DEPARTMENT OF HEALTH & HUMAN SERVICES 2009 JUL -1 AM 8:14 Public Health Service
Food and Drug Administration
Silver Spring, MD 20993

NOTICE OF OPPORTUNITY FOR HEARING (NOOH)

HAND DELIVERED

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:

The Center for Drug Evaluation and Research (the Center) of the Food and Drug Administration (FDA) has information indicating that you repeatedly or deliberately violated federal regulations in your capacity as an investigator in clinical trials with multiple investigational drugs. The Center also has information indicating that you repeatedly or deliberately submitted false information to FDA or the sponsor in required reports. These violations provide the basis for withdrawal of your eligibility as a clinical investigator to receive investigational new drugs.

The Center's findings are based on information relating to your conduct as an investigator for the following clinical studies:

1. **Protocol** (b) (4) entitled: "An Open, Non-Comparative Multicenter Study to Assess the Efficacy and Safety of Oral (b) (4) /125mg Twice Daily for 10 Days in the Treatment of Acute Bacterial Sinusitis in Adults;" and

2. **Protocol** (b) (4) entitled: "A Randomized, Double-Blind, Double Dummy, Multicenter, Parallel Group Study to Assess the Efficacy and Safety of Oral (b) (4) 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 (b) (4).

FDA conducted an inspection between July 29, 2002 and August 28, 2002. After the inspection, and pursuant to section 312.70(a) of Title 21 of the Code of Federal Regulations [21 CFR 312.70(a)], the Center informed you, by letter titled "Notice of Initiation of Disqualification Proceedings and Opportunity to Explain" (NIDPOE) dated May 11, 2006, of numerous concerns

regarding your conduct of these studies, including submission of false information to FDA or to the sponsor in a required report, failure to conduct the study in accordance with the investigational plan, failure to prepare and maintain adequate and accurate records, and failure to report adverse events to the sponsor.

In October 2002, the FDA Field Investigator referred the matter to FDA's Office of Criminal Investigations (OCI) for further investigation. OCI's investigation determined that you falsified documentation that subjects met inclusion criteria and that this documentation was submitted to the clinical study sponsor, (b) (4) and FDA. On September 11, 2007, the United States District Court for the Eastern District of Michigan accepted your guilty plea and entered judgment against you for one count of mail fraud, a federal felony offense under 18 U.S.C. 1341. You were sentenced to nine (9) months in prison for this offense. On September 18, 2008, your sentence was amended to weekend incarceration for seven (7) months, followed by nine (9) months of electronic monitoring and three (3) years of probation.

The following details the underlying facts supporting your felony conviction:
Between 2000 and 2003, you were a licensed physician practicing medicine in the state of Michigan. You agreed to participate in the clinical research trial for (b) (4), including its use in the treatment of adults with Acute Bacterial Sinusitis (ABS). As part of your participation in the clinical study, you agreed to conduct the study in conformity with the protocol established by (b) (4) and comply with FDA regulations. You also agreed to take X-rays, before and after treatment, of persons you diagnosed with ABS, and to have an independent radiologist analyze these and issue reports regarding the X-rays.

As part of your plea agreement, you admitted that instead of having an independent radiologist review the X-rays and issue reports, you allowed certain X-rays to be sent in batch form, which was a direct violation of the protocol. Further, you did not verify the purported signatures of the independent radiologist reports and, instead, failed to disclose to (b) (4) and/or the FDA that the signatures were unverified and possibly forged, with the intent to create a false impression of a state of facts. You were paid by (b) (4) approximately $ (b) (6) in X-ray fees for your participation in the clinical research trial. In so doing, you did cause, on or about March 4, 2003, a check to be mailed to you through the Postal Service at the direction of (b) (4) as partial payment for your participation in the clinical trial for the purpose of executing the scheme to defraud.

