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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service



Food and Drug Administration
9200 Corporate Blvd.
Rockville MD 20850

MAR 13 2008

WARNING LETTER

VIA FEDERAL EXPRESS

Hilton Becker, MD
Oaks Medical Plaza
670 Glades Road, Suite 220
Boca Raton, FL 33431

Dear Dr. Becker:

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 October 30 through November 21, 2007, by an investigator from the FDA Florida District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the studies titled [redacted] (herein referred to as the [redacted] Study), under IDE [redacted], and [redacted] both sponsored by [redacted] complied with applicable federal regulations. [redacted] used for these studies are devices 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 that you promptly implement corrective actions.

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 several serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 812 - Investigational Device Exemptions. At the close of the inspection, the FDA investigator presented a form FDA 483 - "Inspectional Observations" for your review, and discussed the observations listed on the form with you. The deviations noted on the FDA 483 and our subsequent review of the inspection report are discussed below:

1. Failure to maintain accurate, complete, and current records relating to an investigation [21 CFR 812.140(a)].

You failed to adhere to the above stated regulation. Examples of this failure include, but are not limited to, the following:

- a.) FDA regulations require that Clinical Investigators maintain accurate, complete, and current records of the receipt, use, and disposition of an investigational device, including the type and quantity of the device, the dates of its receipt, and the batch numbers or serial numbers [21 CFR 812.140(a)(2)]. At the time of the FDA inspection, there were no device accountability records or device inventory records at your study site for the [redacted] Study. Specifically, the protocol for the [redacted] Study specifies,

[redacted] The log found in your study files listed the names of 7 subjects and the dates they were enrolled into the study in [redacted], but no other required information, including complete dates of [redacted], assigned patient numbers, and catalog and serial numbers of the [redacted] devices. There were also no shipping records in your study files to account for the specific study devices received by you and/or returned to the sponsor, [redacted].

You, as a clinical investigator, are responsible for controlling the use of investigational devices at your facility, including maintaining adequate records of the disposition of all study devices provided to you by the sponsor.

- b.) FDA regulations require that Clinical Investigators maintain accurate, complete, and current records of each subject's case history and exposure to the device [21 CFR 812.140(a)(3)]. The study records for subjects enrolled in the [redacted] Study at your site contained inaccurate and incomplete information regarding their participation in the study. For example:

- i. The study records for Subject [redacted] contained two different serial numbers for the device [redacted] in the right breast. In addition, the serial number assigned by the manufacturer to each device is unique, but some of your study records indicate that the same device was [redacted] in both the left and the right breast of this subject.
- ii. All subjects' records contained the incorrect catalog/reference number used to identify the type and size of the devices implanted in the subjects.

- iii. The protocol for the [redacted] Study specifies,

[redacted] There was no documentation in any of your records for the [redacted] Study subjects reviewed by the FDA investigator to indicate that you evaluated their eligibility for the study prior to their enrollment. Specifically, the FDA investigator reviewed 7 records for subjects enrolled in the [redacted] Study. None of the clinic records contained information to indicate the subjects met the enrollment

criteria specific to the study, including the fact that the subjects were not suitable for saline breast implants.

2. Failure to ensure an investigation is conducted in accordance with the signed agreement with the sponsor, the investigational plan, applicable FDA regulations, and any conditions of approval imposed by FDA or the IRB [21 CFR 812.100, 21 CFR 812.110(b)].

You failed to adhere to the above-stated regulations. Specifically:

- a.) The protocol for the [] Study states, "The subject and witness will sign the consent before any other study procedures occur." None of the consent forms for the [] Study that were reviewed by the FDA investigator contained a witness signature.
- b.) As noted above, you did not maintain all records and logs required by the protocol for the [] Study. Specifically, there were inadequate or missing device accountability and inventory logs that are required to ensure that all study devices received at your site can be properly accounted for, inadequate or missing subject enrollment logs necessary to ensure that all enrolled subjects are properly followed and treated according to the protocols, and inadequate or missing source records necessary to verify the validity and accuracy of data collected during the study.

During the FDA inspection, you told the FDA investigator that you felt it was the responsibility of the IRBs to inform you how to conduct the studies, and that any deficiencies observed during the FDA inspection reflected failures on the part of the IRBs. You also told the FDA investigator that the sponsor of the studies did not tell you that you must follow the protocols or adhere to the investigator agreements that you signed. As the clinical investigator, you are responsible for implementation of study protocols and adherence to FDA regulations. Your general responsibilities as a clinical investigator include ensuring that an investigation is conducted according to the Clinical Study Agreement, the investigational plan, and all applicable FDA regulations, in order to protect the rights, safety, and welfare of subjects under the investigator's care, and to control use of devices under investigation. You failed to supervise the study to ensure that your general responsibilities as a clinical investigator were fulfilled.

Please provide us with documentation of a corrective action plan that addresses each of the violations noted above, such as a written procedure for ensuring study protocol compliance, written verification of training of all study staff on study procedures and requirements, and a plan for ensuring accurate and complete documentation of receipt and disposition of study devices.

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 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. Please send your response to:

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

A copy of this letter has been sent to the FDA Florida District Office, 555 Winderley Place, Suite 200, Maitland, FL 32751. Please send a copy of your response to that office.

If you have any questions, please contact Ms. Doreen Kezer, MSN, at 240-276-0125 or at Doreen.Kezer@fda.hhs.gov.

Sincerely yours,



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