Inspections, Compliance, Enforcement, and Criminal Investigations

Pozner, Jason M.D. 6/25/10

Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

WARNING LETTER

VIA UPS EXPRESS

June 25, 2010

Jason Pozner, M.D.
4800 N. Federal Hwy, Suite 100
Boca Raton, FL 33431

Dear Dr. Pozner:

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 February 12, 2010, to March 24, 2010, by investigators from the FDA's Florida District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical study entitled, "A Multicenter, Randomized, Controlled Study with Independent, Masked Assessment, to Evaluate the Safety and Efficacy of the UltraShape® Contour Plus™ System, for Non-Invasive Abdominal Fat Reduction for the Purpose of Body Contouring," UltraShape® Contour Plus™ System, Investigational Device Exemption (IDE) #**(b)(4)** complied with applicable federal regulations. The UltraShape® Contour Plus™ System 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 April 8, 2010, to the noted violations.

The inspection was conducted under a program designed to ensure that data and information contained in requests for 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 violations of Title 21, Code of Federal Regulations (21 CFR) Part 50 - Protection of Human Subjects, and Part 812 - Investigational Device Exemptions. At the close of the inspection, the FDA investigator presented the 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 adhere with the regulation that prohibits representations that an investigational device is safe or effective for the purposes for which it is being investigated. [21 CFR 812.7(d)].

A sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator shall not represent that an investigational device is safe or effective for the purposes for which it is being investigated. You have failed to adhere to the above-stated regulation. Examples of your failure include, but are not limited to, the following:

- On your website, http://www.smacboca.com/ultra[1] shape.html, the investigational device is being represented as safe and effective. The website states "A unique feature of Ultrashape technology is its highly sophisticated optical tracking and guidance system engineered to ensure safe, effective and uniform treatment." Although the website includes information regarding the device's status as unapproved and under clinical trials, the representation on your website nonetheless indicates that the UltraShape® is safe or effective for the purposes for which it is being investigated.

In your response, you stated that the website was an oversight on your part and that you used an outside public relations firm that was not aware of FDA regulations. You have since added your own marketing department in which you will have complete control of all your marketing efforts. You state that you will seek IRB approval for marketing material in future studies, although IRB approval by itself will not ensure that your labeling and marketing material are in compliance with 21 CFR part 812. Your response appears adequate and may be verified during a future inspection.

2. Failure to conduct the investigation according to the signed agreement, the investigational plan, applicable FDA regulations, and any conditions of approval imposed by an Institutional Review Board (IRB) or FDA. Also failure to adhere to the regulation that governs an investigational device to be used only with subjects under the investigator's supervision. [21 CFR 812.110(b) and (c)].

A clinical investigator is responsible for ensuring that an investigation is conducted according to the signed agreement with the sponsor, the investigational plan, and applicable FDA regulations and any conditions of approval imposed by an IRB or FDA. Also, a clinical investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. You have failed to adhere to the above stated regulations. Examples of your failures include, but are not limited to, the following:

- Section 6.2 of the Study Protocol versions July 29, 2008, and December 1, 2008, states that the Screening Exam must occur up to 30 days prior to Day 0, and must include the collection and review of subjects' laboratory values to determine eligibility. Prior to subjects receiving their first treatment, laboratory reports were to be reviewed for out-of-range values and assessed for clinical significance. However, the following subjects' reports were reviewed by you approximately 2 to 7 weeks after subjects received their first treatment.

  - The **(b)(4)** for Subject **(b)(4)** was collected on September 12, 2008 and reported on September 13, 2008. The first treatment occurred on September 19, 2008; however, you signed the lab report stating you reviewed the report on November 7, 2008. The lab report contained numerous out-of-range values that were determined to be clinically significant. An email exchange between the Safety Monitor, Dr. **(b)(4)** from **(b)(4)**, and **(b)(4)** confirms these out-of-range values and that the subject should have been marked as a screen failure. As a consequence of late reviews, this subject was withdrawn after having received the first treatment.
  - The **(b)(4)** for Subject **(b)(4)** was collected on August 25, 2008 and reported on August 26, 2008. The first treatment occurred on September 3, 2008; however the lab report was not reviewed by you until September 19, 2008, in which you indicated that there were numerous out-of-range values which were clinically significant.

