DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

JUL 6 2001

CERTIFIED MAIL - RESTRICTED DELIVERY
RETURN RECEIPT REQUESTED

Ref: 01-HFD-45-0701

Lori A. Nesbitt, Pharm. D., M.B.A.
Chief Executive Officer
Discovery Alliance, Inc.
(formerly d/b/a Gulf Coast Clinical Services, Inc.)
63 S. Royal Street, Suite 801
Mobile, Alabama 36602

Dear Dr. Nesbitt:

Between June 20 and August 23, 2000, Ms. Patricia S. Smith and Ms. Cynthia R. Crocker representing the Food and Drug Administration (FDA), met with you and your staff 1) to investigate allegations that Gulf Coast Clinical Services, Inc., engaged in regulatory non-compliance, and 2) to review your conduct, as principal investigator, of the following clinical study:

> Protocol[ ][“A Multi-Center, Randomized, Double-Blind, Parallel Group, Placebo-Controlled Study Evaluating the Efficacy and Safety of[ ](15 – 60 mg/day) in Children and Adolescents (aged 6 to 17) with Generalized Anxiety Disorder”], involving the investigational drug[ ] performed for[ ]

This inspection is a part of 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 have been protected.

From our evaluation of the inspection report, the documents submitted with that report, and your September 17, 2000, written response, we conclude that you did not adhere to all pertinent federal regulations and/or good clinical investigational practices. We note that at the conclusion of the inspection, Ms. Smith and Ms. Crocker presented and discussed with you the items listed on Form FDA 483, Inspectional Observations. We accept your explanations and your promised corrective actions regarding inadequate/inaccurate records, the error in obtaining informed consent from subject 908's parent/guardian, and failure to obtain the protocol-required assessments at study visits for one subject. However, we wish to remind you and caution you that in the conduct of your investigation (as a non-physician), you failed to meet your regulatory obligations as an investigator as follows:

SUMMARY OF INVESTIGATOR RESPONSIBILITIES AND PROTOCOL VIOLATIONS (21 CFR 312.60)

1. You failed to adequately protect the safety and welfare of human subjects in the study by failing to involve a physician in clinical assessments and procedures that should be performed by a physician, including the following:

   a. You, or in some cases [ ] Ph.D, a psychologist sub- investigator, wrote orders for study drug, evaluated patient responses to study drug, and, based on responses, made dosage adjustments. You maintain that, as principal investigator, you were authorized to perform these activities. We disagree, and the State Board of Medicine supports our position that these activities are within the practice of medicine. You are not licensed to practice medicine. Moreover, the study protocol doesn't contemplate performance of these functions by a non-physician.

   b. You performed physical examinations on at least eight study subjects. Again, you are not qualified by licensing or training to perform physical examinations.

   c. You failed to rely on a physician to correlate laboratory and ECG assessments with the clinical situations of study subjects on whom such tests were performed. You indicated, and documentation supports, that in some cases you independently assessed test results or discussed test results only with off-site physicians at [ ] or [ ] physicians, and that [ ] M.D., your physician sub-investigator, did not review results. We note that, particularly in the case of ECGs, results must be coordinated with clinical data (the ECG report clearly states that the "report must be correlated with clinical data by a physician"). The [ ] physicians who reviewed the ECGs are not in a position to assess the clinical situation of a subject relative to the ECG (located off-site), and you are not qualified by licensing or training to do so.

2. You failed to adhere to the protocol in that you inappropriately signed end-of-study forms that are part of the case report forms (CRFs). The protocol requires that the completed CRFs must be reviewed, signed, and dated by a qualified physician who is an investigator or sub-investigator.

3. You failed to accurately inform your Institutional Review Board (IRB) about medical oversight of the trial. You initially informed the IRB on February 12, 1999, that Dr. [ ] would "provide any and all procedures required of a physician in addition to medical back-up." As discussed in (1) above, there are numerous instances in which you failed to rely on Dr. [ ] for clinical assessments and oversight, or on any other licensed physician in a position to make needed assessments. Although you did eventually clarify with the IRB the role of [ ] and [ ] the clarification was not timely (after the completion of

the trial) and thus did not allow the IRB to meaningfully assess the adequacy of the study's human subject protections.

4. You failed to obtain IRB approval for recruitment advertisements prior to enrolling subjects in the study. Study records show that the last subject was enrolled in July 1999, and completed the study on September 14, 1999. However, IRB approval of advertisements was not granted until October 4, 1999.

We also note what appears to be an example of deceptive conduct and concealment. Specifically, you denied the existence of, and took steps to conceal, an onsite, unlicensed laboratory. Employees allege that they were instructed to not bring urine and blood specimens to the site while FDA was there and that the centrifuge in the laboratory was concealed in a cabinet whenever FDA inspectors were present. When FDA finally was allowed entrance into the room that was functioning as a laboratory, the centrifuge was discovered in a cabinet. FDA notified Occupational Safety and Health Administration (OSHA), and OSHA fined your company for maintaining unsafe laboratory conditions.

Protocols [_____]

We would like additional information regarding the responsibilities, if any, of Discovery Alliance, Inc., and/or Gulf Coast Clinical Services, Inc., in these three studies. We note that Forms FDA 1572 signed by the principal investigators in these studies identify Discovery Alliance, Inc., and/or Gulf Coast Clinical Services, Inc., as the investigators' mailing address. We also note that your letterhead characterizes Discovery Alliance, Inc., as a clinical trials management firm.

Although you were not listed as the principal investigator in these protocols, it appears that you and/or Discovery Alliance, Inc./Gulf Coast Clinical Services, Inc., may have been responsible for at least some portions of the studies in question. Our FDA investigators were told that firm management of Discovery Alliance, Inc., and/or Gulf Coast Clinical Services, Inc., recruits physicians to conduct FDA regulated clinical research and informs the physicians that they will have **only** limited responsibilities and that the organization will "do the rest." We are concerned about these types of practices and procedures.

Please inform us of the extent to which Discovery Alliance, Inc., and/or Gulf Coast Clinical Services, Inc., was/were involved in these studies and provide documentation that fully describes the relationship between Discovery Alliance, Inc./Gulf Coast Clinical Services, Inc., and these principal investigators as it relates to the conduct of these studies. You should specifically include a description of what investigator responsibilities, if any, were carried out by Discovery Alliance, Inc., and Gulf Coast Clinical Services, Inc.

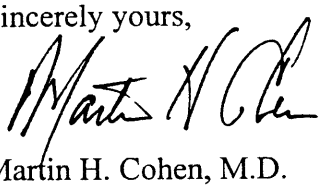
We reserve comment regarding the Form FDA 483 items that pertain to protocols [_____] until we receive your response to this item.

Because of the nature of the violations of FDA regulations discussed above, we request that you inform this office, in writing, within 15 working days of your receipt of this letter, of the actions you have taken or plan to take to prevent similar violations in the future. Failure to adequately and promptly achieve corrections may result in further regulatory action without further notice.

If you have any questions, please contact Dr. Antoine El-Hage, at (301)594-1032, FAX (301)827-5290. Your written response and any pertinent documentation should be addressed to:

Antoine El-Hage, Ph.D.
Branch Chief
Good Clinical Practice II, HFD-47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

Sincerely yours,



Martin H. Cohen, M.D.
Acting Director
Division of Scientific Investigations, HFD-45
Office of Medical Policy
Center for Drug Evaluation and Research