



[Home](#) > [Inspections, Compliance, Enforcement, and Criminal Investigations](#) > [Enforcement Actions](#) > [Warning Letters](#)

## Inspections, Compliance, Enforcement, and Criminal Investigations

### Pioneer Surgical Technology 8/3/10



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 3 2010

#### VIA UPS EXPRESS

Jeff Millen  
President and CEO  
Pioneer Surgical Technology, Inc.  
375 River Park Circle  
Marquette, MI 49855

Dear Mr. Millen:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at Pioneer Surgical Technology, Inc. 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 activities as sponsor of the clinical study titled "A Prospective, Multi-Center, Randomized, Controlled Clinical Trial Evaluating the Safety and Effectiveness of NuBaC® Disc Arthroplasty," (Investigational Device Exemptions (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 USC § 321(h). This letter also requests prompt corrective action to address the violations cited and discusses your written response, dated May 13, 2010, to the noted violations.

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 Mr. Jonathan M. Gilbert, Director of Regulatory Affairs, Ms. Charmaine Henderson, Director of Clinical Affairs, and Mr. Fred Taccolini, Chief Compliance Officer. The deviations noted on the Form FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

#### **Failure to comply with FDA regulation that prohibits the promotion and advertisement of an investigational device as safe and effective. [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. An example of your failure to adhere to this regulation is as follows:

- In the video titled, "Motion Preservation: Understanding and Treating Spinal Pain," which is accessed through the clinical investigator's website, Dr. **(b)(6)** states, "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." Dr. **(b)(6)** also compares NuBac with other devices and procedures, claiming reduction in surgery time and improved recovery time. 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. The video does not describe the risks associated with your investigational device. The claims made in the video and the omission of risk information could unduly influence subjects. You are representing that the NuBac device is safe and effective for the purposes for which it is being investigated in violation of 21 CFR 812.7(d).

Your response states that your firm erroneously defaulted to the Institutional Review Board (IRB) for final approval of the video and that your firm now understands that the video implies that the device is safe and effective, and omits pertinent information. In addition, you state that future plans include engaging an independent agent to review and approve study content that could be viewed by prospective subjects, and conducting annual reviews of all literature and websites available for viewing by prospective subjects. Further, you state that your firm will utilize OCP 4.5 Document Control procedure to approve and document "promotional materials," including any changes to such materials. What is meant by "promotional materials" is unclear. We expect that the Document Control procedure will be used to approve and document materials that could be viewed by prospective subjects and that such materials will comply with the Act and applicable regulations, including 21 CFR 812.7. We acknowledge that the video link has been removed from the website until it can be revised, brought into compliance, and approved by the sponsor and the IRB. Your corrective and preventive actions appear to be adequate if implemented appropriately. In your response, please provide a copy of the OCP 4.5 Document Control procedure.

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

In seeking informed consent (IC) the following basic elements must be included, among others: identification of experimental procedures, statements that describe reasonably foreseeable risks or discomforts to the subject, explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and subjects' right to discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. In addition, the IC must include, when appropriate, a statement that the procedure may involve unforeseeable risks to subjects, embryos, or fetuses, and a statement informing subjects that significant new findings which may relate to the subject's willingness to continue participation will be provided. Your firm failed to include these elements and statements in the November 11, 2008 IC that was drafted by your firm on behalf of the clinical investigator and sent to the IRS for review and later used in the study.

Your response states that Dr. **(b)(6)**, who was an employee of your firm at that time and a clinical investigator, preferred the language in the IC dated November 11, 2008. Therefore, your firm reviewed and approved the language and submitted the IC to the IRS on his behalf. In addition, you state that your firm erroneously defaulted to the IRS for final approval and for overseeing patient protection measures and now understands why the consent dated November 11, 2008 is inadequate and does not meet the requirements of 21 CFR Part 50.

We acknowledge that your firm provided Dr. **(b)(6)** with a copy of an IC template from the October 2009 protocol for personalization and subsequent IRS approval, and that your firm will review the IC documents at the other ten sites to confirm that they meet the requirements of 21 CFR Part 50. We recognize that your firm submitted a new IC template to FDA in May 2010 and that, once approved, your firm plans to submit the IC to all clinical sites for subsequent IRS approval. Your response is inadequate in that you have not provided preventive actions to prevent this deviation from recurring in the future. We recommend that you develop a standard operating procedure (SOP) or a checklist to ensure that all IC meet the requirements of 21 CFR Part 50 and submit a copy of the SOP or checklist along with your response to this letter.