- Sections 6.12.11 and 7.2 of the Study Protocol, version July 29, 2008, and Sections 6.13.11 and 7.2 of the Study Protocol, version December 1, 2008, the clinical investigator is instructed to "refer to the Contour Plus User's Manual." However, the correct user manual for the investigational device, the Contour Plus™ System, was not available at your site. Rather the manual on site was for a different device, the Contour 1 System.

- Section 6.12.3 of the Study Protocol version, July 29, 2008 and Section 6.13.3 of the Study Protocol version, December 1, 2008, state that, "The Principal Investigator (or designed physician) will mark the treatment area prior to each treatment, with a dark non-permanent marker while the subject stands upright." However, you did not perform this procedure for any subjects. You also did not supervise **(b)(4)**, the medical assistant/study coordinator, who performed these tasks.

• Section 6.16 of the Study Protocol version, July 29, 2008 and Section 6.17 of the Study Protocol version, December 1, 2008, state that, **(b)(4)**".” However, you did not perform this global assessment examination for any subjects. You also did not supervise **(b)(4)**, who did perform these examinations.

• Section 15.1.3 of the Study Protocol versions, July 29, 2008, and December 1, 2008, state that "The Investigator will be responsible for the timeliness, completeness, and accuracy of the information on the CRF.” In addition, 21 CFR 812.140(a)(3) requires investigators to maintain accurate, complete, and current records of each subject's case history, which includes all relevant observations, such as the information and data on the condition of each subject upon entering the investigation. However, there is no source documentation (e.g., medical record entries) in your study records to show that "**(b)(4)**" examinations were performed on any subjects, or any results of such examinations, during the physical examination of the treatment area as part of the screening process. The boxes on the case report forms (CRFs) were marked "Yes" to indicate that the "**(b)(4)**" examinations were completed.

Please note that as a result of your non-performance of various study duties listed above and lack of oversight of the clinical trial, FDA has concerns about the Global Assessments examination data validity and accuracy because they are one of the secondary efficacy variables stated in Section 8.0 "Efficacy and Safety" of both study protocol versions.

In your response you stated that the sponsor did not mean that the PI needs to be present at each procedure, but to be responsible for the proper conduct of each procedure. You also stated that delay in the reporting of the blood tests will not happen in future studies. Your response is inadequate in that it does not describe your corrective and preventive actions for performing all physical examinations and global assessments of research subjects and reviewing lab results prior to subjects receiving treatments, as required by the protocol and the investigator agreement. Your response also does not describe your corrective and preventive actions for ensuring the adequate supervision of delegated responsibilities, as stated in the study protocol. Please explain how you plan
to correct these failures and provide mechanisms for preventing any recurrence.

3. Failure to maintain accurate, complete, and current records of receipt, use, or disposition of a device that relate to the type and quantity of the device and the dates of receipt. [21 CFR 812.140(a)(2)].

A clinical investigator is responsible for maintaining accurate, complete, and current records of receipt, use, or disposition of an investigational device that relate to the type and quantity of the device, the dates of receipt, and the names of all persons who received, used, or disposed of each device. You failed to adhere to the above-stated regulation. Examples of your failure include, but are not limited to, the following:

• The "Product Accountability Log" only listed the UltraShape system once and seven **(b)(4)**. There are no records of receipt, use, or disposal of any **(b)(4)** or the UltraShape system. A total of **(b)(4)** subjects were enrolled at your site; however, the log does not provide information related to which subjects were treated with which **(b)(4)**.

