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Inspections, Compliance, Enforcement, and Criminal Investigations

Matthew N. Songer, MD



Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

WARNING LETTER

AUG 27 2010

VIA UPS EXPRESS

Matthew N. Songer, M.D.
Orthopaedic Surgery Associates
1414 W. Fair Avenue, Suite 190
Marquette, Michigan 49855

Dear Dr. Songer:

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 April 19 to April 22, 2010 by an investigator from the FDA Detroit District Office. The purpose of this inspection was to determine whether your activities and procedures related to your participation in the clinical study titled "A Prospective, Multi-Center, Randomized, Controlled Clinical Trial Evaluating the Safety and Effectiveness of NuBac® Disc Arthroplasty," Investigational Device Exemption (IDE) **(b)(4)**, complied with applicable federal regulations. The NuBac® Disc Arthroplasty 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.

The inspection was conducted under a program designed to ensure that data and information contained in requests for IDEs, 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 and Part 50 - Protection of Human Subjects. 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, Dale A. Moilanen, Chief Operating Officer, Orthopaedic Surgery Associates of Marquette (OSAM), **(b)(6)**, RN, Nurse Coordinator and Clinical Staff Supervisor, and **(b)(6)** NP, Research Coordinator. The deviations noted on the Form FDA 483 and our subsequent review of the inspection report are discussed below:

1. Failure to include all elements of informed consent. [21 CFR 50.25(a) and 50.25(b)]

An investigator is responsible for ensuring that all the basic elements of informed consent are provided to each subject when seeking informed consent. Further, the investigator is responsible for ensuring that the informed consent document (ICD) include certain additional elements when appropriate. You have failed to adhere to the above-stated regulations. Examples of your failure include, but are not limited to the following:

All **(b)(4)** subjects who enrolled in the NuBac® Disc Arthroplasty study at your clinical site signed the ICD "Pioneer NUBAC: MGH: November 11, 2008." This ICD does not include the following required information:

- a statement that the study involves research;
- identification of any procedures which are experimental;
- a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable (the investigational plan requires a series of x-rays and Magnetic Resonance Imaging or Computed Tomography evaluations which could be harmful to an embryo or fetus);
- a statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and
- an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights.

In your response, please provide copies of the following: a revised IRB approved ICD that includes all the elements as required by 21 CFR 50.25, documentation of Institutional Review Board (IRB) review and approval of the ICD, and your plan to adequately inform all of the subjects who are receiving experimental treatment.

2. Failure to conduct the investigation according to the signed agreement with the sponsor, the investigational plan, 21 CFR part 812, other applicable FDA regulations, and any conditions of approval imposed by an Institutional Review Board (IRB) or FDA. [21 CFR 812.110(b)]

A clinical investigator is responsible for conducting an investigation according to the signed agreement with the sponsor, the investigational plan, 21 CFR part 812, other applicable FDA regulations and any conditions of approval imposed by an IRB or FDA. In addition to your failure to conduct the investigation in accordance with applicable FDA regulations in 21 CFR part 50 identified above, you failed to conduct the investigation in accordance with the investigational plan and the signed agreement. Examples of your failure include, but are not limited to the following:

The Randomized NuBac® investigational plan requires the patient to follow a clinical study schedule, which includes a series of radiological studies (i.e., Films and Scans) performed within the following time windows: Pre-op (i.e., baseline), discharge, 6 weeks, 3 months, 6 months, 12 months, 24 months and annually thereafter. These films include: Anterior-Posterior (AP), lateral, flexion and extension x-rays; and at least one of the following scans: Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). The schedule of radiographic studies and exams in the protocol specifies that the pre-op films and scan(s) are to be performed within **(b)(4)** of surgery. Please note that radiographs taken more than **(b)(4)** prior to surgery may not represent the subject's true clinical condition prior to surgery which may result in subjects inappropriately being included in the study. You did not take pre-operative films or scan(s) as required by the protocol for seven (7) out of **(b)(4)** subjects enrolled in the Randomized NuBac® study at your clinical site.

- Subject **(b)(6)** received the pre-op MRI on August 25, 2008, followed by surgery on February 11, 2009. The MRI was taken over five (5) months prior to implantation of the investigational device.
- Subject **(b)(6)** received the pre-op MRI on April 4, 2008, followed by surgery on March 4, 2009. The MRI was taken 11 months prior to implantation of the investigational device.
- Subject **(b)(6)** received the pre-op MRI on October 22, 2008, followed by surgery on March 11, 2009. The MRI was taken over four (4) months prior to implantation of the investigational device. Additionally, there is no documentation for both the pre-op Flexion and Extension X-rays as required by the protocol.
- Subject **(b)(6)** received the pre-op MRI on December 4, 2006, followed by surgery on April 22, 2009. The MRI was taken approximately two (2) years and five (5) months prior to implantation of the investigational device.
- Subject **(b)(6)** received the pre-op MRI on February 25, 2009, followed by surgery on July 1, 2009. The MRI was taken over four (4) months prior to implantation of the investigational device. Additionally, there is no documentation for both the pre-op Flexion and Extension X-rays as required by the protocol.
- Subject **(b)(6)** received the pre-op MRI on June 25, 2009, followed by surgery on December 17, 2009. The MRI was taken over five (5) months prior to implantation of the investigational device.
- Subject **(b)(6)** received the pre-op MRI and pre-op AP and Lateral X-rays on July 27, 2009, followed by surgery on February 1, 2010. The MRI and X-rays were taken over six (6) months prior to implantation of the investigational device. Additionally, there is no documentation for both the pre-op Flexion and Extension X-rays as required by the protocol.