**Failure to ensure adequate monitoring of the investigation and failure to supply all investigators participating in the study with copies of the investigational plan. [21 CFR 812.40 and 21 CFR 812.45]**

Sponsors are responsible for selecting qualified investigators and providing them with the information they need to conduct the investigation properly and ensuring proper monitoring of the investigation. In addition, the Sponsor shall supply all investigators participating in the investigation with copies of the investigational plan and the report of prior investigations of the device. Examples of your failure to adhere to these regulations include, but are not limited to the following:

- Your firm did not provide Dr. **(b)(6)** with the revised investigational plan dated October 30, 2009 that was approved by the FDA on December 1, 2009. The protocol in use at Dr. **(b)(6)** site was dated September 19, 2008 on the cover sheet and December 22, 2008 in the footer on each page of the protocol.

In your response, you indicate the following corrective actions:

- Your firm provided the revised investigational plan to Dr. **(b)(6)** and five other clinical investigator sites

to obtain IRS approval;

- Your firm developed and released a checklist ((b)(4)) to ensure that all pre-study documentation is reviewed for accuracy and completeness prior to enrollment of subjects; and
- Your firm plans to develop a Work Instruction ((b)(4)), which will include a detailed process for confirming completeness and accuracy of investigator study documents.

Your corrective and preventive actions appear to be adequate if implemented appropriately. We recommend that your checklist and/or Work Instruction include a provision for ensuring proper distribution of any revised version of the investigational plan or other study documents to all investigators. In your response, please provide a copy of the checklist and the Work Instruction discussed above.

**Failure to obtain signed investigator agreements that include sufficient accurate financial disclosure information. [21 CFR 812.43(c)(5) and 21 CFR Part 54]**

A sponsor shall obtain from each participating investigator a signed agreement that includes sufficient accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement as required under 21 CFR Part 54. Examples of your failure include, but are not limited to the following:

- Financial disclosure information was not obtained from Dr. (b)(6) who implanted a device on February 1, 2010, nor was financial disclosure information obtained from Dr. (b)(6) who implanted devices in September and December 2009 until April 21, 2010.
- The financial disclosure statements were incomplete for Drs. (b)(6) and (b)(6) all of whom signed investigator agreements and implanted the investigational device. For example:
  - Dr. (b)(6) did not mark "yes" or "no" to whether any financial interests or arrangements were applicable, or certify that none of the financial interests or arrangements were applicable.
  - Drs. (b)(6) and (b)(6) did not mark "yes" or "no" to whether any financial interests or arrangements were applicable, and they did not describe the significant equity interest in the sponsor, as required by the form.

Your response states that lack of a checklist and the assumption that signed investigator agreements included signed financial disclosure forms resulted in this oversight. We acknowledge that your firm obtained financial disclosure forms from Drs. (b)(6) and (b)(6) as well as amended statements from Drs. (b)(6) and (b)(6). Your response again refers to the checklist ((b)(4)) to ensure that all pre-study documentation is reviewed for accuracy and completeness prior to enrollment of a patient in the study and the development of a Work Instruction ((b)(4)). Your corrective and preventive actions appear to be adequate if implemented appropriately. We recommend that your checklist and/or Work Instruction include a provision for ensuring that any revisions to the financial disclosure information are properly documented and an updated signed and completed financial disclosure form is obtained, if appropriate. In your response, please provide a copy of the checklist and the Work Instruction discussed above.

**Failure to maintain accurate, complete, and current device shipment records. [21 CFR 812.140(b)(2)]**

Sponsors are responsible for maintaining accurate, complete, and current records relating to shipment and disposition of devices. Examples of your failure include, but are not limited to the following:

- Your firm did not have documentation of the investigational devices that were hand-delivered to the operating rooms by the Pioneer representatives. Additionally, your firm provided a device location summary that did not include Dr. (b)(6) site, which implanted one investigational device in April 2010.

We recommend that your firm develop written procedures that address the inventory control process.

In addition to the checklist and Work Instruction discussed above, we acknowledge that your firm has developed and released a checklist ((b)(4)) that details the training elements required for each investigator, whether a principal or sub-investigator, and that a more detailed Work Instruction ((b)(4)) will be released. Please revise to include the required training elements from your protocol, and submit a copy of the revised as well as the Work Instruction ((b)(4)). Your firm also indicated that it plans to conduct an internal system audit by August 30, 2010. Please submit a copy of all policies and procedures developed as part of your corrective and preventive actions, including any actions taken as a result of your system audit.

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 study sponsor 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 study sponsor. 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.

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.

The Division of Bioresearch Monitoring has developed introductory training modules in FDA regulated device clinical research practices, which are available on the FDA website. The modules are for persons involved in FDA regulated device clinical research activities. These modules are located at the following website address: <http://www.fda.gov/Training/CDRHLearn/ucm162015.htm>.

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

Sincerely yours,

/s/

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

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**Links on this page:**