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JUN 8 2005

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

WARNING LETTER

Wesley Kinzie, M.D.
1401 Spanos Court, Suite 101
Modesto, California 95355

Dear Dr. Kinzie:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site. This letter also discusses your written response, dated April 20, 2004, to the noted violations and requests that you implement prompt corrective actions. Mr. Jeffrey W. Shrifter, an investigator from the FDA's San Francisco District Office, conducted an inspection between April 13 and April 20, 2004, of the [redacted] clinical study in which you participated.

The product under investigation is a device as that term is defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act ("the Act"), 21 U.S.C. 321(h).

This inspection was conducted as a follow-up to a previous inspection conducted at your clinical site from April 28, 2003 through May 8, 2003 by Mr. Carl Lee, FDA investigator. These inspections were conducted as part of the FDA's [redacted] which includes inspections designed to monitor the conduct of research involving investigational products.

Our review of the inspection report submitted by the San Francisco District Office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions, and Part 50 - Protection of Human Subjects, and Section 520(g) of the Act. At the close of the inspection, Mr. Shrifter presented a Form FDA 483 "Inspectional Observations" to you for review and discussed the listed deviations. The deviations noted on the Form FDA 483, our subsequent review of the inspection report, and your response to the observations are discussed below:

- 1. You failed to follow the Investigator's Agreement, Investigational Plan, applicable FDA regulations, and any conditions of approval imposed by the IRB; you failed to ensure that informed consent is obtained in accordance with 21 CFR Part 50 (21 CFR 812.100, 812.110(b); 21 CFR 50.20, 50.25(a)).**

A clinical investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations, and for ensuring that informed consent is obtained in accordance with 21

CFR Part 50. (21 CFR 812.100). An investigator shall also conduct an investigation in accordance with any conditions of approval imposed by an IRB or FDA. (21 CFR 812.110(b)). The investigational plan includes the study protocol. (21 CFR 812.25(b)).

Also, in accordance with 21 CFR 50.20, an investigator can not involve a human being as a subject in research unless the investigator obtains the legally effective informed consent of the subject or the subject's legally authorized representative. The informed consent must be documented by the use of written consent forms approved by the IRB. The basic elements required of informed consent are set forth in 21 CFR 50.25(a) and include requirements for a description of all study procedures, anticipated circumstances for a participant's termination, and contact information for research-related injury and questions.

You failed to follow the Investigator's Agreement, which you signed on June 25, 2001. The Agreement provides that any non-emergency deviation from the Investigational Plan requires prior approval from FDA, the sponsor, and the IRB. The Agreement further provides that any unapproved, emergency deviation shall be reported to the IRB, sponsor, and FDA as soon as possible but not later than five working days from the deviation. Examples of your failure to follow the Investigator's Agreement include:

- You did not notify or obtain approval of changes from the [redacted] [redacted] for revised versions of the study protocols. Specifically, the protocols dated [redacted] - which you used to conduct the study prior to May 2003 -- were never approved by the [redacted] was the IRB of record for the study from April 2001 to April 2002, and the [redacted] IRB was the IRB of record for the study from April 2002 onward. During the May 2003 inspection, you were informed of the protocol revisions and you stated in your February 5, 2004 written response to a November 7, 2003 FDA Warning Letter (WL) that any modifications to the study protocol or informed consent will be reviewed and approved by the IRB prior to use. However, during the April 2004 inspection, you were using the [redacted] protocol, which had never been approved by the [redacted] and which was not up-to-date.
- You did not follow the inclusion/exclusion criteria set forth in the protocol. Specifically, the need for [redacted] was exclusionary. As a result, at least one subject who did not meet the inclusion/exclusion criteria [redacted] was included in the study.
- You did not notify or obtain IRB approval to utilize the [redacted] which was approved for use with the investigational device on February [redacted] 2003. On June 16, 2003, you [redacted] device into Subject [redacted]

