DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

CERTIFIED MAIL-RESTRICTED DELIVERY
RETURN RECEIPT REQUESTED

NOV 28 2003

[ ]

NOTICE OF OPPORTUNITY FOR HEARING

Dear Mr.[ ]

The Center for Drug Evaluation and Research (the Center) of the Food and Drug Administration (FDA) has information indicating that your client, Dr. Carl Andrew DeAbate, M.D., repeatedly or deliberately violated federal regulations in his capacity as an investigator for the following clinical studies:

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

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

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," sponsored by [ ]

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.

The Center also has information indicating that your client submitted false information to FDA or the sponsor in required reports.

The repeated or deliberate violation of federal regulations and submission of false information, described below, provide the basis for withdrawal of Dr. DeAbate's eligibility as a clinical investigator to receive investigational new products or drugs.

The Center's findings are based on our evaluation of information obtained from, but not limited to, the Form FDA 483 and the establishment inspection report (EIR) for the FDA inspection conducted between May 30, 2000, and June 27, 2000; the documents submitted with the EIR; information received from sponsors; and Dr. DeAbate's written response to the Form FDA 483, dated July 20, 2000.

Pursuant to section 312.70(a) of Title 21 of the Code of Federal Regulations (21 CFR 312.70(a)), the Center informed Dr. DeAbate, by letter titled "Notice of Initiation of Disqualification Proceedings and Opportunity to Explain" (NIDPOE) dated April 13, 2001, of the specific matters complained of and offered him an opportunity to respond in writing or at an informal conference. The NIDPOE also offered Dr. DeAbate the option of entering into a consent agreement with the FDA, thereby terminating any administrative proceeding against him.

Dr. DeAbate provided the FDA a written response to the NIDPOE, dated June 8, 2001. In addition, Dr. DeAbate, Ms.[ ] Mr.[ ] and you (as the attorney representing Dr. DeAbate), met with the FDA at an informal conference on July 18, 2001. As a follow-up to the informal conference, you submitted additional documentation dated August 9, 2001, and April 3, 2003. After a review of all available documentation, and Dr. DeAbate's explanations, the Center has concluded that Dr. DeAbate's explanations are unacceptable because they fail to adequately address the violations set forth below.

Accordingly, Dr. DeAbate is being offered an opportunity for a regulatory hearing pursuant to 21 CFR parts 16 and 312, on the question of whether he should be entitled to receive investigational new products or drugs. Dr. DeAbate has 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. Please note that the Center has dropped items I.C. and I.D. from the NIDPOE, and is including item II.C, which covers the same facts as those described in I.B. from the NIDPOE, to reflect the scope of the violation. Applicable provisions of the CFR are cited for each violation.

I. Dr. DeAbate submitted false information to the sponsor (21 CFR 312.70(a)).

A. In protocol[ ] Dr. DeAbate 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 Dr. DeAbate's 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 of these 35 subjects actually came from 3 individuals (17 specimens matched profile A, 4 matched profile B, and 5 matched profile C). Dr. DeAbate admitted in his written response to the NIDPOE, and in the informal conference, that some of the data provided from his study site to the sponsor were false (*i.e.*, sputum samples from at least 26 of the study subjects actually came from 3 individuals). However, Dr. DeAbate appeared to dispute the exact number of sputum specimens that did not match their serum counterpart. Our review of the records confirmed that the numbers presented above are accurate (*i.e.*, DNA in sputum specimens did not match the DNA in each subject's blood serum for 35 of the 84 subjects).

B. In protocol[ ]subject[ ](#66013), whom Dr. DeAbate reportedly enrolled and followed to completion in the study, did not exist as a unique subject. Dr. DeAbate admitted in his written response to the NIDPOE, and in the informal conference, that subject[ ] was enrolled twice in protocol[ ]under two different names, as[ ] (#66003) and[ ](#66013). The protocol prohibited the re-enrollment of study subjects. Therefore, the data generated for subject[ ](#66013) is falsely represented and subject [ ]was re-enrolled in the study in violation of the protocol.

II. Dr. DeAbate failed to conduct the study in accordance with the investigational plan, in violation of 21 CFR 312.60.

A. For protocols[ ]and[ ]Dr. DeAbate failed to collect sputum samples in accordance with the investigational plan. During the FDA inspection, Dr. DeAbate acknowledged that qualifying sputum specimens for an unidentifiable number of subjects were not obtained at the pre-therapy visit, because some subjects were unable to produce a sputum specimen on demand. However, the sponsor[ ] informed FDA that during the investigator's meeting for both protocols, all clinical investigators were specifically instructed to "be present when patient produces sputum into collection cup." Documentation provided by the sponsor indicates that Dr. DeAbate and his staff were in attendance at the investigator's meeting for protocol[ ]on October 9, 1997 in Orlando, Florida. Attendees were also 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 was unable to produce a sputum specimen at the pre-therapy visit or, if the specimen was unacceptable, the patient was ineligible for the study at that time. This answer was presented to, and discussed with, the audience immediately after the question. In Dr. DeAbate's written response to the NIDPOE, he stated that he did not attend the meeting with the sponsor in which the sputum collection procedures were discussed. However, during the informal conference, Dr. DeAbate contradicted himself and stated that he did attend the investigator's meeting. In addition, two of Dr. DeAbate's study coordinators also attended that investigator's meeting

during which the sponsor provided supplemental documentation specifying the sputum collection procedure. Therefore, as the clinical investigator, Dr. DeAbate should have known the correct procedure for collecting the subject's sputum specimens.

B. In protocol [ ] Dr. DeAbate failed to collect sputum samples in accordance with the investigational plan. Evidence discussed under item I.A, of this letter shows that, for 35 of the 84 subjects enrolled in the study, Dr. DeAbate submitted data from sputum samples that did not belong to the subjects identified with the samples.

C. As noted in I.B., Dr. DeAbate failed to conduct study [ ] in accordance with the protocol.

III. Dr. DeAbate failed to personally conduct or supervise the clinical investigation as he committed to do when he signed the Investigator Statement, Form FDA 1572, in violation of 21 CFR 312.60.

The violations documented above in I. and II. resulted, at least in part, from a serious lack of Dr. DeAbate's direct involvement in the conduct of the study, or lack of personal supervision of personnel involved in assisting him with the conduct of those studies. Although Dr. DeAbate was entitled to delegate duties to other qualified personnel during the studies in question, it was his responsibility to ensure that information submitted to the sponsor and FDA was accurate.

Dr. DeAbate's 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, Dr. DeAbate 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 Dr. DeAbate wishes to respond but does not desire a hearing, you, or Dr. DeAbate, should contact Dr. McCormack within the time period specified above and send a written response containing his reply. The letter should state that Dr. DeAbate waives his right to a hearing and that he wants a decision on the matter to be based on his written response and other information available to FDA.

FDA's offer to enter into a consent agreement, attached to the NIDPOE dated April 13, 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 Dr. DeAbate's eligibility to continue to receive investigational new products or drugs. Moreover, there will be no prejudgment of this matter if Dr. DeAbate declines to enter into a consent agreement and decides 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 Dr. DeAbate wishes to request a hearing or to have this matter resolved by consent agreement or information available to FDA.

Sincerely yours,

John M. Taylor, III
Associate Commissioner
for Regulatory Affairs

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