



AUG 2 2004

WARNING LETTER

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

Via Federal Express

Miers Johnson, M.D.
[REDACTED]

215 East Hawaii Avenue
Nampa, ID 83686

Dear Dr. Johnson:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site. This letter also discusses your written responses, dated April 6, 2004 and dated May 15, 2004, to the noted violations and requests that you implement prompt corrective actions. We take note of your request that your May 15, 2004 letter supercedes your April 6, 2004 response. Catherine J. Laufman, an investigator from FDA's Seattle District Office conducted the inspection from March 22, through March 26, 2004. The purpose of the inspection was to determine whether your activities as a clinical investigator of the study entitled [REDACTED] complied with applicable regulations. The investigational [REDACTED] system used in your study is a device defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 321 (h)).

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. 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 submitted by the district office revealed serious violations of requirements of Title 21, Code of Federal Regulations, (CFR), Part 812 - Investigational Device Exemptions and Part 50 - Protection of Human Subjects. At the conclusion of the inspection Ms. Laufman presented you with a Form FDA 483, "Inspectional Observations," that listed the deviations noted and those deviations were discussed with you. The deviations noted on the FDA 483, your written response dated May 15, 2004 to those deviations, and our subsequent review of the inspection report are discussed below:

1. Failure to conduct the investigation according to the signed agreement with the sponsor, the investigational plan, and any conditions imposed by the institutional review board (IRB) (21 CFR 812.100 and 21 CFR 812.110(b)).

Under FDA regulations, you are required to conduct your clinical investigation in accordance with your signed agreement with the study sponsor and with your investigational plan, which includes the study protocol. Our investigation revealed deviations from the signed agreement and investigational plan including, but not limited to, the following:

- You failed to exclude subjects from the study who met the exclusion criteria identified in the protocol. The protocol listed "[REDACTED]" as an exclusion criteria. You enrolled [REDACTED] subjects who had received [REDACTED]. In addition, the protocol listed "[REDACTED]" as an exclusion criteria. You enrolled [REDACTED] patients who had a [REDACTED] of over [REDACTED], although the study monitor had indicated to you that patients with a [REDACTED] over [REDACTED] should be excluded from the study. Your staff indicated at the time of inspection that your former study coordinator used [REDACTED] calculations to determine whether subjects should be excluded from the study due to [REDACTED] but no records of this could be located during the inspection.
- You failed to submit amendments to the protocol dated May 8, 2002 and June 17, 2002, involving changes to the study inclusion and exclusion criteria, to the reviewing IRB. The IRB approval letter dated May 21, 2002 indicates that protocol changes are to be submitted to the IRB for review and approval prior to implementation. In addition, the Investigator's Agreement, Section I, contains a certification that you will conduct the investigation in accordance with FDA regulations, the Investigational Plan, and any *other conditions of approval imposed by the IRB, FDA, and the sponsor*. You signed the agreement and are obligated to follow it.
- Case report forms (CRFs) for the study contained a signature block that required the investigator's signature to show review and approval of the CRF as described in the Investigator's Agreement, page 2, Section IV. On [REDACTED] of [REDACTED] CRFs reviewed, the CRFs were not signed. Instead, your study coordinator used an ink stamp of your signature.

In your written response you refer to the protocol change on June 17, 2002 stating that patients who "require surgery on a [REDACTED] are acceptable as long as long as the period of 9-12 months has passed since the initial surgery on the [REDACTED]" This response is inadequate since you failed to submit the June 17, 2002 protocol amendment to the IRB and it was not approved prior to the surgery on the [REDACTED] of these [REDACTED] subjects.

In addition you state that you were not provided with a specific [REDACTED] chart by the sponsor to determine [REDACTED]. You further state that, as a result, this issue was

"overlooked at the time of consent." This response is inadequate because as a clinical investigator it is your responsibility to follow the protocol, including its exclusion criteria.

You stated that you would submit the two protocol amendments to the reviewing IRB at its May 17, 2004 meeting. In your written response to this letter, please confirm that you have taken this action. You also state that you have signed and dated each of the CRFs that were stamped with your signature. In your written response, please confirm whether you reviewed the documents that now bear your original signature.

2. Failure to ensure IRB approval of informed consent form (21 CFR 812.100 and 21 CFR 50.27(a)).

An investigator is responsible for ensuring that informed consent is obtained in accordance with 21 CFR Part 50 and 21 CFR 812.100. In accordance with 21 CFR 50.27(a), the investigator is required to document informed consent using a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative, and maintain all correspondence with an IRB.

Examples of your failure to satisfy these requirements include but are not limited to the following:

There were [REDACTED] different versions of the informed consent document (ICD). You did not have documentation that [REDACTED] of the versions had been approved by the reviewing IRB. [REDACTED] of the [REDACTED] subjects enrolled into the [REDACTED] study signed one of these [REDACTED] versions of the ICD. For example:

- [REDACTED] subjects signed documents that had significantly different language than the IRB approved versions on the opening page.
- [REDACTED] different subjects signed the [REDACTED] unapproved document which had significantly different language on the signature page.

Your response states that the unapproved versions of the informed consent forms, among other changes, corrected mistakes in the approved versions and "had a much clearer description of the Purpose Of The Study." This response is not adequate. As stated above, there are significant differences in the unapproved versions that you have not mentioned. Also, regardless of the improvements that you cite, it is your responsibility to use informed consent forms that have been approved by the reviewing IRB prior to initiating any study related procedures.

We acknowledge that you have submitted an informed consent form to the reviewing IRB and that it was approved at the IRB's May 18, 2004 meeting. You have also attached proposed SOPs to your May 15, 2004 letter. Proper implementation of your

proposed SOPs should help correct the deviation and prevent recurrence of similar deviations in the future.

3. Failure to submit progress reports to the sponsor (21 CFR 812.150(a)(3)).

FDA regulations require the submission of complete and accurate periodic progress reports on the investigation, at least yearly, to the sponsor, monitor, and reviewing IRB. There are no records of you preparing or submitting progress reports to the sponsor or IRB during the period of your conduct of the study, beginning October 22, 2002.

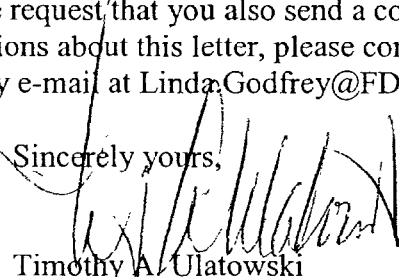
Your response regarding progress reports submitted to the sponsor indicates that you plan to contact the sponsor to determine how and when progress reports are to be submitted. In your written response to this letter, please describe how and when you intend to submit these reports. Your response also indicates that you planned to submit an annual report to your reviewing IRB on May 21, 2004, on a form provided by the IRB. In your response to this letter, please include a copy of this annual report.

The above described deviations are not intended to be an all-inclusive list of deficiencies that may exist in your clinical study. It is your responsibility as a clinical investigator to assure adherence to each requirement of the Act and all applicable federal regulations.

Within 15 working days after receiving this letter please provide written documentation of the additional specific steps you have taken or will take to correct these violations and prevent 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. 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 Seattle District Office, 22201 – 23rd Drive S.E., Bothell, WA 98021. We request that you also send a copy of your response to that office. If you have any questions about this letter, please contact Ms. Godfrey at (301) 594-4720, extension 134, or by e-mail 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]

[REDACTED]

[REDACTED]

(purged)

Chairman

Institutional Review Board

[REDACTED]

[REDACTED]

[REDACTED]