009, documenting (b)(4). Based on these endoscopy results, this subject should have been excluded from enrollment into both studies.

We emphasize our concern that you failed to fully evaluate the eligibility criteria, designed specifically for each clinical investigation by the sponsor to optimize the interpretability of the data to the disease process under study, and to minimize foreseeable harm to enrolled subjects due to comorbidities. Enrollment of subjects who do not meet eligibility criteria jeopardizes subject safety and welfare and compromises the interpretation and validity of the investigational endpoints.

4. You did not obtain informed consent in accordance with the provisions of 21 CFR part 50 [21 CFR 312.60, 21 CFR 50.20, and 21 CFR 50.27].

As a clinical investigator, you are required to obtain legally effective informed consent prior to involving a subject in research. An investigator shall seek such consent only under circumstances that provide the prospective subject sufficient opportunity to consider whether or not to participate, and that minimize the possibility of coercion or undue influence. In addition, the regulations require that information given to the subject or the subject's legally authorized representative (LAR) shall be in language understandable to the subject or the LAR, and that the consent document be signed and dated by the subject or the subject’s LAR at the time of consent. You failed to obtain informed consent from subjects in accordance with these provisions of 21 CFR part 50. Examples include, but are not limited to, the following:

a. You failed to ensure that the consent documents were signed and dated by the subject or the subject’s LAR at the time of consent. Specifically, you failed to obtain signatures that reflected the subjects’ true identities or informed consent documents in that you permitted your study coordinators, (b)(6) and (b)(6), to enroll into studies under fictitious identities and to sign consent documents using these fictitious identities. You permitted your study coordinator, (b)(6), to sign consent documents as falsified subject DCJ in Studies (b)(4) and (b)(4), and you permitted your study coordinator, (b)(6), to sign consent documents as falsified subject MD for Study (b)(4).

b. You failed to obtain legally effective informed consent from Subject 1007 in Study (b)(4) in that you failed to ensure that the information given to the subject or the subject's LAR was in a language understandable to the subject or the LAR. Both you and your study coordinator told the Contract Research Organization (CRO) that the subject only spoke Spanish. The SMO administrator had to translate the consent form orally for this subject at the time of consent. You did not provide a Spanish version of the consent form to this subject or the subject’s LAR. In addition, there was no written documentation that a witness was present during the oral presentation of informed consent.

Subject 1007 signed the ICD for Study (b)(4) on November 17, 2008, and had the endoscopy procedure with gastric biopsy for screening purposes on December 12, 2008. Endoscopy and biopsy are both invasive procedures with potential adverse events for the study subject. By not providing the subject with proper informed consent, you jeopardized this subject’s safety by not assuring that he/she understood all the risks associated with screening for the study, including but not limited to the endoscopic procedure and biopsy.

c. You failed to obtain informed consent prior to involving subjects in research. Specifically, for Study (b)(4), Subject 1012 completed the patient medical history questionnaire, inclusion/exclusion form, and subject screening records on December 3, 2008. However, you did not obtain informed consent from Subject 1012 until December 22, 2008. In addition, Subject 1012’s informed consent form was signed under a fictitious name.

d. You failed to obtain legally effective informed consent from your study coordinators, (b)(6) and (b)(6), in that their enrollment raised concerns regarding coercion and undue influence. As your study site staff, (b)(6) and (b)(6) were not free to give informed consent that was independent of their status as employees. You did not minimize the potential for coercion and undue influence by enrolling them as subjects in your studies.
Your failure to ensure that informed consent documents were properly signed and dated by the subject or the subject's LAR; your failure to provide subjects with informed consent documents in a language that is understandable to the subject; and your failure to obtain informed consent prior to involving subjects in research jeopardize the safety and welfare of subjects by denying them an opportunity to assess the risks and benefits of their participation in the clinical investigation.

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 or employed as a control in the investigation [21 CFR 312.62(b)].

As clinical investigator, you were required to prepare and maintain adequate and accurate case histories that recorded 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 case report forms and supporting data, including, for example, subject medical records and signed and dated informed consent forms.

As discussed above, you enrolled two members of your study staff into your study under fictitious names. Thus, you did not maintain accurate case histories for these subjects because their medical records, case report forms, and informed consent forms contained false names.

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 issues, including an explanation of why you should remain eligible to receive investigational products 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) days of receipt of this letter, write or call me at 301-796-3150 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:

Leslie K. Ball, M.D.
Acting Director
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Building 51, Room 5342
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 free from bias or prejudice and who has not participated in this matter will conduct the hearing. Such a hearing will determine whether or not you will remain entitled to receive investigational products.
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}

Leslie K. Ball, M.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

Page Last Updated: 04/22/2012
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewer: and Players.

