DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

CERTIFIED MAIL - RESTRICTED DELIVERY
RETURN RECEIPT REQUESTED

Ref: 01-HFD-45-0802

AUG 30 2001

Martin B. Scharf, Ph.D.
Center for Research in Sleep Disorders
1275 East Kemper Road
Cincinnati, Ohio 45237

Dear Dr. Scharf:

Between February 6 and 23, 2001, and again between May 7 and 11, 2001, Messrs. Joseph X. Kaufman and Michael P. Sheehan and Dr. Constance Lewin, representing the Food and Drug Administration (FDA), met with you to review your conduct as a sponsor-investigator and to validate data submitted by the sponsor to support a major amendment of the following clinical study:

Protocol [redacted] in the Treatment of Narcolepsy/Cataplexy"), involving the investigational drug [redacted] (also known as [redacted]

These inspections are 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 written responses dated March 13, March 21, and May 24, 2001, 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 each inspection, our representatives presented and discussed with you the items listed on Form FDA 483, Inspectional Observations. The discussions included, but were not limited to, inadequate drug accountability and other recordkeeping inadequacies/inaccuracies; failure to report all serious adverse events (SAEs) to the IRB; and informed consent deficiencies, including failure to obtain consent from some subjects. We note that you have adequately addressed most of the inspectional observations, and that you appear to have taken adequate corrective measures to ensure that the violations discussed above do not recur in any ongoing or future clinical studies conducted by you. However, your response regarding your failure to terminate the study once the IRB rescinded its approval is unacceptable and failed to meet your obligations as an investigator as follows:

SUMMARY OF VIOLATIONS RELATED TO REQUIREMENTS FOR IRB APPROVAL AND REVIEW (21 CFR 312.66)

You failed to ensure IRB approval for protocol _____for the duration of the clinical study. Study records document that you dispensed study drug to at least 18 subjects after the IRB withdrew its approval and informed you that your appeal for continued approval was denied.

Your response to the issue of treating subjects without IRB approval is not satisfactory. You stated that in an undocumented telephone discussion, you were granted permission to continue to dose subjects for 30 days while you appealed the IRB's termination. Even if you were granted such permission, that would have given you approval until August 25, 2000, you did not terminate the study until October 9, 2000.

In your response, you failed to acknowledge the seriousness of this violation and the unacceptability of your actions. In addition, your response fails to include any assurance that this would not be repeated in any future studies. Instead, your response appears to represent an attempt to rationalize violating FDA regulations.

Because of the departures from FDA regulations discussed above, please 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 explain the violations noted above may result in further regulatory action.

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 Practices II, HFD-47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
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Sincerely yours,

Martin H. Cohen, M.D.
Acting Director
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