The NIPDOE offered you an opportunity to respond in writing or at an informal conference. It also offered you the option of entering into a consent agreement with FDA, thereby terminating the disqualification proceeding against you. After the NIDPOE was issued in 2006, you requested, and were granted, several extensions to the deadline for responding to the NIDPOE while you addressed the criminal proceedings, guilty plea, and sentencing, described above. On June 1, 2007, FDA officials contacted your attorney, Michael Manley, to determine the status of your response to the NIDPOE. Mr. Manley confirmed that it was your intention to offer a revised proposed Consent Agreement (CA) to FDA and that this would be sent promptly. FDA made repeated attempts over the next several months to contact your attorney after FDA did not

receive a revised proposed Consent Agreement. On April 24, 2008, Michael Manley responded to FDA via teleconference that he was no longer representing you with regard to FDA related matters. Mr. Manley identified your new attorney as James Burdick, and indicated that Mr. Burdick would promptly contact FDA on your behalf.

In response to the NIDPOE, Mr. Burdick, on your behalf, proposed a revised Consent Agreement, dated July 31, 2008. Your proposed revisions, provided without explanation, excluded all references to submitting false documents to the sponsor or to FDA. After negotiations in September and October 2008, FDA and your attorney were unable to agree upon terms of a Consent Agreement. Mr. Burdick then requested an informal conference with the agency to present explanations for the violations set forth in the NIDPOE. An informal conference was held via teleconference on October 21, 2008 with FDA, you and your legal counsel participating. During the informal conference, you requested that FDA provide you with a copy of the response letter you submitted to FDA, dated September 10, 2002, to the Form FDA 483, and that FDA return to you all documents that were seized by FDA OCI during the OCI investigation. You stated that these documents were essential to preparing a response to the violations set forth in the NIDPOE. On October 23, 2008, FDA sent you by facsimile a copy of your response letter to the Form FDA 483. DSI obtained permission from the Assistant United States Attorney who prosecuted the criminal matter to release documents seized by OCI in that matter to you. On December 5, 2008, OCI agent (b) (7)(C) handed over to your attorney all documents seized by OCI during the criminal investigation. You then requested another extension, which DSI granted, of the response time in order to review these documents. On November 17, 2008, FDA received by email documents pertinent to subject (b) (6) from your attorney, Mr. Walter Piszczatowski, related to violations included in the NIDPOE. On January 9, 2009, you submitted an additional response to the NIDPOE.

We have evaluated the inspection report and all related documents, your response to the Form FDA 483, other pertinent information obtained by the Agency, your plea agreement, the informal conference, and your responses to the NIDPOE. After a review of all applicable information and documentation, the Center has accepted your response to the NIDPOE Item 2 as it pertains to subject (b) (6), and decided to delete reference to subject (b) (6) under Item 2 from the matters to be considered. However, we do not find your explanations acceptable in addressing the remaining matters under complaint because they fail to adequately address the violations set forth below. Therefore, in accordance with 21 CFR 312.70, FDA proposes that you be disqualified as a clinical investigator entitled to receive investigational drugs.

Accordingly, you are being offered an opportunity for a regulatory hearing pursuant to 21 CFR parts 16 and 312, to determine whether you are entitled to receive investigational new drugs. You have the right to be advised and represented by counsel at all times. Any regulatory hearing on this matter will be governed by the regulations in 21 CFR part 16 and FDA's guidelines on electronic media coverage of administrative proceedings, 21 CFR part 10, subpart C. Enclosed you will find copies of these regulations. A listing of the specific violations follows. These are matters that will be considered at the regulatory hearing. 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 (b) (4) and Protocol (b) (4), 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 (b) (4) 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 (b) (4). Protocol (b) (4) 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 (b) (4), M.D. for at least 129 subjects that you enrolled in these protocols. These reports were purportedly from two sources: (1) (b) (4) and (2) (b) (4), although all were allegedly completed by Dr. (b) (4). Dr (b) (4) worked only for (b) (4).

