

*Via Federal Express*

AUG 22 2006

Food and Drug Administration  
Center for Devices and  
Radiological Health  
2098 Gaither Road  
Rockville, MD 20850

### WARNING LETTER

Barry L. Eppley, M.D.  
Riley Hospital for Children  
702 Barnhill Drive, Rm. 3540  
Indianapolis, Indiana 46202-5125

Dear Dr. Eppley:

This Warning Letter is to inform you of objectionable conditions observed during a Food and Drug Administration (FDA) inspection conducted at your clinical site from May 18 through 31, 2006, by an investigator from FDA's Detroit District Office (DET-DO). The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical study entitled [REDACTED], sponsored by [REDACTED], complied with applicable FDA regulations. [REDACTED] products are devices as defined under 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 Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), 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 serious violations of Title 21, Code of Federal Regulations (21 C.F.R.), Part 50 – Protection of Human Subjects, and Part 812-Investigational Device Exemptions. 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, and our subsequent review of the inspection report are discussed below:

**Failure to ensure that informed consent was obtained in accordance with FDA regulations [21 CFR 812.100, 21 CFR 50.27 and 21 CFR 812.140(a)(3)(i)]**

An investigator is responsible for ensuring that informed consent is obtained in accordance with FDA regulations, including requirements that consent be documented in writing using an IRB-approved consent document prior to any study-related procedures and that records of consent be maintained in accordance with FDA regulations. Our investigation revealed that two out of four subjects enrolled in the study were not properly consented. Examples of this failure include, but are not limited to the following:

- Patient records show that [REDACTED] was implanted with the study device on [REDACTED]. However, there is no signed informed consent available for this subject.
- [REDACTED] was implanted with the study device on [REDACTED]. The subject signed the informed consent form on [REDACTED].

**Failure to ensure an investigation is conducted in accordance with the signed agreement, the investigational plan, and applicable FDA regulations and any conditions of approval imposed by FDA or the reviewing IRB [21 CFR 812.100 and 21 CFR 812.110(b)]**

As a clinical investigator it is your responsibility to conduct the clinical investigation in accordance with the signed investigator agreement, investigational plan, and applicable FDA regulations. You failed to adhere to the above-stated regulations. Examples of this failure include but are not limited to the following:

- The IRB initially approved the study from [REDACTED]. No further documentation was available onsite to indicate that the IRB conducted further continuing review of the study, although IRB's are required to conduct continuing review no less than once a year, and although you are required to maintain records of all correspondence with an IRB. 21 CFR 56.109(f); 21 CFR 812.140(a)(1). You implanted the following three subjects with the study device after [REDACTED], although there is no evidence of IRB review and approval to cover these periods.
  - [REDACTED] was implanted on [REDACTED].
  - [REDACTED] was implanted on [REDACTED].
  - [REDACTED] was implanted on [REDACTED].
- The study protocol required that follow-up visits be conducted as follows: 1 month, 3 months, 6 months, 1 year, 1.5 years and 3 years. Of the 24 follow-up visits required by the protocol, three visits were missed entirely and many of the others were conducted outside the timeframe required by the protocol. For example:

- [REDACTED], whose study surgery was performed on [REDACTED] had no record of being seen for the following follow-up visits; 6 months, 1.5 years and 3 years.
- [REDACTED] was implanted on [REDACTED]. The one-month follow-up visit was performed on [REDACTED], 60 days after surgery
- [REDACTED] was implanted on [REDACTED]. The three-month follow-up visit was performed on [REDACTED], approximately 120 days after surgery.

In addition, the FDA investigator noted that no source documentation for the [REDACTED] subjects' previous medical history, radiographic assessments, or other relevant records were available for review. These records are required to be maintained in accordance with 21 CFR 812.140 and should have been readily available at your site.

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.

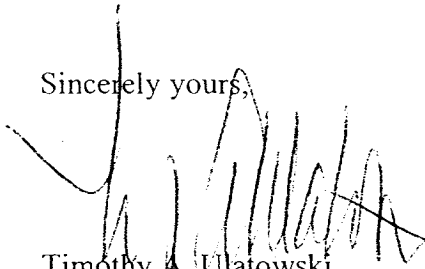
Within fifteen (15) working days of receiving this letter, please provide written documentation of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. In addition, 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: Michael E. Marcarelli, PharmD, Director, Division of Bioresearch Monitoring, Office of Compliance, Food and Drug Administration, Center for Devices and Radiological Health, 2098 Gaither Road, HFZ-310, Rockville, Maryland 20850.

A copy of this letter has been sent to FDA's Detroit District Office, 300 River Place, Suite 5900, Detroit, Michigan 48207. Please send a copy of your response to that office.

If you have any questions, please contact Dr. Marcarelli at (240) 276-0125, or by email at Michael.Marcarelli@fda.hhs.gov.

Sincerely yours,

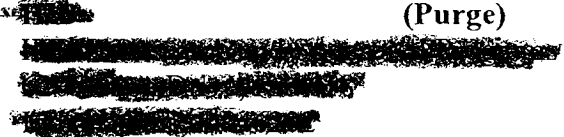


Timothy A. Ulatowski  
Director  
Office of Compliance  
Center for Devices and  
Radiological Health

cc:



(Purge)



(Purge)