



MAR 21 2006

**WARNING LETTER**

VIA FEDERAL EXPRESS

Paul Fenster, M.D.  
Associate Professor of Medicine  
University of Arizona  
1501 North Campbell Ave.  
P.O. Box 245037  
Tucson, AZ 85724-5037

Dear Dr. Fenster:

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 October 3, 2005, through November 22, 2005, by an investigator from the FDA Los Angeles District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical study for the [REDACTED], that ultimately resulted in approval under PMA [REDACTED] complied with applicable federal regulations. The [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 responses to the noted violations.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (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 C.F.R.) Part 812 -- Investigational Device Exemptions, Part 50 -- Protection of Human Subjects, and Section 520(g) (21 U.S.C. 360j(g)) of the Act. 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 FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

1. **Failure to ensure that the investigation is conducted in accordance with the signed agreement with the sponsor, the investigational plan, applicable FDA regulations for protecting rights, safety and welfare of subjects under the investigator's care, and for control of devices under investigation, and any conditions of approval imposed by the FDA or the IRB. [21 CFR 812.100 and 21 CFR 812.110(b)] In addition, you failed to supervise device use. An investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. [21 CFR 812.110(c)]**

Examples of these failures include but are not limited to the following:

- a. Over a six month period, from February 2001 until August 2001, a physician, who had not been approved as a study physician until October 2001, attempted to implant a device in one subject and did implant devices into three other subjects. As the principal investigator, you are responsible for the supervision of the investigational device. Such supervision includes not supplying the investigational device to any person not authorized to receive it. A physician who is not approved as a study physician would not be authorized to receive the investigational device.
- b. Subject [REDACTED] was enrolled prior to a determination of eligibility, as that determination is explained in the protocol. Such a determination is required in the investigational plan under inclusion/exclusion criteria.
- c. Screening/enrollment logs were not maintained for any of the subjects as required in the investigational plan. The screening logs were created retrospectively, in some cases years, after-the-fact from appointment notebooks and memory.
- d. The IRB required all unanticipated adverse effects and all serious or fatal anticipated events must be reported within 5-days of learning of the occurrence. You have failed to adhere to this IRB requirement. Examples of your failure include but are not limited to the following:
  - i. You were aware that Subject [REDACTED] died on June 21, 2002, however, you failed to notify the IRB of this death until December 18, 2002.
  - ii. Subject [REDACTED] underwent a kidney transplant on November 16, 2002, however, the IRB was not notified of the adverse event until June 9, 2004.

Each of the above occurred outside of the required time frame.

You have provided responses related to the events surrounding these failures, including responses to the IRB, the Blue Ribbon Panel, and to the FDA inspector's observations. You have not explained how you will assure compliance with all elements of the protocol

if and when you are allowed permission by your IRB to conduct research at the University of Arizona or any other institution. Please describe your corrective actions to assure these events will not recur.

- 2. Failure to ensure that informed consent was obtained in accordance with 21 CFR Part 50 and failure to document informed consent. [21 CFR 812.100, 21 CFR 812.140(a)(3)(i), and 21 CFR 50.27(a)]**

Examples of these failures include but are not limited to the following:

- a. Subject [REDACTED] did not sign the "Additional Testing Studies for [REDACTED] consent form.
  - b. Subject [REDACTED] did not sign the consent form bearing the IRB's approval stamp.
- 3. Failure to maintain complete, accurate, and current records of all relevant observations and information, including those related to each subject's case history. [21 CFR 812.140(a)(3)(ii)]**

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

- a. Progress notes in the case report form binder had unsigned, undated additions and annotations for the following subjects: [REDACTED], [REDACTED] and [REDACTED]
- b. The baseline EKG dated July 26, 2001 for subject [REDACTED] could not be located at the time of the FDA inspection.

You have provided responses related to the events surrounding these failures. However, you have not explained how you will assure compliance with all elements of the protocol if and when you are allowed permission by your IRB to conduct research at the University of Arizona or any other institution. Please describe your corrective actions to assure these events will not recur.

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.

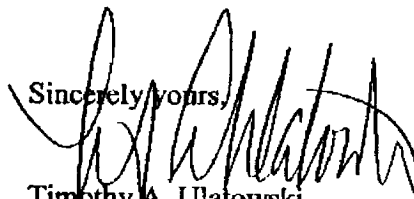
Within fifteen (15) working days of receiving this letter, please provide written documentation of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. In addition, 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 C.F.R. 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 must include projected completion dates for each action to be accomplished. Send your response to: Attention: Ms. Doreen Kezer, BSN, MSN, Chief, Special Investigations Branch, 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 the Los Angeles District Office 19701 Fairchild, Irving, CA 92612. Please send a copy of your response to that office.

If you have any questions, please contact Ms. Doreen Kezer, BSN, MSN, at 240-276-0125.

Sincerely yours,



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

cc:

**PURGED COPY:**

  
Director, Human Subject Protection Program