- You did not ensure that the versions of the informed consent forms (ICF) were approved by [redacted] or [redacted] prior to using the ICFs at both sites. As a result, 22 subjects signed an unapproved version of the consent form. For example, 18 subjects at [redacted] signed the ICF versions dated June 15, 2001 or July 5, 2001, which had not been approved by [redacted] and 4 subjects signed the ICF version dated July 5, 2001 at [redacted]. Although [redacted] IRB approved three versions of the ICFs for use at that site, you utilized the ICF approved by [redacted] IRB. During the May 2003 inspection and in the WL, you were cited for utilizing ICFs which were not approved by the [redacted] IRB. After the May 2003 inspection, you continued to fail to ensure that the version of the ICF used at [redacted] was the approved version.

Moreover, the ICFs (revised June 15, 2001; July 5, 2001; May 15, 2002; and April 15, 2003) that were utilized prior to and after the May 2003 inspection did not contain all of the required elements of informed consent in accordance with 21 CFR 50.25(a). Specifically, you did not ensure that the informed consent forms included all study procedures, anticipated circumstances that the subject's participation may be terminated by the investigator, or contacts.

2. You failed to prepare and submit complete, accurate, and timely reports (21 CFR 812.150(a)).

In accordance with 21 CFR 812.150(a)(3), investigators must prepare and submit complete, accurate, and timely progress reports to the sponsor, monitor, and IRB at least annually. The investigator must also prepare and submit complete, accurate, and timely reports of unanticipated adverse device effects to the IRB and sponsor as soon as possible, but in no event later than 10 working days after the investigator learns of the effect (21 CFR 812.150(a)(1)), as well as complete, accurate, and timely reports of deviations from the investigational plan to the sponsor and IRB (21 CFR 812.150(a)(4)).

The Investigator's Agreement you signed also requires that routine reports and/or final reports be provided to the IRB and sponsor as requested. In addition, an [redacted] IRB letter, dated April 11, 2002, requires you to notify the IRB of any unforeseen risk or complications.

You did not submit timely reports of unanticipated adverse device effects to the IRB. The following item was not reported:

- On June [redacted] 2003, when Subject [redacted] received the investigational device, you observed [redacted]

In addition, after the May 2003 inspection, you failed to submit progress reports of protocol deviations in a timely manner to the sponsor and did not submit a report to the IRB. During 2002, your clinical site reported protocol deviations to the sponsor only and did not submit a progress report of the deviations to the IRB until April 11, 2003.

In your response, you state that due to lack of support from the sponsor you will “no longer be involved in this L.D.E. study...” Your response does not address the observations annotated on the Form FDA 483; and therefore is inadequate.

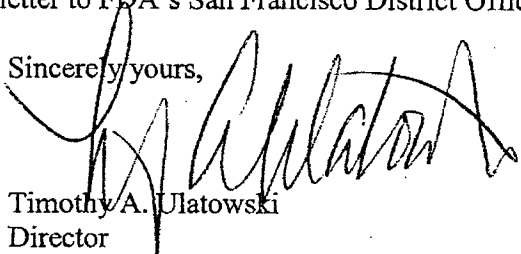
The deviations cited above are not intended to be an all-inclusive list of deficiencies at your site. As a clinical investigator, it is your responsibility to ensure that investigations that you participate in are conducted in accordance with applicable FDA regulations.

Within 15 working days after receiving this letter, please provide written documentation of the additional specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations in current and future studies. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. In addition, please provide a list of your current investigational studies and include the name of the study sponsor and the date of IRB approval. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action, including initiation of disqualification procedures pursuant to 21 C.F.R. 812.119, without further notice.

Please send your response to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch (HFZ-312), 2094 Gaither Road, Rockville, Maryland 20850, Attention: Viola Sellman, Chief, Program Enforcement Branch.

We are also sending a copy of this letter to FDA’s San Francisco District Office,

Sincerely yours,



Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health