DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

N13L

Food and Drug Administration
Rockville MD 20857

APR 13 2001

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

CERTIFIED MAIL – RESTRICTED DELIVERY
RETURN RECEIPT REQUESTED

Carl Andrew DeAbate, M.D.
Medical Research Centers, Inc.
1020 Gravier Street
New Orleans, Louisiana 70112

Dear Dr. DeAbate:

Between May 30 and June 27, 2000, Food and Drug Administration (FDA) investigators, Ms. Barbara D. Wright and Dr. Mathew T. Thomas, 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 [ ]

The FDA inspection was expanded to review your enrollment of subjects for other clinical studies that included:

3. Protocol [ ] titled, "A Multicenter, Randomized, Double-Blind, Active-Controlled, Comparative Three-Arm Study, Evaluation of the Efficacy and Safety of Oral [ ] 800 mg Once a Day for 5 Days Versus [ ] 800 mg Once a Day for 10 Days Versus Amoxicillin/Clavulanic acid 500/125 mg Three Times a Day for 10 days in the Treatment of Acute Maxillary Sinusitis (AMS) in Adults," and

4. Protocol [ ] titled, "A Multicenter, Randomized, Double-Blind, Comparative Study of Oral [ ] (800 mg Once Daily) Versus Oral Cefuroxime Axetil (500 mg Twice Daily) for Outpatient Treatment of Acute Exacerbation of Chronic Bronchitis in Adults," sponsored by [ ]

5. Protocol[ ] titled, "A Comparative Study of the Efficacy and Safety of Clarithromycin Immediate Release Tablets and Loracarbef Pulvules for the Treatment of Patients with Secondary Bacterial Infection of Acute Bronchitis," sponsored by Abbott Laboratories.

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 of those studies are protected.

We note that at the conclusion of the inspection Ms. Wright 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 response to the items listed on the Form FDA 483 and find your responses to be unacceptable.

Based on our evaluation of a number of materials including, but not limited to, the establishment inspection report, the documents submitted with that report, information received from sponsors, and your written response dated July 20, 2000, 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 listing of the violations follow. The applicable provisions of the CFR are cited for each violation.

1. You submitted false information to the sponsor, in violation of 21 CFR 312.70(a).

   A. In protocol[ ] you submitted data from sputum samples that did not belong to the subjects identified with the samples. The study sponsor provided FDA with data from its audit of your study site, which revealed that the DNA in sputum specimens did not match the DNA in each subject's blood serum for 35 of the 84 subjects. Furthermore, the results demonstrate that sputum specimens that were purportedly obtained from 26 different subjects actually came from 3 individuals (17 specimens matched profile A, 4 matched profile B, and 5 matched profile C).

B. In protocol [ ] subject [ ] (#66013), whom you reportedly enrolled and followed to completion in the study, did not exist as a unique subject. In your verbal response to the FDA investigator, you stated that subject [ ] was enrolled twice in protocol [ ] under two different names as [ ] (#66003) and [ ] (#66013). Therefore, the data generated for subject [ ] (#66013) is falsely represented. Your response does not adequately explain how this alleged instance of re-enrollment occurred and why it was not detected.

C. In protocol [ ] you reportedly enrolled and followed to study completion a subject identified as [ ] (#3525). We were not able to document that [ ] is a real person.

D. An individual, to whom you entrusted study-related responsibilities, signed an affidavit stating that the data submitted to sponsors regarding subjects' study drug compliance were inaccurate. In the affidavit this individual states that, "...the subject's 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."

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

A. For protocols [ ] and [ ] you failed to collect sputum samples in accordance with the investigational plan. During the FDA inspection, you acknowledged that qualifying sputum specimens were obtained from an unidentifiable number of subjects from outside the clinic because some subjects were unable to produce a sputum specimen on demand. 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. In your written response you state that this was not explicitly required by the protocol. However, the sponsor (TAP Pharmaceuticals) informed FDA that, it specifically instructed all clinical investigators during the investigator's meeting that it 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 response 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. In protocol [ ] you failed to collect sputum samples in accordance with the investigational plan.

3. 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 a serious lack of your direct involvement in the conduct of the study or personal supervision of personnel involved in 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 a 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 cited regulations 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
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 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. 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 yours,

Stan W. Woollen

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

Enclosures:
#1 - 21 CFR Part 312
#2 - 21 CFR Part 16
#3 - Agreement