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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

JUN - 2 2008

WARNING LETTER

VIA FEDERAL EXPRESS

Charles Hamlin, M.D.
Hand Surgery Associates, PC
2535 S. Downing St., Suite 500
Denver, CO 80210

Dear Dr. Hamlin:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your clinical site from January 30, 2008 to February 21, 2008 by investigators from the FDA Denver District Office. The purpose of this inspection was to determine whether your activities as both sponsor and investigator in the [redacted], complied with applicable federal regulations. The [redacted] prosthesis (also known as [redacted] used in the [redacted] 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 letter also requests prompt corrective action to address the violations cited and discusses your written response dated February 22, 2008 to the noted violations.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval (PMA) applications, and Premarket Notification submissions (510(k)) 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.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 812 -- Investigational Device Exemptions, Part 50 -- Protection of Human Subjects, and Section 520(g) (21 U.S.C. 360j(g)) of the Act. At the close of the inspection, the FDA investigator presented an inspectional observations Form FDA 483 for your review and discussed the observations listed on the form with you. The deviations noted on the Form FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

1. Failure to submit an investigational device exemption (IDE) application to FDA, failure to obtain FDA approval before beginning the investigation, and failure to await FDA approval before allowing subjects to participate in the investigation [21 CFR 812.20(a), 21 CFR 812.40, 21 CFR 812.42, 21 CFR 812.100, and 21 CFR 812.110(a)].

You acted as both sponsor and clinical investigator in the [redacted]. As a sponsor, you are required to submit to FDA and obtain FDA approval of an IDE application if you intend to use a significant risk device in an investigation. 21 CFR 812.20(a) and 21 CFR 812.40. As a sponsor, you must not begin such an investigation until you have obtained FDA approval. 21 CFR 812.42.

As a clinical investigator, you are responsible for ensuring that an investigation is conducted according to applicable FDA regulations and that FDA approval is obtained before allowing any subjects to participate. 21 CFR 812.100 and 21 CFR 812.110(a).

Examples of your failure to adhere to these regulations include, but are not limited to, the following:

You failed to ensure that an FDA-approved IDE was obtained before allowing subjects to participate in the [redacted]. Specifically, you [redacted] device, a significant risk device as defined in 21 CFR 812.3(m), in forty-seven (47) subjects prior to FDA approval.

2. Failure to ensure that informed consent is obtained in accordance with 21 CFR part 50 and failure to properly document informed consent [21 CFR 50.20, 21 CFR 50.27(a), 21 CFR 812.100, and 21 CFR 812.140(a)(3)(i)].

As an investigator, you are responsible for ensuring that informed consent is obtained in accordance with 21 CFR part 50. 21 CFR 812.100. Informed consent shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. 21 CFR 50.20, 21 CFR 50.27(a), and 21 CFR 812.140(a)(3)(i). Examples of your failure to adhere to these regulations include, but are not limited to, the following:

- There is no written documentation that informed consent was obtained for the following subjects: [redacted] on [redacted], [redacted] or [redacted], and [redacted] on [redacted].

- [redacted] and [redacted] IRB approved a 3-page informed consent document in [redacted]. Subject [redacted] was consented on [redacted] using an unapproved 1-page informed consent document. Subject [redacted] was consented on [redacted] using an unapproved 4-page informed consent document.

- The IRB-approved informed consent document was signed after study devices were [redacted] in three subjects:

Subject		Informed Consent Date

3. Failure to conduct the investigation in accordance with the investigational plan [21 CFR 812.25, 21 CFR 812.100, and 21 CFR 812.110(b)].

As an investigator, you are responsible for ensuring that an investigation is conducted according to the investigational plan, which includes the protocol, and any conditions of approval imposed by an IRB or FDA. 21 CFR 812.25, 21 CFR 812.100, and 21 CFR 812.110(b). Examples of your failure to adhere to these regulations include, but are not limited to, the following:

- was approved by the IRB for enrollment of a maximum of 12 subjects. You enrolled and forty-seven (47) subjects.
- Section 3.7 of the protocol states that case report forms (CRFs) shall be completed only by authorized personnel at the time of the patient visit. Many CRFs were completed several months to more than a year after the patient visit.
- Section 3.8 of the protocol states that follow-up visits must be conducted within the following time windows: – prior to – at the time of surgery; You failed to adhere to these time windows for at least four (4) subjects:

Subject	

*** Denotes that visits were not conducted within the specified time window**

4. Failure to prepare and submit complete, accurate and timely reports of unanticipated adverse device effects [21 CFR 812.150(a)(1) and 21 CFR 812.150(b)(1)].

As a sponsor/investigator, you are responsible for preparing and submitting complete, accurate, and timely reports to the reviewing IRB of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after you first learn of the effect. 21 CFR 812.150(a)(1) and 21 CFR 812.150(b)(1). Examples of your failure to adhere to this regulation include, but are not limited to, the following:

You failed to report within the required timeframe that investigational devices were [redacted] from three patients.

Subject	[redacted]	Reported to IRB
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

5. Failure to maintain accurate, complete, and current records of receipt, use or disposition of a device [21 CFR 812.140(a)(2)].

You failed to retain records regarding the dates of receipt and batch number or code mark of the device, as required under 21 CFR 812.140(a)(2). For example, the only information in the source documentation regarding the devices is mention of the size of the device [redacted] Therefore, you are unable to identify which subjects received which device.

In your written response, you stated that the FDA-summary report demonstrated significant flaws, errors, and missteps in the IRB and application process for the [redacted] You stated that the findings were accurate, and you acknowledged that you did not understand the depth of the FDA process. Your response is inadequate in that you did not describe a corrective and preventive action plan. Please provide copies of policies, procedures, and training with expected completion dates that are being developed and implemented to prevent the recurrence of these violations in future clinical studies.

The violations described above are not intended to be an all-inclusive list of problems that may exist with your clinical study. It is your responsibility as a sponsor/clinical investigator to ensure compliance with the Act and applicable regulations.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. In addition, please provide a complete list of all clinical trials in which you have participated for the last five years, including the name of the study and test article, the name of the sponsor, the number of subjects enrolled, and the current status of the study. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 CFR 812.119.

You will find information to assist you in understanding your responsibilities and planning your corrective actions in the FDA Information Sheets Guidance for Institutional Review Boards and Clinical Investigators, which can be found at http://www.fda.gov/oc/ohrt/irbs/. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Send your response to:

Attention: Doreen Kezer, MSN, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-311, Rockville, Maryland 20850.

A copy of this letter has been sent to Denver District Office, P.O. Box 25087, 6th Ave. & Kipling St., Bldg. 20, Denver, CO 80225. Please send a copy of your response to that office.

If you have any questions, please contact Ms. Doreen Kezer by telephone at (240) 276-0125 or via e-mail at doreen.kezer@fda.hhs.gov.

Sincerely yours,

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