   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 (b) (4) and completed by Dr. (b) (4), were visibly different from (b) (4) X-ray reports verified as authentic. The letterheads and format of authentic reports from (b) (4) were not the same as other reports identified as being from (b) (4). In addition, all authentic (b) (4) 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 numbers and the majority lack an assessment date and the subjects' birth dates. Those with birth dates depict the dates in a different position and format than that found on an authentic (b) (4) report. In addition, during an interview with Dr. (b) (4) 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 by (b) (4)" and listed Dr. (b) (4) as evaluator. Dr (b) (4) stated in sworn testimony that she provided radiological interpretations for (b) (4), she had no agreement with you to perform assessments outside of (b) (4) and that she was "not a member of (b) (4)

." Furthermore, our personnel could not confirm the existence of (b) (4).

Specifically, our investigation found the following:

Protocol (b) (4)

1) There were 22 sinus X-ray assessments for 12 subjects ((b) (6) (7/3/01, 7/24/01), (b) (6) (5/8/01, 5/30/01), (b) (6) (5/14/01, 5/31/01), (b) (6) (3/13/01), (b) (6) (7/11/01, 7/31/01), (b) (6) (2/27/01, 3/20/01), (b) (6) (12/27/00, 1/18/01), (b) (6) (1/4/01, 1/26/01), (b) (6) (2/27/01, 3/23/01), (b) (6) (3/26/01), (b) (6) (12/8/00, 12/27/00) (b) (6) (12/7/00, 12/26/00)) that were reported on (b) (4) letterhead and listed Dr. (b) (4) as the evaluator. In sworn testimony, Dr. (b) (4) stated that she did not interpret these X-rays.

   During the course of the FDA inspection, our personnel requested (b) (4) staff to search its database (by subject name, requesting physician, and requesting group) for evidence that sinus X-rays were performed or interpreted at (b) (4) for the above subjects. (b) (4) could find no evidence in their database to indicate that these X-rays or assessments were done at (b) (4).

2) There were 22 additional sinus X-ray assessments for 12 subjects ((b) (6) (12/4/01), (b) (6) (12/6/01), (b) (6) (11/28/01, 12/17/01), (b) (6) (12/20/01, 1/8/02), (b) (6) (12/20/01, 1/7/02), (b) (6) (12/26/01, 1/15/02), (b) (6) (1/8/02, 1/25/02), (b) (6) (1/8/02, 1/29/02), (b) (6) (1/10/02, 1/28/02), (b) (6) (2/12/02, 3/5/02), (b) (6) (2/28/02, 3/18/02)), and (b) (6) (3/19/02, 4/11/02) that were printed on stationery bearing the letterhead "Flushing Research Center, P.C… Interpreted by (b) (4)," and listed Dr. (b) (4) as the evaluator.

   As stated above, Dr. (b) (4) stated that she was not "… a member of (b) (4) and our personnel could not confirm the existence of (b) (4).

3) FDA personnel compared the list of X-ray interpretations verified as generated by (b) (4) 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. (b) (4) for evaluation for the same time period. Only two of the 195 X-ray assessments that you claim were performed by Dr. (b) (4) were performed at (b) (4), and neither of these assessments were performed by Dr. (b) (4). Specifically, Dr (b) (4) confirmed that she did not perform the 3/7/01 assessment for Subject (b) (6); (b) (4) corroborated that another of their radiologists performed this assessment, with the finding of clear paranasal sinuses. (b) (4) also confirmed that a radiologist other than Dr. (b) (4) evaluated the sinus X-rays for Subject (b) (6) 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 Dr. (b) (4) reviewed and signed sinus X-ray reports for subjects enrolled in Protocol (b) (4) [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. (b) (4) 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 (b) (4) 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. (b) (4) has confirmed that she signed.

Protocol (b) (4)

4) There were 25 sinus X-ray assessments for 13 subjects (b) (6) that were reported on (b) (4) letterhead and listed Dr. (b) (4) as the evaluator. In sworn testimony, Dr. (b) (4) reported that she did not interpret these X-rays.