Accessibility Contact FDA Careers FDA Basics FOIA No Fear Act Site Map Transparency Website Policies
NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS
AND OPPORTUNITY TO EXPLAIN (NIDPOE)

CERTIFIED MAIL – RESTRICTED DELIVERY
RETURN RECEIPT REQUESTED

Kim C. Hendrick, M.D.
Flushing Family Care PC and
Flushing Research Center PC
6429 West Pierson Road, Suite 12
Flushing, Michigan 48433

Dear Dr. Hendrick:

Between July 29, 2002 and August 28, 2002, Ms. Laureen F. Kononen, representing the
Food and Drug Administration (FDA), conducted an inspection and met with you to
review your conduct of the following clinical investigations:

Protocol[ ] entitled: "An Open, Non-Comparative Multicenter Study
to Assess the Efficacy and Safety of Oral[ ] 125mg Twice
Daily for 10 Days in the Treatment of Acute Bacterial Sinusitis in Adults;"

and

Protocol[ ] entitled: "A Randomized, Double-Blind, Double
Dummy, Multicenter, Parallel Group Study to Assess the Efficacy and Safety
of Oral[ ] 320 mg Once Daily for 7 Days Compared with Oral
Cefuroxime Axetil 250 mg Twice Daily for 10 days in the Treatment of Acute
Bacterial Sinusitis (ABS) Infections," performed for[ ]

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

At the conclusion of the inspection, Ms. Kononen presented and discussed with you the
items listed on the Form FDA 483, Inspectional Observations. We have reviewed your
letter of September 10, 2002, in response to the inspecional observations, and accept
your response regarding protocol[ ] that subjects 19343[ ] and 19289[ ] met the inclusion criteria. We also acknowledge that the same radiologist was
not required to assess sinus X-rays for study subjects and screen failures. However, we
do not find your explanation acceptable in addressing the remaining matters under complaint.

Based on our evaluation of the information obtained by the agency, FDA’s Center for Drug Evaluation and Research (the Center) believes that you have repeatedly or deliberately violated regulations governing the proper conduct of clinical studies involving investigational drugs as published under Title 21, Code of Federal Regulations (CFR), Part 312 (copy enclosed) and that you submitted false information to the sponsor or FDA in a required report.

This letter provides you with written notice of the matters under complaint and initiates an administrative proceeding, described below, to determine whether you should be disqualified from receiving investigational drugs as set forth under 21 CFR 312.70.

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

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

   a. The sinus X-ray assessments for subjects enrolled in Protocol[] and Protocol[] which were used, in Case Report Forms or other documents you submitted to the sponsor, to confirm that the subjects met the inclusion criteria, were false. These false X-ray assessments provided the basis for the submission of false information to the sponsor or FDA in a required report.

   Both protocols required that the diagnosis of acute bacterial sinusitis (ABS) be confirmed by an independent radiological evaluation of the involved sinus(es) for subjects to qualify for inclusion in the studies. Protocol[] requires screening procedures at visit 1 including a sinus x-ray (Water's view) or a CAT scan, with the results of either study "consistent with a diagnosis of ABS of a maxillary sinus" for the patient to be enrolled (see Protocol Section 5.4.1). No CAT scan was purported to have been conducted in protocol[]. Protocol[] requires that the radiologist "radiologically confirm ABS of the affected sinus(es) via a Water's view X-ray" at the screening visit (see Protocol Section 5.3.1). You falsely represented that sinus X-ray assessments were performed by radiologist[] M.D. for at least 129 subjects that you enrolled in these protocols. These reports were purportedly from two sources: (1)[] and (2)[] although all were allegedly completed by Dr.[]. Dr.[] worked only for [].

   The X-ray reports found in your case files that were used to confirm that subjects met the inclusion criteria for the studies and identified as being from[] and completed by Dr.[] were visibly different from[] X-ray reports verified as authentic. The letterheads and format of authentic reports from[] were not the same as other reports.
identified as being from . In addition, all authentic X-ray reports have an assessment date under the electronic signature, most contain subject identifiers (i.e., birth date, social security number), and some are initialed by the radiologist performing the assessment. Of the assessments that we reviewed for enrolled subjects at your site, all lack the subjects' social security number and the majority lack an assessment date and the subjects' birth date. Those with birth dates depict the dates in a different position and format than that found on an authentic report. In addition, during an interview with Dr. on August 8, 2002, she stated to Ms. Kononen, the FDA investigator, that all assessments that did not document the date of the electronic signature, i.e., assessment date, were not performed by her.

