



2017

Food and Drug Administration
Rockville MD 20857

JUN 27 2001

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS
AND OPPORTUNITY TO EXPLAIN (NIDPOE)

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Chavaramplakil P. Mathew, M.D.
Westbank Research Centers, Inc.
1101 Westbank Expressway
Gretna, Louisiana 70053

Dear Dr. Mathew:

Between May 30 and June 27, 2000, Ms. Dana M. Daigle and Dr. Mathew T. Thomas, representing the Food and Drug Administration (FDA), conducted an inspection of the following clinical studies in which you participated:

1. Protocol [] titled, "Comparative Safety and Efficacy of []
and Cefuroxime Axetil in the Treatment of Acute Bacterial Exacerbation of Chronic
Bronchitis"; and
2. Protocol [] titled, "Comparative Safety and Efficacy of [] and
Clarithromycin in the Treatment of Acute Bacterial Exacerbation of Chronic Bronchitis,"
sponsored by []

This inspection is part of the FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects in those studies are protected.

At the conclusion of the inspection Ms. Daigle presented and discussed with you the items listed on the Form FDA 483, Inspectional Observations. We have reviewed your letter dated July 20, 2000, in which you provided written responses to the items listed on the Form FDA 483. We accept your responses to items 2, 3b, 3c, and 3d. However, we do not accept your responses to items 1 and 3a.

Based on our evaluation of the inspection report and the documents submitted with that report, 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 new drugs as published under Title 21, Code of Federal Regulations (CFR), Part 312 (copy enclosed) or you repeatedly or deliberately submitted false information.

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

1. You submitted false data to the sponsor, in violation of 21 CFR 312.70(a).
 - a. In protocol [] you submitted data for subject #5508 [] for clinic visits on 10-29-98 and 11-05-98. The subject could not possibly have made those visits because the subject was incarcerated at the Jefferson Parish Correctional Center from 10-23-98 to 12-08-98. The false data included:
 1. Results of a physical examination performed by you on 10-29-98, as evidenced by your signature.
 2. Results of a physical examination performed by another physician on 11-05-98, as evidenced by the initial/signature (reportedly made by Dr. [])
 3. Assessment of subject's clinical progress reportedly obtained through direct conversations between the subject and Study Coordinator [] on 10-29-98 and 11-05-98, as evidenced by documentation in the subject's source records.
 4. Blood chemistry results for specimen collected on 10-29-98, as evidenced by laboratory reports.
 5. Assessment of study drug administration and compliance on 10-29-98, as evidenced by documentation in the subject's source records.

In your response, you state that the above mentioned false data were generated either by Ms. [] Study Coordinator, or that in all likelihood you and your staff were misled by a "third party." This explanation is unacceptable. As the investigator of record, you are responsible for the proper conduct of the clinical studies and must ensure the validity and veracity of the data generated from subjects who participated in your clinical studies.

- b. An individual to whom you entrusted study-related responsibilities has signed an affidavit stating that data submitted to the sponsor regarding subjects' study drug compliance were inaccurate. This individual stated that, "...the subjects' returned drug was disposed of and 100% drug compliance was recorded. I occasionally disposed of returned drug and recorded 100% compliance myself. I estimate that this occurred no more than 20% of the time." This individual further stated that the subject identified in Item 1a. above was imprisoned and was unable to visit the center to complete the study. This individual stated that the subject was

reported to have taken all of his medications at completion of the study, when in fact, this individual received and discarded some of the subject's returned study drug. This individual also stated that it was routine practice at the center to record that a patient "left town" when they failed to return, or, as in the case of the subject identified in 1a. above, were imprisoned and unable to return to the center.

2. You failed to conduct the study in accordance with the investigational plan, in violation of 21 CFR 312.60.

a. For both protocols [] and [] you failed to collect sputum samples in accordance with the investigational plan. During the FDA inspection and in your written response to the Form FDA 483, you acknowledged that qualifying sputum specimens were obtained from an unidentifiable number of subjects from outside the clinic. Furthermore, you failed to document the specific instances of sputum collection obtained outside the clinic thereby providing a false impression that all sputum specimens were collected as instructed by the sponsor. The sponsor, [] informed FDA that all clinical investigators were specifically instructed during the investigators' meeting that the study required the collection of subjects' sputum in the presence of the clinical investigator. Documentation of that meeting indicates that you and your staff were in attendance. Attendees were specifically tested via an interactive audience system on the question of what to do if a patient is unable to produce a sputum specimen at the pre-therapy visit or if the specimen is unacceptable. The unambiguous answer to this question was that if a patient is unable to produce a sputum specimen at the pre-therapy visit or if the specimen is unacceptable, the patient is ineligible for the study. This answer was presented to and discussed with the audience immediately after the question.

b. Both protocols required that subjects' blood samples be collected and sent to the laboratory for testing so that "any clinically significant abnormal values" could be evaluated. In the instances listed below, however, the coagulation samples for these subjects were not sent to the laboratory and there was no documentation as to why the specimens were not sent:

1. In protocol [] subject #3342 [] visit 1 on 1-22-98.

2. In protocol []

a) Subject #5198 [] visit 3 on 8-28-98.

b) Subject #5352 [] visit 1 on 9-28-98.

3. You failed to maintain adequate and accurate case histories, in violation of 312.62(b) and (c).

a. In protocol [] subjects #3014 [] and #3015 [] were enrolled with identical identification information including social security numbers, addresses and telephone numbers.

b. In protocol []

1. The follow-up clinic visits for visit 4 of subject #5199 [] on 9-8-98, and for visit 1 of subject #5337 [] on 9-1-98, were not documented in the sign-in logs maintained in your clinic.
2. A sign-in log to document visit 4 of subject #5513 [] on 11-20-98 was not available for inspection.

4. You failed to personally conduct or supervise the clinical investigation as you committed to do when you signed the investigator statement (Form FDA 1572), in violation of 21 CFR 312.60.

The violations documented above resulted, at least in part, from your failure to be directly involved in the conduct of the studies or to adequately supervise personnel assisting you with the conduct of those studies. You should recognize that although duties may be delegated, it is the principal investigator who is ultimately responsible for the conduct of the study, and the submission of accurate information to the sponsor and FDA.

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 repeatedly or deliberately failed to comply with the requirements of 21 CFR 312 or repeatedly or deliberately submitted false information to the sponsor or the FDA. The Center proposes that you be disqualified as a clinical investigator. You may reply in writing or at an informal conference in my office 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. 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:

Stan W. Woollen
Acting Director
Division of Scientific Investigations, HFD-45
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place, Room #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 all pertinent documents with you, and 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 30 days of your request.

At any time during this administrative process, you may enter into a consent agreement with the Center 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 the Center.

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 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. After such a hearing, the Commissioner 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,



Stan W. Woollen
Acting Director
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research

Enclosures:

- #1 - 21 CFR 312
- #2 - 21 CFR 16
- #3 - Agreement