DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
9200 Corporate Boulvard
Rockville, Maryland 20850

WARNING LETTER

VIA FEDERAL EXPRESS

Steven J. Morgan, M.D.
777 Bannock Street
Department of Orthopaedics Trauma Service
Denver, CO 80204

OCT 3 2006

Dear Dr. Steven Morgan

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 June 5 through June 9, 2006, by an investigator from the FDA Denver District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical study, "Treatment of Atrophic Long Bone Nonunions with [redacted] in Combination with Autograft or Allograft," complied with applicable federal regulations. [redacted] 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 July 10, 2006.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 812 -- Investigational Device Exemptions, 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. The deviations noted on the Form FDA 483, our subsequent review of the inspection report, and your written response are discussed below:

Failure to obtain FDA approval prior to initiation of an investigation for which an FDA-approved IDE was required. [21 CFR 812.20(a)(2)]

You failed to obtain an FDA-approved investigational device exemption (IDE) prior to initiating a clinical investigation of the [redacted]

In your response you state that you were using the [redacted] as the "standard of care" and that your intent was to give your patients the best possible care. Use of a legally marketed device for an indication that has not been FDA-approved or cleared is permissible within the context of a legitimate health care practitioner-patient relationship.

A physician that conducts an investigation, which is defined as a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device, 21 CFR 812.3(h), with a device for an indication that has not been FDA-approved or cleared must obtain an FDA-approved investigational device exemption (IDE). [21 U.S.C. 360j(g), 21 CFR Part 812]

The FDA approved indication for the [redacted], "It is authorized by Federal law for use as [redacted]." Thus the approved indication is for use of the [redacted] alone. Your protocol titled "Treatment of Tibial Atrophic Nonunions with [redacted] in Combination with Autograft or Allograft" indicates that you were conducting an investigation to determine the safety and effectiveness of the [redacted] in combination with either an autograft or allograft. This clinical investigation of the safety and effectiveness of a new indication for the [redacted] requires an FDA-approved IDE. You failed to obtain approval of an IDE prior to the conduct of this investigation.

You implanted [redacted] without a FDA-approved IDE in eleven of eleven subjects' charts reviewed. Examples of this failure include but are not limited to the following:

Patient Code	Patient Initials	Autograft/Allograft	Date Implanted
[redacted]	[redacted]	Autograft	11/30/2004
[redacted]	[redacted]	Autograft	10/16/2003
[redacted]	[redacted]	Autograft	10/27/2003
[redacted]	[redacted]	Autograft	11/11/2003
[redacted]	[redacted]	Autograft	12/16/2003
[redacted]	[redacted]	Autograft	1/12/2004
[redacted]	[redacted]	Allograft	1/13/2004
[redacted]	[redacted]	Allograft	7/16/2004
[redacted]	[redacted]	Autograft	7/1/2003
[redacted]	[redacted]	Autograft	6/24/2003
[redacted]	[redacted]	Autograft	8/7/2003

Your response is incomplete in that you mentioned steps to "evaluate and upgrade training" but did not discuss a specific plan to evaluate the use of the device in the clinical investigation to ensure all applicable approvals are obtained prior to the conduct of the investigation. Please provide copies of policies, procedures, and training with expected completion dates that are being developed and implemented to determine whether to continue the study and obtain an FDA-approved IDE. In addition, please provide copies of policies, procedures, and training with expected completion dates that are being developed and implemented to ensure FDA and IRB approval are obtained prior to the conduct of any studies.