Other X-ray reports in your files that were used to confirm inclusion criteria contained the following identifier: "Flushing Research Center, P.C. Interpreted

and listed Dr. as evaluator. Dr. stated in sworn testimony that she provided radiological interpretations for she had no agreement with you to perform assessments outside of and that she was "not a member of Furthermore, our personnel could not confirm the existence of

Protocol

1) There were 22 sinus X-ray assessments for 12 subjects (7/3/01, 7/24/01), (5/8/01, 5/30/01), (5/14/01, 5/31/01), (7/31/01), (3/13/01) (7/11/01, 7/31/01), (2/27/01, 2/30/01), (7/1/01), (1/26/01), (2/27/01, 3/23/01), (2/27/01, 3/26/01), (2/27/00, 12/27/00), and (12/8/00, 12/26/00) that were reported on letterhead and listed Dr. as the evaluator. In sworn testimony, Dr. stated that she did not interpret these X-rays.

During the course of the FDA inspection, our personnel requested staff to search its database (by subject name, requesting physician, and requesting group) for evidence that sinus X-rays were performed or interpreted at for the above subjects. could find no evidence in their database to indicate that these X-rays or assessments were done at

2) There were 22 sinus X-ray assessments for 12 subjects (12/4/01), (11/28/01, 12/17/01), (12/20/01, 1/7/02), (12/6/01, 1/25/02), (12/20/01, 1/7/02), (12/26/01, 1/5/02), (12/26/01, 1/8/02), (1/8/02), (1/29/02), (1/10/02, 1/28/02), (2/12/02, 3/5/02), (2/28/02, 3/18/02), and (3/19/02, 4/11/02) that were printed on stationery bearing the letterhead "Flushing Research Center, P.C. . Interpreted by and listed Dr. as the evaluator.
As stated above, Dr. stated that she was not "... a member of and our personnel could not confirm the existence of

3) FDA personnel compared the list of X-ray interpretations verified as generated by for the time period 12/1/00-12/31/01 with your study log listing the sinus X-rays that you reportedly sent to Dr. for evaluation for the same time period. Only two of the 195 X-ray assessments that you claim were performed by Dr. were performed at and neither of these assessments were performed by Dr. Specifically, Dr. confirmed that she did not perform the 3/7/01 assessment for subject that she did not perform the 3/7/01 assessment for subject corroborated that another of their radiologists performed this assessment, with the finding of clear paranasal sinuses. also confirmed that a radiologist other than Dr. evaluated the sinus X-rays for subject on 12/28/00, with the finding of mucosal thickening. The protocol required radiologically confirmed ABS of a maxillary sinus, and specifically stated that mucosal thickening alone was not sufficient to make a subject eligible, so neither of these subjects met the inclusion criteria for the study. However, you enrolled both subjects in the study. Note that this is also a protocol violation under item 2, set forth below.

To support your claim that reviewed and signed sinus X-ray reports for subjects enrolled in Protocol (as set forth in items 1.a.1), 1.a.2), and 1.a.3) above), you submitted to the sponsor a memorandum dated 8/29/01 that Dr. purportedly signed. This memorandum reads, "This is to certify that I received copies of previously read and electronically signed sinus x-ray reports from Flushing Family Care, PC on August 27, 2001. I reviewed the reports and signed all such copies provided me on August 28, 2001, as requested by Dr. Hendrick." You also presented this memorandum to Ms. Kononen during the FDA inspection in July/August 2002 when she questioned the different format of the sinus X-ray assessments for the enrolled subjects. Dr. has given sworn testimony that she did not write or sign this memorandum. We note that the signature on the 8/29/01 memorandum is markedly different from other documents that Dr. has confirmed that she signed.

Protocol

4) There were 25 sinus X-ray assessments for 13 subjects that were reported on letterhead and listed Dr. as the evaluator. In sworn testimony, Dr. reported that she did not interpret these X-rays.

During the course of the FDA inspection, our personnel requested staff to search its database (by subject name, requesting physician, and requesting group) for evidence that sinus X-rays were performed or interpreted at
Page 5—Dr. Hendrick

for the above subjects. [ ] could find no evidence of these X-rays in their database.

