

Inspections, Compliance, Enforcement, and Criminal Investigations

Jones, Thomas M.D.



Department of Health and Human Services

Public Health Service
Food and Drug
Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

WARNING LETTER

VIA FEDERAL EXPRESS

JUL 1 2009

Thomas K. Jones, M.D.
4800 Sand Point, Wy, NE
Seattle, Washington 98105

Dear Dr. Jones:

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 March 6, 2009 to March 19, 2009, by an investigator from the FDA Seattle District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical study **(b)(4)** Investigational Device Exemption (IDE) **(b)(4)** Premarket Approval (PMA) **(b)(4)** sponsored by **(b)(4)** complied with applicable federal regulations. The **(b)(4)** 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 April 17, 2009, to the Form FDA 483 "Inspectional Observations."

The inspection was conducted under a program designed to ensure that data and information contained in requests for IDE, 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 serious violations of Title 21, Code of Federal Regulations (21 C.F.R.) 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 you and **(b)(6)** Clinical Research Coordinator. The deviations noted on the FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

Failure to ensure that informed consent is obtained in accordance with 21 CFR Part 50, failure to conduct the investigation in accordance with the investigational plan and conditions of approval imposed by an IRB. [21 CFR 50.20, 50.27(a), 812.100 and 812.110(b)]

As an investigator, you are responsible for ensuring that informed consent is obtained in accordance with 21 CFR Part 50.20. Informed consent shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. In addition, a clinical investigator must conduct an investigation in accordance with the signed agreement, the investigational plan, applicable FDA regulations, and any conditions of approval imposed by FDA or the IRE. You failed to adhere to the above stated regulations. Examples of this failure include, but are not limited to, the following:

1. The Institution Review Board (IRB) conditionally approved the study on **(b)(4)**. This letter explained, "Until you received final approval you may not recruit or contact research subjects," and conditioned final approval upon receipt of the data safety monitoring board's (DSMB) report and a revision to the informed consent form (ICF) notifying subjects of the risk of device embolization. On January 26, 2005, the ICF was revised to reflect the risk of embolization and the DSMB report was submitted. However, four subjects **(b)(6)** were implanted with the device between **(b)(4)** and **(b)(4)** prior to receipt of the DSMB report and revised ICF, and prior to final IRE approval.

2. After the approval of the revised ICF by the IRE on **(b)(4)** ten subjects **(b)(6)** were consented using the ICF version dated **(b)(4)** which did not include the risk of embolization.

3. The legally authorized representative of subject **(b)(6)** signed the ICF; however, it was not dated.

Your response related to items 1,2 and 3 above acknowledges that the subjects did not sign the revised and approved ICF; however, you did not address the issue of ensuring proper consenting of subjects. You stated that your IRE has introduced more stringent protections to prevent the use of outdated consent forms, which include using a dated approval stamp. You also stated that you have hired one full time research nurse and one part time assistant to oversee these activities. Although you have hired additional staff, you are ultimately responsible for the conduct of the study and following the regulations. Your response is inadequate in that you did not provide any documentation of corrective or preventative actions to ensure that subjects are not enrolled prior to IRE approval and that the correct ICF is signed and dated by all subjects or their authorized representatives. Please submit documentation of training and procedures that you have implemented or plan to implement to prevent the above deviation from recurring.

4. The investigational plan requires **(b)(4)** to be reviewed by the **(b)(4)** There was no documentation in your study records of the shipment of the data to the **(b)(4)**

Your response states that you did not send copies of any **(b)(4)** to the sponsor to be forwarded to the **(b)(4)** Your response is inadequate in that it does not provide corrective or preventative actions to avoid recurrence of the violations, such as new or revised standard operating procedures (SOPs), policies, or other means that would ensure compliance with the study protocol and FDA regulations.

Failure to submit progress reports on the investigation to the sponsor at regular intervals, but in no event less often than yearly. [21 CFR 812.150(a)(3)]

5. Section 8.1 of the protocol indicates that progress reports are to be sent to the sponsor and the IRB. However, there was no documentation or evidence in your

study records that indicate that the annual progress reports were submitted to the sponsor.

In your response, you state the annual reports were forwarded to the sponsor in electronic form and the email confirmations were available. You also stated that, in the future, you will maintain paper records of email correspondence to study sponsors in the regulatory binders to address this concern. Your response is inadequate in that you did not provide copies of the email confirmations of the annual reports to the sponsor. Please provide copies of email confirmations of the annual reports and any new or revised procedures, along with documentation demonstrating staff training in these procedures, when you respond to this letter.

Failure to maintain accurate, complete, and current records of receipt, use, or disposition of a device that relate to the type and quantity of the device, the dates of receipt and the batch number or code mark. [21 CFR 812.140(a)(2)]

Your device receipt and disposition records were inadequately maintained. Examples of these failures include, but are not limited to, the following:

6. There are no records of receipt for 29 of the **(b)(6)** devices received.
7. According to your records, one device **(b)(4)** was returned to the sponsor on **(b)(4)** Your records also indicate that the same device was **(b)(4)** subject **(b)(6)** on **(b)(4)** There is no documentation that indicates the device was returned to your site between **(b)(4)** and **(b)(4)**
8. There are no records of disposition for 10 of the **(b)(6)** devices.

In your response, you state that there were no devices unaccounted for during the span of this study and that you verified with the sponsor that all devices shipped to your site during the course of the study were properly accounted for. You also stated that the serial numbers for all **(b)(4)** devices, investigational or not, are now noted on shipping records maintained electronically in your hospital's central supply inventory system and this system will adequately address the new auditing standard. Your response is inadequate in that you did not provide any documentation of your corrective actions. We recommend that you re-evaluate any preventative actions related to the electronic system within three to six

months to ensure their adequacy and that there is no recurrence of these deviations. Please submit documentation of training on the electronic system and procedures that you have implemented or plan to implement to prevent the above deviation from recurring.

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. 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.

Please also note that as an investigator you are responsible for maintaining accurate, complete, and current records of each subject's case history and exposure to the device, which includes the case report forms (CRFs) and supporting data. The FDA investigator identified a number of subject's records in which the CRFs did not match the source data.

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: Levering Keely, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-310, Rockville, Maryland 20850.

A copy of this letter has been sent to FDA's Seattle District Office, 22201 23rd Drive, SE, Bothell, Washington 98021-4421. Please send a copy of your response to that office.

If you have any questions, please contact Levering Keely, 301-796-5663, or email: Levering.Keely@fda.hhs.gov.

Sincerely yours,

/S/

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