DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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JUL 27 2001

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Via Federal Express

WARNING LETTER

Jerry Engelberg, M.D.
The University of Tennessee Health Sciences Center
College of Medicine
Department of Neurosurgery
847 Monroe Avenue, Suite 427
Memphis, Tennessee 38163

Dear Dr. Engelberg:

This Warning Letter informs you of objectionable conditions found during Food and Drug Administration (FDA) inspections conducted at your clinical site and requests from you a prompt written reply informing us of your corrective actions. You participated as a clinical investigator in a study entitled, "[redacted] sponsored by [redacted], to investigate the device [redacted]). Data from the study conducted at your site was submitted to the FDA in support of the premarket approval application, [redacted].

During the periods of February 5 through February 22, 2001, and April 2 through April 11, 2001, you were visited by David R. Heiar, an investigator from the FDA's New Orleans District Office. The purpose of Mr. Heiar's visits was to conduct inspections to determine whether your activities and procedures as a clinical investigator for the [redacted] study complied with applicable regulations. The [redacted] product is a device as that term is defined under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspections were conducted under a program designed to ensure that data and information contained in applications for Investigational Device Exemptions (IDE), Premarket Approval (PMA), and Premarket Notification (510(k)) submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

We have completed our review of the inspection reports submitted by the New Orleans District Office. The reports reveal significant violations of the requirements under Title 21, Code of Federal Regulations (21 CFR), Part 50 - Protection of Human Subjects; 21 CFR, Part 56 - Institutional Review Boards; and 21 CFR, Part 812 - Investigational Device Exemptions. These violations are listed on the Forms FDA 483, "Inspectional Observations," which were presented to and discussed with James T. Robertson, M.D., at the conclusion of the first inspection, and with you at the conclusion of the second inspection.

We acknowledge the letter from Dr. James T. Robertson dated May 30, 2001, addressed to Mr. Michael R. Duran, Supervisory Investigator, FDA. Dr. James T. Robertson's letter responds to the items listed on the Forms FDA 483 issued in your name.

The violations noted on the Forms FDA 483 and our subsequent review of the inspection reports are summarized below:

1. **Failure to maintain accurate, complete, and current records relating to the investigator's participation in an investigation *(21 CFR 812.140).***

- You failed to maintain accurate, complete, and current records relating to your participation in the [redacted] study. For example, you transferred to The Lee Group, Inc. (Lee Group) custody of the study records without providing to FDA a notice of transfer not later than 10 working days after the transfer occurred (21 CFR 812.140(e)). When Mr. Heiar arrived at your site on February 5, 2001 to inspect the study records, there were no study records available to inspect and there was no documentation showing that the custody of records was transferred to the Lee Group. On March 28, 2001, the former President of the defunct Lee Group transferred to you all study documents and records including case report forms, source documentation, screen failure records, drug accountability and dispensing records, and regulatory documents. Upon his return visit to your site on April 2, 2001, Mr. Heiar inspected the available study records and found numerous regulatory violations, some of which are outlined below.

- You failed to maintain accurate, complete, and current records for follow-up visit evaluations. For example, [redacted] for the [redacted] study, submitted incorrect information on certain case report forms for as many as twelve study subjects. The [redacted] protocol schedule of visits requires follow-up visits at 1, 2, 6, and 12 months post-operatively. On September 21, 1996, [redacted] recorded information on 6-month case report forms for patient [redacted]. Patient [redacted] reported to [redacted] during his visit on October 28, 1996, that he recalled seeing study personnel one time only. On October 28, 1996, [redacted] interviewed patient [redacted] and completed again case report forms for his 6-month visit. The information on the 6-month case report forms for patient [redacted] filled out and signed by [redacted] does not match the information on the 6-month case report forms filled out and signed by [redacted]. This is only one example of questionable information entered by [redacted] on case report forms.

2. **Failure to supervise investigational device use *(21 CFR 812.110(c)).***

You failed to properly supervise and control the use of the investigational device by allowing an unauthorized person to have access to and perform implantation of investigational devices into patients. For example, on January 12, 1996, you signed the [redacted] Statement of Investigator (Investigator's Agreement). By signing the Investigator's Agreement, you agreed that patients would be under your direct care or the care of designees who were responsible to you. Article 6 of the Investigator's Agreement lists your designees (Sub-Investigators) who were responsible to you for the conduct of the [redacted] study.

Article 6 of the Investigator's Agreement does not include the name of Bernie G. McHugh, Jr., M.D. Dr. McHugh operated on eight patients participating in the [redacted] study as follows: Patient [redacted] surgery date [redacted]; Patient [redacted], surgery date [redacted]; Patient [redacted] surgery date [redacted]; Patient [redacted] surgery date [redacted]; Patient [redacted] surgery date [redacted]; Patient [redacted] surgery date [redacted]; Patient [redacted] surgery date [redacted]; Patient [redacted] surgery date [redacted]

On June 21, 1996, [redacted], Berger-Boyer & Associates, Inc., sent to you a letter requesting that Dr. McHugh sign the Investigator's Agreement. Dr. McHugh signed the Investigator's Agreement without placing a date next to his signature. Based on [redacted] letter, Dr. McHugh signed the Investigator's Agreement as a Sub-Investigator sometime after June 21, 1996. Dr. McHugh was not authorized to operate on the eight study patients listed above.

In addition, Dr. McHugh failed to ensure proper informed consent of patients [redacted] and [redacted] by using the wrong informed consent document. Patients [redacted] and [redacted] signed the informed consent document meant for study subjects who were operated on at the Baptist Memorial Hospital rather than signing the appropriate informed consent document for study subjects operated on at the Veterans Administration Medical Center.

The violations listed above are not intended to be an all-inclusive list of deficiencies at your site. As a clinical investigator, it is your responsibility to ensure that investigations that you participate in are conducted in accordance with applicable FDA regulations. To assist you, we have enclosed a copy of the *FDA Information Sheets,* guidance for clinical investigators.

Please advise this office, in writing, **within fifteen (15) working days of receipt of this letter**, of the specific steps that you have taken to correct these violations and other violations known to you, and to prevent the recurrence of similar violations in current or future studies. Failure to respond may result in regulatory action, including disqualification, without further notice.

You should direct your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kathleen E. Swisher, J.D., R.N., Consumer Safety Officer.

A copy of this letter has been sent to our New Orleans District Office, 6600 Plaza Drive, Suite 400, New Orleans, Louisiana 70122. We request that a copy of your response be sent to that office as well.

Sincerely yours,

Channa M. Connor, RPh

for Larry Spears
Acting Director
Office of Compliance
Center for Devices and
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Enclosure

cc:

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