DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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

MAR 11 2004

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS AND OPPORTUNITY TO EXPLAIN

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Burton L. Redd, M.D.
400 West Mineral King
Visalia, California 93291

Dear Dr. Redd:

From June 2 through 6, 2003, Mr. Jeffrey W. Shrifter, a Food and Drug Administration (FDA) inspector, conducted an inspection of the [redacted] clinical study in which you participated as a principal investigator. This inspection was conducted as part of the FDA's Bioresearch Monitoring Program which includes inspections designed to monitor the conduct of research involving investigational products.

Based on our evaluation of information obtained by the Agency, we believe that you have repeatedly or deliberately violated regulations governing the proper conduct of clinical studies involving investigational products as published under Title 21, Code of Federal Regulations (CFR), Part 812, Investigational Device Exemptions (copy enclosed) and Part 50, Protection of Human Subjects (copy enclosed).

This letter provides you with written notice of the matters under complaint and initiates an administrative proceeding, described below, to determine whether you should be disqualified from receiving investigational products as set forth under 21 CFR 812.119.

A listing of the violations follows. The applicable provisions of 21 CFR 812 and Part 50 are cited for each violation.

1. **You allowed subjects to participate in the study before obtaining approval from the reviewing institutional review board (IRB) (21 CFR 812.100 and 812.110(a)).**

   You implanted subjects [redacted] and [redacted] with the investigational device prior to obtaining IRB approval. On May 10, 2002, you obtained the [redacted] IRB approval to conduct the [redacted] study. The study, however, was initiated on or prior to November 2001. The

following subjects were implanted with the investigational device prior to IRB approval: 1) subject [redacted] received the investigational device on November 28, 2001 on the first side and [redacted] on the second side; 2) subject [redacted] received the investigational device on [redacted], 2002.

Accordingly, you conducted research on human subjects without IRB approval. During the inspection, you stated that you wrote a prescription for the device and sent it to [redacted], the sponsor, and that you had no recollection of a note on the device mentioning FDA approval. Your response is not acceptable in that it does not adequately address the reasons for treatment use of the investigational device. FDA regulations do not provide for the "prescription" use of an unapproved device currently under IDE. Your records contain nothing to demonstrate that the investigational device was implanted in subjects [redacted] and [redacted] in accordance with 21 CFR 812.36, FDA's regulations governing treatment use of an investigational device, and our records do not indicate that FDA has approved treatment use of this device.

An investigator is responsible for not allowing any subject to participate in an investigational study before obtaining IRB approval and may determine whether potential subjects would be interested in participating in an investigation but may not request the written informed consent of any subject to participate and not allow any subject to participate prior to obtaining IRB and FDA approval (21 CFR 812.100 and 812.110(a)).

2. **You failed to conduct the study in accordance with the approved investigational plan, the investigator's agreement, and any conditions of IRB approval (21 CFR 812.100 and 812.110(b)).**

You failed to follow the protocol and investigational plan. For example, prior to implantation with the investigational device, subject [redacted] had [redacted] pain and needed [redacted] surgery. Consequently, subject [redacted] did not meet the inclusion/exclusion criteria specified in the investigational plan; yet, subject [redacted] was included in the study. Furthermore, the Investigator's Agreement includes a requirement that any deviation from the plan be reported to the IRB, the sponsor, and FDA as soon as possible but not later than 5 working days from the deviation. You did not exclude subject [redacted] per the study protocol, nor did you report your implantation of the study device into subject [redacted] to the IRB or FDA, and thus you did not follow the Investigator's Agreement.

3. **You failed to adhere to informed consent requirements (21 CFR 812.100, 21 CFR 50.20, 50.25(a) and 50.27(a)).**

- You did not ensure that there was written documentation of informed consent for all study subjects. There was no informed consent form for subjects [redacted] and [redacted] treated with the investigational device at your clinical site. During the inspection, you stated that the subjects signed the standard hospital informed consent form prior to surgery; you ensured that subject [redacted] was aware that the device was

investigational; and you did not know what your co-investigator, Dr. McConnaughey, told subject [redacted] Although subject [redacted] record contained evidence that the subject was informed verbally, not all subject records included documentation of the subjects being informed verbally of the investigational device status.

- You failed to ensure that the informed consent form has a contact for questions regarding the subject's rights.

An investigator is required to comply with the following: protect the rights, safety, and welfare of subjects, and ensure that informed consent is obtained (21 CFR 812.100 and 21 CFR 50.20). Further, an investigator is required to have written documentation of informed consent 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 (21 CFR 50.27(a)). Page three of the Investigator Agreement has a statement of certification that written informed consent will be obtained from subjects or their legal representatives. You signed this agreement; therefore, you are obligated to follow it, as well as the regulations that require written informed consent. The basic required elements for informed consent are set forth in 21 CFR 50.25(a). An investigator is responsible for providing each subject with an explanation of whom to contact for answers to pertinent questions about the research and the research subjects' rights (21 CFR 50.20 and 50.25(a)(7)).

