DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

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 inspectional 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 by[ ]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),[ ] (3/13/01)[ ](7/11/01, 7/31/01)[ ](2/27/01, 3/20/01),[ ] (12/27/00, 1/18/01),[ ](1/4/01, 1/26/01),[ ](2/27/01, 3/23/01),[ ] (3/26/01),[ ](12/8/00, 12/27/00), and[ ](12/7/00, 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),[ ](12/6/01),[ ](11/28/01, 12/17/01),[ ](12/20/01, 1/8/02),[ ](12/20/01, 1/7/02),[ ](12/26/01, 1/15/02),[ ](1/8/02, 1/25/02),[ ](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[ ]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 Dr.[ ]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[ ]

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