Please provide information on what actions you plan to take to prevent the above deviations from recurring in

the future. If you develop standard operating procedures, then submit a copy of these procedures, along with documentation demonstrating staff training in these procedures, when you respond to this letter.

3. Failure to maintain accurate, complete, and current records related to your participation in the investigation. [21 CFR 812.140(a)(1), 812.140(a)(3)(ii) and 812.140(a)(4)]

A clinical investigator shall maintain accurate, complete and current records relating to the investigator's participation in an investigation. These records include all correspondence with the IRS, each Subject's case history and exposure to the device, all relevant observations, including data and information on the condition of each subject upon entering and during the course of the investigation, the current protocol for the study of the investigational device, and documentation showing the dates of and reasons for each deviation from the protocol. Examples of your failure to adhere to the above stated regulations include, but are not limited to the following:

- There is no documentation for IRS review and approval for the following: the study guide dated February 2009, the investigational plan referenced in this study guide, and the revised investigational plan dated December 22, 2008.
- The June 2, 2009 amended protocol was approved by the IRS on August 12, 2009; yet your site did not maintain it.
- Exclusion criteria # 25 of the investigational plan includes pregnancy or interested in becoming pregnant within the next two years. There is no documentation about how this exclusion criterion was met. For example, there is no documentation of negative pregnancy testing or birth control consultation for the following child-bearing age female subjects: Subject **(b)(6)** (33 year old female) and subject **(b)(6)** (37 year old female).

We acknowledge that the sponsor's representative provided a copy of the amended protocol to your site on April 21, 2010, during the FDA inspection. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations to protect the rights, safety, and welfare of subjects and for the control of devices under investigation [21 CFR 812.100]. Please provide information on what actions you plan to take to ensure that all study documentation, including protocols, subject case histories, test results, and correspondence between your site, the IRB, and sponsor are maintained in order to prevent the above deviations from recurring in the future. If you develop standard operating procedures, please submit with your response, a copy of these procedures, along with documentation demonstrating staff training in these procedures.

Please note that there was no documentation of financial disclosure for Dr. **(b)(6)** at your clinical site; however, Dr. **(b)(6)** implanted the investigational device in one subject and was listed as the doctor to contact on the ICD. We acknowledge that Dr. **(b)(6)** provided a signed financial disclosure statement and curriculum vitae prior to the FDA inspection close-out meeting.

In addition to the violations described above, we have concerns about a 2009 video titled "UMotion Preservation: Understanding & Treating Spinal Pain" that was made available through your office at OSAM and on your website, www.upbonedoctors.com¹. You stated in the video that "Artificial Disc is a new technology that allows for movement. ...The next wave of advancement in the treatment of the spine is a minimally invasive artificial disc and that is where the NuBac comes in... with the NuBac, we're able to preserve the patient's normal movement. If they still need a total disc at some point, the more invasive procedure, we can still do that; if they still need a fusion in the future, we can still do that. So you don't burn any bridges whereas once you fuse somebody, that bridge is burned - you never can go back." The video also presents a testimonial from a 2005 NuBac recipient who claims that she has had no complications from the surgery or placement of the device. In addition, in the video you compare NuBac with other devices and procedures, claiming reduction in surgery time and quicker recovery. Although the video contains a brief written disclaimer at the bottom of the screen which states that the device is investigational, the claims made in the video suggest that NuBac is safe and effective and the video does not describe any of the potential risks associated with this investigational device.

The claims made in the video and the omission of risk information could unduly influence subjects to participate. Since the inspection, we have reviewed your website and acknowledge that you have removed the video from your website. FDA believes it is important that materials which could be viewed by prospective subjects are accurate and include appropriate risk information. In your response, please provide information on any actions that you plan to take to make sure that any such materials in the future are accurate and include appropriate risk information.

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. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. 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/>².

Your response should reference "CTS # **(b)(4)**" and be sent to:

Attention: Linda D. Godfrey
Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
10903 New Hampshire Avenue
Building 66, Room 3462
Silver Spring, Maryland 20993-0002

A copy of this letter has been sent to the FDA Detroit District Office, 300 River Place, Suite 500, Detroit, MI 48207. Please send a copy of your response to that office.

If you have any questions, please contact Linda D. Godfrey at (301) 796-5654 or Linda.Godfrey@fda.hhs.gov.

Sincerely yours,

/S/

Larry D. Spears
Deputy Director of Regulatory Affairs
Office of Compliance
Center for Devices and
Radiological Health

cc:

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Links on this page:

1. <http://www.upbonedoctors.com/>
2. <http://www.fda.gov/oc/ohrtlirbs/>