In addition, Mr. Shrifter noted the use of technical language in the informed consent form. The information given to the subject or the subject's representative must be in language understandable to the subject or the subject's representative (21 CFR 50.20).

4. **You failed to maintain accurate and complete device accountability and subjects' records (21 CFR 812.140(a)(2) and 812.140(a)(3)).**

- You failed to maintain device accountability records documenting receipt, use, and disposition of the device. There were no device accountability logs or records of the devices shipped, received, dispensed or returned.

- You failed to maintain source documents. Several Case Report Forms (CRFs) were incomplete, in that, the CRFs were completed at a later date, signed and dated at a later date, or not signed or dated. For example, the following subject records were incomplete:

  - Subject [redacted] had surgery on [redacted] 2002; yet, the following CRFs are dated January 27, 2003: operative CRF and the X-ray Evaluation CRF.,
  - Subject [redacted] X-ray Evaluation CRF is not dated or signed.

During the inspection, you stated you had not completed some of the CRFs, or had filled some of them out incorrectly. An investigator is required to maintain accurate,

complete, and current records of each subject's exposure to the investigational device, as well as records of receipt, use, or disposition of the device and each subject's case history (21 CFR 812.140(a)(2) and 812.140(a)(3)).

5. **You failed to submit timely progress reports to the IRB (21 CFR 812.150(a)).**

   You failed to submit timely progress reports to the IRB. During 2002, your clinical site reported protocol deviations to the sponsor only. You did not submit a progress report of the protocol deviations to the IRB until April 11, 2003. Page three of the Investigator Agreement, section XI, has a statement of certification that routine reports and/or final reports will be provided to the IRB **and** [redacted] the sponsor, as requested. You signed this agreement and are obligated to follow it. During the closing discussion, you stated that you did not realize that an annual report was required. FDA's regulation pertaining to Investigator Reports requires the submission of complete, accurate and timely reports which includes progress reports to the sponsor, monitor and the reviewing IRB at least annually (21 CFR 812.150(a)(3)).

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study of investigational [redacted] It is your responsibility to ensure adherence to each requirement of the law and relevant regulations.

On the basis of the violations listed above, FDA asserts that you have repeatedly and deliberately failed to comply with the cited regulations and failed to comply with the conditions of the exempting regulations. Accordingly, FDA proposes that you be disqualified as a clinical investigator. You may reply to the above stated issues, including an explanation of why you should remain eligible to receive investigational products and not be disqualified as a clinical investigator, in a written response or at an informal conference in my office. This procedure is provided for by regulation 21 CFR 812.119.

Within fifteen (15) days of receipt of this letter, write or call Michael E. Marcarelli, Pharm.D., at 301-594-4720 ext. 120 to arrange a conference time or to indicate your intent to respond in writing. Your written response must be forwarded within thirty (30) days of receipt of this letter. Your reply should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-310), 2094 Gaither Road, Rockville, Maryland 20850, Attention Michael E. Marcarelli.

Should you request an informal conference, we ask that you provide us with a full and complete explanation of the above listed violations. You should bring with you all pertinent documents that include documentation of prescription use of the investigational device, and you may be accompanied by a representative of your choosing. Although the conference is informal, a transcript of the conference will be prepared. If you choose to proceed in this manner, we plan to hold such a conference within 30 days of your request.

At any time during this administrative process, you may enter into a consent agreement with FDA regarding your future use of investigational products. Such an agreement would terminate this disqualification proceeding. Enclosed you will find a proposed agreement between you and FDA.

The Center will carefully consider any oral or written response. If your explanation is accepted by the Center, the disqualification process will be terminated. If your written or oral responses to our allegations are unsatisfactory, or we cannot come to terms on a consent agreement, or if you do not respond to this notice, you will be offered a regulatory hearing before FDA, pursuant to 21 CFR Part 16 (enclosed) and 21 CFR 812.119. Before such a hearing, FDA will provide you notice of the matters to be considered, including a comprehensive statement of the basis for the decision or action taken or proposed, and a general summary of the information that will be presented by FDA in support of the decision or action. A presiding officer free from bias or prejudice and who has not participated in this matter will conduct the hearing. Such a hearing will determine whether or not you will remain entitled to receive investigational products. You should be aware that neither entry into a consent agreement nor pursuit of a hearing precludes the possibility of a corollary judicial proceeding or administrative remedy concerning these violations.

Sincerely yours,

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