• The product accountability log shows the receipt date for one investigational device and five **(b)(4)** on June 30, 2008, and lists receipt of two additional **(b)(4)** but no receipt date.

• There are no records of the disposition of the , including any shipping receipts.

In your response you acknowledge these errors and you indicate that in future studies you will make sure that the "Product Accountability Log" is complete, accurate and contains all study-related inventory. Your response is inadequate in that it does not describe your corrective and preventive actions for maintaining complete and accurate device records, including receipt and return of the UltraShape system, **(b)(4)**, and other supplies (e.g., treatment packets, etc.). Please explain how you plan to correct these failures and provide mechanisms for preventing any recurrence.

4. Failure to maintain accurate, complete, and current records of each subject's case history. [21 CFR 812.140(a)(3)].

A clinical investigator is responsible for maintaining accurate, complete, and current records of each subject's

case history and exposure to the device, which encompasses the case report forms (CRFs) and supporting data. You have failed to adhere to the above-stated regulation. Examples of your failure include, but are not limited to, the following:

- A note-to-file dated, September 9, 2008, states that subjects through were brought back to the site for reassessment; however, there is no documentation in the subjects' files or on-site to show that the subjects returned for the reassessment.

- The "Signature Authorization Log" that delegated study-related responsibilities is incomplete and inaccurate in that you did not initial and date the log or change the study coordinator listing. The Signature Authorization Log shows **(b)(4)**, as the study coordinator for the study; however, **(b)(4)** was only involved in part of the study. **(b)(4)** became the study coordinator, though she is listed as a "treater" in the Signature Authorization Log

In your response you acknowledge these errors and indicate that in future studies you will make sure that the "Signature Authorization Log" is complete, accurate and closely supervised by the investigator. Your response is inadequate in that it does not describe your corrective and preventive actions for maintaining complete and accurate CRFs, maintaining and updating the subjects' visits log, recording results from physical examinations performed during the visits, maintaining a current and accurate Signature Authorization Log, and maintaining on-site an accurate investigational device user manual. Please explain how you plan to correct these failures and provide mechanisms for preventing any recurrence.

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.

Please note that when the IRB approves subsequent substantial changes to the informed consent it is a best practice to notify subjects that signed previous versions of the informed consent of these changes. Four subjects (**(b)(4)**) were enrolled in the study with no documentation on file to show that they signed the revised informed consent version, dated December 1, 2008. The December 2008 version of the informed consent document contained the following additional information: **(b)(4)**"

Within fifteen (15) working days of receiving this letter, please provide written documentation of the additional 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/[2].

Any submitted corrective action plan must include projected completion dates for each action to be accomplished.

Your response should reference "CTS #:**(b)(4)** " and be sent to: Attention: Linda Godfrey, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 10903 New Hampshire Avenue, WO66-3462, Silver Spring, Maryland, 20993-0002.

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

For further information concerning the Bioresearch Monitoring program, please visit our Internet homepage at http://www.fda.gov/cdrh/comp/bimo.html[3]. Valuable links to related information are included at this site. The Division of Bioresearch Monitoring also developed introductory training modules in FDA-regulated medical device clinical research practices, which are available on the FDA website. The modules are for anyone involved in the

clinical research enterprise and, can be found at http://www.fda.gov/Training/CDRHLearn/ucm162015.htm[4].

If you have any questions, please contact Ms. Linda Godfrey by telephone at (301) 796-5490 or via email at Linda.Godfrey@fda.hhs.gov.

Sincerely yours,

/S/

Michael E. Marcarelli, Pharm.D., M.S.

Director

Division of Bioresearch Monitoring

Office of Compliance

Center for Devices and Radiological Health

Links on this page:

1. http://www.smacboca.com/ultra
2. http://www.fda.gov/oc/ohrt/irbs/
3. http://www.fda.gov/cdrh/comp/bimo.html
4. http://www.fda.gov/Training/CDRHLearn/ucm162015.htm