2. You failed to conduct the study in accordance with the investigational plan [21 CFR 312.60].

Protocol[ ]

You failed to adhere to the protocol in that you did not perform a screening sinus puncture for subject [ ] As a result of this failure, the primary efficacy measure could not be determined for this patient. In addition, as noted in item 1.a.3) above, the protocol required radiologically confirmed ABS of a maxillary sinus, and specifically stated that mucosal thickening alone was not sufficient to make a subject eligible. The radiological assessment for subject [ ] found clear paranasal sinuses and the radiological assessment of subject [ ] found mucosal thickening, so neither subject was qualified for the study. However, you enrolled both subjects in the study.

3. You failed to prepare and maintain adequate and accurate records [21 CFR 312.62(b)].

Protocol[ ]

You failed to document in the case report forms the reasons why 41 subjects were considered screen failures. The protocol required that you record the reason for exclusion of any patient from the study to document the lack of systemic bias in selecting patients.

4. You failed to report adverse events to the sponsor [21 CFR 312.64].

Protocol[ ]

As you acknowledged in your September 10, 2002, response to the 483, you failed to report to the sponsor the diarrhea and yeast infection experienced by subject [ ] during the study.

This letter is not intended to be 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, the Center asserts that you have submitted false information and repeatedly or deliberately failed to comply with the cited regulations for investigational new drugs and it proposes that you be disqualified as a clinical investigator. You may reply to the above stated issues, including an explanation of why you should remain eligible to receive investigational products 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) days of receipt of this letter, write or call me at (301) 594-0020 to arrange a conference time or to indicate your intent to respond in writing. Your written response must be forwarded within thirty (30) days of receipt of this letter. Your reply should be sent to:

Joseph Salewski  
Director (Acting)  
Division of Scientific Investigations (HFD-45)  
Food and Drug Administration  
7520 Standish Place, Suite 103  
Rockville, Maryland 20855

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 you may be accompanied by a representative of your choosing. 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 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 (enclosed) and 21 CFR 312.70. 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 free from bias or prejudice and who has not participated in this matter will conduct the hearing. Such a hearing will determine whether or not you will remain entitled to receive investigational products.
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,

(See appended electronic signature page)

Joseph Salewski
Director (Acting)
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research

Enclosures:
21 CFR 312
21 CFR 16
Consent Agreement
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Joseph Salewski
5/11/2006 02:50:59 PM
References. References 76 through 184 from the main article


77. Form 483 and EIR regarding Nasim Golzar, August 29, 2007.


81. Warning letter issued to Dmitri Sirakoff, September 12, 2013.


83. NIDPOE issued to Jamie Kapner, August 15, 2007.


89. NIDPOE issued to Christopher M. Phillips, January 20, 2006.


94. NIDPOE issued to James Vestal, May 9, 2007.


100. NIDPOE issued to Matthew J. Guy, January 24, 2008.


102. NIDPOE issued to Eduardo Caro Acevedo, August 28, 1998.

103. NOOH issued to Eduardo Caro Acevedo (via Nelson Rivera-Cabrera), August 18, 1999.


107. Warning letter issued to James Williams, April 9, 1999.


116. NIDPOE issued to Ramon Ramirez, October 21, 2008.


125. Form 483 and EIR regarding Joseph B. Michelson, August 24, 2010.

126. Warning letter issued to Laura Teasley, October 14, 2011.


136. Other Review, NDA022406, July 1, 2011.
140. Form 483 issued to David Craig Loucks, May 7, 2008.
141. EIR regarding David Craig Loucks, May 7, 2008.
151. Form 483 and EIR regarding Martha Hagaman, March 14, 2002.
152. NIDPOE issued to Martha Hagaman, March 1, 2005.


159. NOOH issued to Jacques R. Caldwell, March 8, 2006.


166 70: Medical Review, NDA021774, August 31, 2005.


168. NIDPOE issued to Maria Carmen Palazzo, December 3, 2003. (document 49.)

169. NIDPOE issued to Gabriel P. Lasala, February 16, 2012 (document 5.)


171. Center for Drug Evaluation and Research. NDA022406, compliance review (document 22.)

172. Center for Drug Evaluation and Research. NDA022406, other review(s) (document 24).


176. “TAX327” study of docetaxel.
177. United States of America v. Paul H. Kornak, 03-cr-00436 (Northern District of New York)


179. Center for Drug Evaluation and Research. NDA202145, medical review(s) (document 29); 185.


182. Center for Drug Evaluation and Research. NDA202145, medical review(s) (document 29).

183. EIR regarding Joseph B. Michelson (document 18).

184. As described by 5 USC §552(b)(4).