Inspections, Compliance, Enforcement, and Criminal Investigations

Scully, Sean M.D. 7/30/10

10903 New Hampshire Avenue
Silver Spring, MD 20993

WARNING LETTER

VIA UPS EXPRESS

JUL 30 2010

Sean Scully, M.D.
University of Miami Hospital
1400 North West 12th Avenue
Suite 2 Cedar Medical Center
Miami, FL 33136

Dear Dr. Scully:

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 March 15, 2010, to April 15, 2010, by the 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, "ReCap® Total Resurfacing System," Investigational Device Exemption (IDE) **(b)(4)** complied with applicable federal regulations. The ReCap™Metal-Metal Resurfacing is a device as that term is defined in section 201 (h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 USC 321 (h). This letter also requests prompt corrective action to address the violations cited.

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 812 - Investigational Device Exemptions. At the close of the inspection, the FDA investigators 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, and our subsequent review of the inspection report are discussed below:

1. 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. [21 CFR 812.100 and 812.110(b)].

A clinical investigator is responsible for ensuring that an investigation is conducted according to the signed agreement with the sponsor, the investigational plan, applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA. You have failed to adhere to the above-stated regulations. Examples of your failures include, but are not limited to the following:

• The Study Protocol version, dated March 25, 2008, states that, "The safety of the system will be monitored by

recording adverse events throughout the follow-up period. All adverse events, device related or otherwise; will be reported and recorded on the Adverse Event/Follow-Up Form." The Adverse Events Reporting section of the Investigator's Agreement, dated August 23, 2007, states that, "All adverse events, seemingly device-related or not, will be reported to Biomet." Subjects **(b)(6)**, **(b)(6)**, **(b)(6)**, and experienced adverse events (AE). There is no documentation to show that the following AE's were recorded on the AE form and reported to the sponsor as required by the protocol and to the IRB as required by the IRB approval letter dated December 27, 2006.

o Subject visited your clinical site on April 30, 2008, ahead of her scheduled appointment, and again on September 10, 2008, because of a sensation of grinding in the hip.

o Subject visited your clinical site on March 19, 2008, and reported increasing lower back pain similar to his pre-operative symptoms.

o Subject visited your clinical site on May 27, 2009. The subject reported experiencing increasing right lower extremity pain that radiates to the dorsum of the right foot due to descending a ladder and having a hard landing. On October 7, 2009, the subject returned to your clinical site and reported to have several episodes of pain, particularly about the right hip in the anterior inguinal region. Again on February 17, 2010, the subject reported increasing right hip pain for a two-day period.

o Subject visited your clinical site on September 10, 2008. The subject reported increasing pain around the left hip and buttock, which had worsened over the last three months. The subject returned again on March 3, 2010, and reported pain with deep squats and with other maneuvers at extreme of flexion.

• The Study Protocol version dated March 25, 2008, states, "All adverse events, .device related or otherwise; will be reported and recorded on the Adverse event/Lost to Follow-up Form. The date and reason for the patient becoming "Lost to Follow-up will also be recorded on this form."

o Subject **(b)(6)** was implanted with the investigational device on November 20, 2007, and was scheduled for the follow-up visit for November 20, 2009, **(b)(4)**. The subject did not return to the clinical site for the **(b)(4)** follow-up visit.

o Subject **(b)(6)** had the investigational device implanted on April 29, 2008, and was scheduled for the **(b)(4)** follow-up visit for April 29, 2009, **(b)(4)**. The subject did not come to the clinical site for the first year annual follow-up visit.

Both of the above subjects were lost to follow-up; however, the "Lost to Follow-Up" form was not completed for either subject. In addition, there is no
documentation to show that you have attempted to contact or inquire about the subjects' follow-up visits.

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

A clinical investigator is responsible for maintaining accurate, complete, and current records of each subjects' case history and exposure to the device, which encompasses the case report forms (CRFs) and supporting data. In addition, 21 CFR 812.140(a)(3)(ii) mandates that case histories shall contain all relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated). Also, a clinical investigator shall maintain complete and current protocol, with documents showing the dates of and reasons for each deviation from the protocol. You have failed to adhere to the above-stated regulations. Examples of your failures include, but are not limited to, the following:

• Your site did not complete the Harris Hip Score (HHS) 200 CRF for follow-up visits related to Subject **(b)(6)**(September 10, 2008, and May 6, 2009) and Subject **(b)(6)** (May 27, 2009, October 7, 2009, and February 17, 2010).

• The "Miller School of Medicine University of Miami - Orthopaedic History" form dated March 19, 2008, for Subject **(b)(6)** show that medications for blood pressure and diabetes were prescribed but the dose, reason for medication, and side effects of the medications were not recorded.

- Prior to FDA's inspection, the current version of the study protocol, dated March 28, 2008, for the ReCap® Total Resurfacing System, was missing or not maintained at your site. During the inspection, the sponsor provided your site with a copy of this protocol.

3. Failure to submit progress reports on the investigation to the sponsor and reviewing IRB at regular intervals. [21 CFR 812.150(a)(3)].

A clinical investigator shall submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly. You have failed to adhere to the above-stated regulations. Examples of your failures include, but are not limited to, the following:

- During the period of August 18, 2008, through June 2, 2009, there was no IRB oversight of the ReCap® Total Resurfacing System study; therefore, no continuing report was submitted to an established IRB even though subjects were still completing their **(b)(4)** follow-up visits. In addition, there is no documentation on site to show that you have notified the sponsor of your request for study closure with the Western IRB nor was there notification of a lack of IRB oversight of the study during that time.

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 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/ohrtlirbs/[1]. 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[2]. 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.govlTraining/CDRHLearn/ucm162015.htm[3].

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

Sincerely yours,

/S/
Timothy A. Ulatowski

Director

Office of Compliance
Center for Devices and
Radiological Health

Links on this page:

1. http://www.fda.gov/oc/ohrtlirbs/
2. http://www.fda.gov/cdrh/comp/bimo.html
3. http://www.fda.govlTraining/CDRHLearn/ucm162015.htm