DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUN - 3 2002

CERTIFIED MAIL-RESTRICTED DELIVERY
RETURN RECEIPT REQUESTED

Chavaramplakil P. Mathew, M.D.
3239 Bienville Avenue
New Orleans, Louisiana 70119

NOTICE OF OPPORTUNITY FOR HEARING

Dear Dr. Mathew:

The Center for Drug Evaluation and Research (the Center) of the United States Food and Drug Administration (FDA) has information that you repeatedly or deliberately violated federal regulations in your capacity as an investigator for the following clinical studies:

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

Protocol [ ] titled, "Comparative Safety and Efficacy of [ ] and Clarithromycin in the Treatment of Acute Bacterial Exacerbation of Chronic Bronchitis," sponsored by [ ]

The Center also has information indicating that you submitted false information to FDA or the sponsor in required reports. These violations and submission of false information provide the basis for withdrawal of your eligibility as a clinical investigator to receive investigational new drugs.

The Center's findings are based on our evaluation of information obtained from, but not limited to, the establishment inspection report for the FDA inspection conducted between May 30 and June 27, 2000, the documents submitted with that report, information received from sponsors, and your written responses dated July 20, 2000, and July 15, 2001.

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 June 27, 2001, of the specific matters complained of and offered you an opportunity to respond in writing or at an informal conference. The NIDPOE also offered you the option of entering into a consent agreement with the FDA, thereby terminating any administrative proceeding against you.

In response to the NIDPOE, you submitted a written response dated July 15, 2001. After a review of all available documentation, and your explanations, the Center has concluded that your explanations are unacceptable because they fail to adequately address the violations set forth below.

Accordingly, you are being offered an opportunity for a regulatory hearing pursuant to 21 CFR parts 16 and 312, on the question of whether you should be entitled to receive investigational new products or 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.

I. You submitted false data to the sponsor, in violation of 21 CFR 312.70(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:

A. Results of a physical examination performed by you on 10/29/98, as evidenced by your signature.

B. Results of a physical examination performed by another physician on 11/05/98, as evidenced by the initials/signature (reportedly made by Dr.[ ]

C. 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.

D. Blood chemistry results for specimen collected on 10/29/98, as evidenced by laboratory reports.

E. Assessment of study drug administration and compliance on 10/29/98, as evidenced by documentation in the subject's source records. In addition, an individual to whom you entrusted study-related responsibilities has signed an affidavit stating that data submitted to the sponsor regarding this subject's study drug compliance were inaccurate. This individual stated that the subject was imprisoned and was unable to visit the center to complete the study. This individual further stated that at the completion of the study a report was prepared to show that the subject took all the study medications, when in fact, this individual received and discarded some of the subject's returned study drug.

II. 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.

III. You failed to maintain adequate and accurate case histories, in violation of 21 CFR 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 visit for subject #5199 [ ] on 9/8/98, and visit 1 for subject #5337 [ ] on 9/1/98, were not documented in the sign-in logs maintained in your clinic.

2. A sign-in log documenting visit 4 for subject #5513 [ ] on 11/20/98 was not available for inspection.

IV. You failed to personally conduct or supervise the clinical investigation as you committed to do when you signed the 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. Although you could delegate duties as the investigator of record, it is your responsibility to ensure that accurate information is submitted to the sponsor and FDA.

Your request for a hearing must be made, in writing, within ten (10) business days after receipt of this letter and should be directed to Dr. James F. McCormack, Coordinator, Bioresearch Monitoring Program, Office of Enforcement, Division of Compliance Policy (HFC-230), 5600 Fishers Lane, Rockville, Maryland 20857, Telephone (301) 827-0425, FAX (301) 827-0482. 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. No hearing will be held.

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 the material submitted had raised no genuine and substantial issue of fact. 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 Dr. McCormack 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 June 27, 2001, remains available. Entering into a consent agreement would terminate the administrative procedures, but would not preclude the possibility of a corollary judicial proceeding.

No final decision by FDA has been made at this time on your eligibility to continue to receive investigational new products or 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 Dr. McCormack 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 yours,

Dennis E. Baker
Associate Commissioner for Regulatory Affairs

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