During the course of the FDA inspection, our personnel requested (b) (4) staff to search its database (by subject name, requesting physician, and requesting group) for evidence that sinus X-rays were performed or interpreted at (b) (4) for the above subjects. (b) (4) could find no evidence of these X-rays in their database.

No explanations were provided in your NIDPOE responses to address this violation. As part of your plea agreement, you admitted that you did not verify the purported signatures of the independent radiologist reports, and instead, failed to disclose to the sponsor or FDA that the signatures were unverified and possibly forged, with the intent to create a false impression of a state of facts.

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

Protocol (b) (4)

You failed to adhere to the protocol in that, 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. Two subjects were enrolled into the study who failed to meet this eligibility criterion. The radiological assessment for Subject (b) (6) found clear paranasal sinuses and the radiological assessment of Subject (b) (6) found mucosal thickening, so neither subject was qualified for the study. However, you enrolled both subjects in the study.

No explanations were provided in your NIDPOE responses to address this violation.

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

Protocol (b) (4)

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.

No explanations were provided in your NIDPOE responses to address this violation.

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

Protocol (b) (4)

As you acknowledged in your September 10, 2002, response to the Form FDA 483, you failed to report to the sponsor the diarrhea and yeast infection experienced by Subject (b) (6) during the study.

No explanations were provided in your NIDPOE response email to FDA, dated November 17, 2008 or letter to FDA, dated January 9, 2009, to address this violation.

For the violations outlined above, your responses to the NIDPOE, in an email to FDA, dated November 17, 2008, and letter, dated January 9, 2009, are unacceptable because, except for the findings pertinent to Subject (b) (6) referenced under Item 2 of the NIDPOE, they do not adequately address the remaining violations set forth in the NIDPOE letter.

Your request for a regulatory hearing pursuant to 21 CFR parts 16 and 312, must be made, in writing within ten (10) business days after receipt of this letter, and should be directed to Eugene R. Leger, Director, Division of Compliance Management and Operations (HFC-210), Office of Enforcement, ORA, FDA, 15800 Crabbs Branch, Rockville, MD 20855, Telephone (240) 632-6868, FAX (240) 632-6859. If no response to this letter is received by that time, you will be deemed to have waived any right to a regulatory hearing, and a decision in these matters will be made based on the facts available to FDA.

A request for a hearing may not rest upon mere allegations or denials but must present specific facts showing that there is a genuine and substantial issue of fact that warrants a hearing.

Pursuant to 21 CFR 16.26, a request for a hearing may be denied, in whole or in part, if the Commissioner or his delegate determines that no genuine and substantial issue of fact had been raised by the material submitted. A hearing will not be granted on issues of policy or law. Written notice of a determination of summary judgment will be provided, explaining the reasons for denial of the hearing.

If you wish to respond but do not desire a hearing, you should contact Mr. Leger within the time period specified above and send a written response containing your reply. The letter should state that you waive your right to a hearing and that you want a decision on the matter to be based on your written response and other information available to FDA.

FDA's offer to enter into a consent agreement, attached to the NIDPOE dated May 11, 2006, remains available. Entering into a consent agreement would terminate these administrative proceedings, but would not preclude the possibility of a corollary judicial or other administrative proceeding.

No final decision by FDA has been made at this time on your eligibility to continue to receive investigational new drugs. Moreover, there will be no prejudgment of this matter if you decline to enter into a consent agreement and decide instead either to request a regulatory hearing or to request that the decision be based on information currently available to FDA.

Please inform Mr. Leger within ten (10) business days of whether you wish to request a hearing or to have this matter resolved by consent agreement or information available to FDA.

Sincerely,

Michael Chappell
Acting Associate Commissioner
for Regulatory Affairs

Enclosures:
21 CFR part 10, subpart C
21 CFR part 16
21 CFR 312.70