Failure to ensure that informed consent was obtained in accordance with 21 CFR Part 50, and failure to ensure all required elements of informed consent were provided to study subjects. [21 CFR 812.100, 50.20, and 50. 25(a)]

It is the investigator's responsibility to ensure that informed consent is obtained in accordance with 21 CFR Part 50. Although the IRB reviews and approves the informed consent document, it is ultimately the responsibility of the investigator to ensure the informed consent process meets the regulatory requirements. Your consent document does not include all the essential elements listed in 21 CFR 50.25. Research subjects voluntarily agree to participate in a clinical investigation. In order to make an informed decision to participate, they must be given all applicable information. An example of this failure includes but is not limited to the failure of the form to identify all experimental procedures. Specifically, the informed consent document does not identify that the device being used in the study is investigational for the indication it is being used for. The consent document states the benefit of this study is to "learn more about the effectiveness of [redacted] when used in your type of injury." You also state, "It is standard practice at Temple University to use a [redacted] is needed to help heal your type of fracture." This suggests that the use of the device with [redacted] is an approved indication. Further, the consent form requests the patient's consent only for administration of two questionnaires and states, "If you decide that you do not want to participate . . . your surgical treatment and follow-up care will not be changed in any way." This further suggests that use of the device for this indication is not investigational and also indicates that you failed to obtain for use of the device in an experimental procedure.

In your response, you state that all patients who agreed to participate in this study were provided with a written consent form which described the use of an allograft or autograft with the [redacted]. Your response is incomplete in that you did not address the fact that the informed consent document did not state that the [redacted] was an investigational device for the indication in this study. You state in your response that your study "was suspended by the IRB pending further review." Although the trial is suspended by the IRB, it is essential that the subjects receive follow-up care. Please provide a plan for obtaining adequate informed consent if the study is resumed and for following up with study subjects if it is not resumed, including follow-up evaluations. In addition, please provide copies of policies, procedures, and training with expected completion dates that are being developed and implemented to ensure informed consent documents contain all the applicable regulatory elements.

Failure to conduct the investigation according to the signed agreement, the investigational plan, and applicable FDA regulations. [21 CFR 812.100 and 21 CFR 812.110(b)]

It is your responsibility to ensure the investigation is conducted in accordance with the signed agreement, the investigational plan, and applicable FDA regulations.

Examples of this failure include but are not limited to the following:

1) The project summary-protocol [redacted] submitted to the [redacted] indicated that the [redacted] was to be used

according to the product label indication. In eleven of eleven subjects' medical histories reviewed, you indicated the [redacted] was used with either an autograft or an allograft. This is contrary to the FDA approved indication.

2) The protocol states the "Site study coordinators will collect all required data elements on pre-printed study forms provided by the Data Coordinating Center (DCC). Within one week following data collection the site study coordinators will enter the data into the electronic, internet database provided and managed by the DCC." The FDA investigator asked to the see study forms for this study and was informed that there were none.

In your response you state that you did not fully comprehend that the use of [redacted] in your study was not the indicated usage. This response is inadequate in that you did not discuss a plan to evaluate the indications for use of a device in clinical investigation and describe this usage completely and accurately in the investigational plan. Please provide copies of policies, procedures, and training with expected completion dates that are being developed and implemented to ensure the investigation plan is complete and accurate. In addition, please provide copies of policies, procedures, and training with expected completion dates that are being developed and implemented to ensure the study is conducted in accordance with the investigational plan.

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.

The regulations in 21 CFR Part 812 describe sponsor responsibilities as well as those of investigators. IRB responsibilities are spelled out in 21 CFR Part 56, Institutional Review Boards. These three sets of responsibilities overlap to ensure appropriate conduct of clinical studies and the protection of the rights and welfare of participating subjects. You are held responsible for knowing and following the regulations pertinent to your activities as a clinical investigator and sponsor of FDA-regulated studies.

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 should include

projected completion dates for each action to be accomplished. Send your response to: Attention: Doreen Kezer Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-311, Rockville, Maryland 20850.

A copy of this letter has been sent to Denver District Office, Building 20, PO Box 25087, Denver Federal Center, 6th Avenue and Kipling Street, Salt Lake City, CO 80225. Please send a copy of your response to that office.

If you have any questions, please contact [redacted]

Sincerely yours,

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

cc.

[redacted]