DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

94837d

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

JUL 13 2004

WARNING LETTER

VIA FEDERAL EXPRESS

Thomas J. Peters, M.D.
651 West Mingus Avenue, Suite 1F
Cottonwood, Arizona 86326

Dear Dr. Peters:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site. Ms. Diane C. Van Leeuwen, an investigator from FDA's Los Angeles District Office, conducted the inspection on April 12, 2004. The purpose of the inspection was to determine if your activities as a clinical investigator for the [redacted] study complied with applicable FDA regulations. The [redacted] is a device as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act)

The FDA conducted the inspection 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 [510(k)] submissions are scientifically valid and accurate. The program also ensures that human subjects are protected from undue hazard or risk during scientific investigations.

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, 21 CFR Part 50-Protection of Human Subjects, and Section 520(g) of the Act. At the close of the inspection, Ms. Van Leeuwen presented a Form FDA 483 "Inspectional Observations" to you for review and discussed the listed deviations. The deviations noted on the FDA 483 and our subsequent inspection report review are discussed below:

1. **Failure to adhere to the general and specific responsibilities of an investigator (21 CFR 812.100, 21 CFR 812.110, 21 CFR 50.20 and 812.150(a)(5)).**

In accordance with 21 CFR 812.100 and 812.110, investigators are responsible for maintaining control of devices under investigation and for ensuring that an investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations. As required by 21 CFR 812.100 and 21 CFR 50.20, an investigator must ensure informed consent is obtained from the subject or the subject's legally authorized representative prior to his or her participation in an investigational study. If

informed consent is not obtained because of emergency use, investigators are responsible for reporting such use of the investigational device to the sponsor and reviewing IRB within five working days after the use occurs (21 CFR 812.150(a)(5)).

You failed to satisfy these requirements. Examples of this failure include but are not limited to the following:

> On May 6, 2002, you implanted the investigational device into Subject [redacted] who was not enrolled in the study and who did not sign the required informed consent form. Furthermore, you did not have IRB approval, did not ensure informed consent was obtained prior to implanting the investigational device into Subject [redacted], and did not report use of the investigational device to the reviewing IRB. The IRB initially approved the study on February 27, 2003, which was nine months after the implantation into Subject [redacted]

During the inspection, you stated that the use of the investigational device with respect to Subject [redacted] was as a custom device and for prescription and compassionate uses; you said that you were not sure why you thought that the device was acceptable to be used; and you acknowledged that you did not have the appropriate approval for compassionate use.

The custom device exemption applies to devices that meet a narrow and specific set of statutory requirements set forth in section 520(b) of the Act. The devices you implanted did not meet these requirements, nor those described in 21 CFR 812.3(b) for custom devices. Custom devices are limited to those intended for use by an individual patient named in a physician's order and made in a special form for that patient. (21 CFR 812.3(b)(5)). These devices also fail to meet the exemption set forth in 21 CFR 812.2(c)(7).

Furthermore, FDA regulations do not provide for the "prescription" use of an unapproved device currently under an IDE. It is important for clinical investigators to understand that unless the physical safety of a subject demands otherwise, treatment of study subjects must adhere to the requirements of an investigational plan. (21 CFR 812.36).

In accordance with 21 CFR 812.35(a)(2), deviations from the investigational plan are permitted when necessary to protect the life or physical well-being of a subject in an emergency. FDA's "Guidance on IDE Policies and Procedures," which includes a section on emergency use of unapproved devices, can be found on the Internet at http://www.fda.gov/cdrh/ode/idepolcy.html. The guidance document speaks to those situations in which an investigational or unapproved device, respectively, is needed to save the life of a patient or to prevent irreversible morbidity. At the same time, however, FDA recognizes that there are circumstances in which an investigational device is the only option available for a patient faced with a serious, albeit not life-threatening condition (hereinafter referred to as "compassionate use"). In these circumstances, FDA uses its regulatory discretion in determining whether such use of an investigational device

should occur. For more information about compassionate use, you may also refer to the above-referenced guidance document.

Unlike emergency use of an unapproved device, prior FDA approval is needed before compassionate use may occur. In order to obtain Agency approval, the sponsor should submit an IDE supplement requesting approval for a protocol deviation under 21 CFR 812.35(a).

2. **Failure to maintain accurate, complete, and current records (21 CFR 812.140(a)).**

   FDA regulations require investigators to maintain accurate, complete, and current records of receipt, use, or disposition of a device (21 CFR 812.140(a)(2)).

   You failed to satisfy this requirement. Examples of this failure include but are not limited to the following:

   - Copies of receipt and disposition of the investigational devices were missing from the study records. For example, the Kit Router document shows that [redacted] investigational devices were returned and [redacted] investigational device with lot [redacted], part [redacted] was missing. However, the implant usage ticket for Subject [redacted] shows that this patient received lot [redacted], part [redacted]

   - Furthermore, the Kit Router shows that the investigational device with lot [redacted], part [redacted] was returned; however, the implant usage ticket for Subject [redacted] shows that this patient received this device. Due to this discrepancy, FDA could not determine which investigational device was implanted into the patient.

   - In addition, during the close-out discussion, Ms. Van Leeuwen mentioned to you that the [redacted] month postoperative follow-up x-ray films and reports were missing from the records of Subject [redacted] Please provide copies of the x-ray report for this patient with your response.

The above-described deviations are not intended to be an all-inclusive list of deficiencies that may exist at your clinical site. As a clinical investigator, it is your responsibility to ensure that investigations in which you participate are conducted in accordance with all applicable requirements of the Act and FDA's regulations.

Within 15 working days after receiving this letter please provide written documentation of the specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations in current and future studies. 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.

Send your response to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II, HFZ-312, 2094 Gaither Road, Rockville, Maryland 20850, Attention: Linda Godfrey.

We are also sending a copy of this letter to FDA's Los Angeles District Office, and request that you also send a copy of your response to that office. If you have any questions, please contact Linda Godfrey by phone at 301-594-4723 extension 134 or by email at linda.godfrey@FDA.HHS.GOV.

Sincerely yours,

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

cc:

[redacted] (purged)
General Manager
[redacted]

[redacted] (purged)
Chair, Institutional Review Committee
[redacted]