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

Via Federal Express

WARNING LETTER

JUL 30 2003

James Yanney, DDS, MD
1830 Blankenship #175
West Linn, OR 97068

Dear Dr. Yanney:

This warning letter informs you of objectionable conditions found during the Food and Drug Administration (FDA) inspection conducted at your clinical site and requests from you a prompt written reply informing us of your corrective actions. You participated as a clinical investigator in a study entitled, the [REDACTED], sponsored by [REDACTED]. Data from the study conducted at your site has been submitted to the FDA by [REDACTED] in support of the investigational device exemptions application.

During the period of May 5 through 7, 2003, you were visited by Mr. Carl A. Anderson, an investigator from the FDA's Seattle District Office. The purpose of Mr. Anderson's visit was to determine whether your activities and procedures as a clinical investigator for the [REDACTED] study complied with applicable regulations. This product is a device as that term is defined under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

This inspection was conducted under a program designed to ensure that data and information contained in applications for Investigational Device Exemptions (IDE), Premarket Approval (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 the scientific investigation.

We have completed our review of the inspection report submitted by the Seattle District Office. The report reveals significant violations of the requirements under Title 21, Code of Federal Regulations (21 CFR), Part 50 - Protection of Human Subjects; and 21 CFR Part 812 - Investigational Device Exemptions. These violations were listed on the Form FDA 483, "Inspectional Observations," which was presented to and discussed with you on May 7, 2003. The violations noted on the Form FDA 483 and our subsequent review of the inspection report are summarized below:

Failure to obtain the legally effective informed consent documented by the use of a written consent form approved by the IRB and signed and dated by the subject at the time of the consent. Failure to provide a copy to the person signing the informed consent form. (21 CFR Part 50.27(a) and 21 CFR 812.100)

No subjects enrolled in the study had signed legally effective informed consent forms. All subjects had notations in the informed consent indicating that the consent document had been read to them over the telephone. The informed consent forms were signed by the investigator and/or witnesses rather than by the subject or the subject's legally authorized representative as required. None of the subjects were provided a copy of the informed consent.

Failure to provide the basic elements of informed consent. (21 CFR 50.25 (a)(1) and 6))

The IRB's "Guide to Informed Consent" and FDA regulations provide the elements required in the informed consent document. The informed consent you allegedly read to each subject did not include certain required elements, including a description of the research procedures, the expected duration the subject's participation, and identification of procedures that are experimental. In addition, it did not include any explanation as to whether any compensation would or would not be provided.

Failure to submit progress reports to the reviewing IRB and sponsor at regular intervals but in no event less often than yearly and failure to submit a final report to the reviewing IRB and sponsor within 3 months after termination or completion of an investigation. (21 CFR 812.150 (a)(3) and (6))

You failed to submit any annual progress reports to your IRB. The IRB made numerous requests for periodic reporting. You failed to respond to their requests, thus the IRB withdrew approval of your participation in this study.

Failure to report the withdrawal of IRB approval to the sponsor. (21 CFR 812.150(a)(2))

On November 8, 2000, your IRB withdrew approval for your participation in this study due to failure to respond to requests for an annual report to be submitted by you to the IRB. This withdrawal of IRB approval was not documented to have been reported to the sponsor.

Failure to submit reports of unanticipated adverse device effects to the reviewing IRB and to the sponsor. (21 CFR 812.150(a)(1))

Subjects [REDACTED] and [REDACTED] had reactions to the polyethylene in the prostheses that resulted in removal and or replacement. Subject [REDACTED] had excision of the polyethylene insert. Subject [REDACTED] reported significant pain as a result of the

surgery. These events were not reported to the IRB or the sponsor as adverse events or in progress or final reports.

Failure to maintain accurate, complete, and current records relating to the subjects' case history including case report forms and supporting data. (21 CFR 812.140 (a)(3))

You failed to complete all worksheets for the post-operative evaluation of subjects. The records for subject [REDACTED] did not contain page 2 (complications and adverse events) for 9 evaluation visits.

Failure to maintain complete records of correspondence with the IRB and sponsor relating to your participation in the investigation (21 CFR 812.140(a)(1)) and failure to maintain records of receipt, use and disposition of devices. (21 CFR 812.140(a)(2))

Your records fail to include any letter of approval from the IRB allowing you to participate in the study. There are no records of any communication with the sponsor concerning phone conversations you have had with the sponsor. There are no records of receipt, use, or disposition of the devices. In your verbal reply to the investigator, you stated that you thought the hospital maintained these files.

As a clinical investigator, it is your responsibility to ensure that investigations in which you participate are conducted in accordance with applicable FDA regulations.

You stated to Mr. Anderson that you would provide a written response to the identified Form FDA 483 Inspectional Observations to this office. We have not received such a reply as yet.

During the inspection, Mr. Anderson discussed with you some possible corrective actions that you could take in the future including training, hiring a study coordinator, and working with an experienced sponsor of clinical research who would provide ongoing contact through monitoring.

We would like to reinforce these recommendations and add several other recommendations. In the future, you might consider attending and having your staff attend training sessions that focus on the operations of investigational studies. Such programs are available from various professional associations such as the Association of Clinical Research Professionals (ACRP), The Food and Drug Law Institute (FDLI), and the Regulatory Affairs Professional Society (RAPS) to name a few. You will want to ensure that future studies in which you find yourself involved are adequately sponsored with well defined sponsor responsibilities. You will want to determine that they are well monitored. There needs to be close cooperation and communication between all participants of the study including the sponsor, IRB, investigator, and staff. Having adequate resources at your clinical site including a coordinator, assists immensely in adequately meeting your investigator responsibilities.

In addition to the above recommendations, you should carefully review the regulations located in 21 CFR Parts 50 and 812. In these regulations the sponsor, investigator, and IRB responsibilities are outlined. You can refer to the following web site for additional information:

Investigational Device Exemptions -
http://www.access.gpo.gov/nara/cfr/waisidx_00/21cfr812_00.html

Please advise this office, in writing, **within fifteen (15) working days of receipt of this letter** of the specific steps you have taken to correct these violations and other violations known to you, and to prevent the recurrence of similar violations in current or future studies. Failure to respond can result in regulatory action without further notice.

You should direct your response to the:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
Program Enforcement Branch II, (HFZ-312)
2098 Gaither Road
Rockville, Maryland 20850
Attention: Mr. G. Levering Keely, BSN, MPA,
Consumer Safety Officer.

A copy of this letter has been sent to our Seattle District Office, 22201 23rd Dr., SE Bothell, Washington, 98021. We request that a copy of your response be sent to that office as well.

Sincerely yours,


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