



M3020N

WARNING LETTER

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

OCT - 4 1999

FEDERAL EXPRESS

Adam B. Smith, D.O.
University of North Texas
Health Science Center at Fort Worth
Office of Clinical Trials
3500 Camp Bowie Boulevard
Ft. Worth, Texas 76107

Dear Dr. Smith:

During the period of May 3 through May 20, 1999, Ms. Elvia Cervantes, an investigator with the Food and Drug Administration (FDA), Dallas District Office, visited your facility. The purpose of that visit was to conduct an inspection to determine whether your activities and procedures as a clinical investigator of the investigational study of the [REDACTED] device [REDACTED] complied with applicable FDA regulations. This product is a device as that term is defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), and Premarket Notifications [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 inspectional report submitted by the District Office revealed violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 – Investigational Device Exemptions and Part 50 – Protection of Human Subjects. These violations were listed on Form FDA-483, "Inspectional Observations" (see enclosed copy), which was presented to and discussed with you at the conclusion of the inspection. Also present were [REDACTED] [REDACTED]. The following list of violations is not intended to be an all-inclusive list of deficiencies in the above referenced clinical study:

1. Failure to prepare and submit complete, accurate, and timely adverse reports to the sponsor and to the reviewing IRB as required by 21 CFR 812.150(a)(1).

You failed to report unanticipated and anticipated adverse events in a timely manner, for example:

- a) [REDACTED] – This subject underwent a transmetatarsal amputation for gangrenous left foot, first, second, and fifth toes on 11/7/97; this event was reported to the sponsor on 4/29/98 and to the IRB on 4/30/98.
- b) [REDACTED] – This subject had four adverse events which were not reported to the sponsor or the IRB within the timeframe established by the IRB. For example, adverse events which occurred on 5/13/98, 5/19/98, 6/2/98, and 6/5/98 were reported to the IRB on 12/9/98, 12/8/98, 12/8/98, and 12/9/98 respectively. These same events were reported to the Sponsor on 10/09/98, 11/23/98, 10/09/98, and 10/09/98 respectively.

The IRB guidelines require that a detailed written report of unexpected, fatal or life-threatening experiences be completed and forwarded, along with supporting documentation, to the IRB within 10 working days of the event.

2. Failure to maintain accurate, complete, and current records relating to your participation in an investigational study [21 CFR 812.140(a)(2)(i) and (a)(3)].

- a) You failed to record data accurately on the subjects' case report forms and failed to complete source documents. Comparison of source documents to case report forms revealed discrepancies and inconsistencies in data reported in approximately 98 percent of the 40 subject files reviewed. For example, source document Adverse Event sheets and Concomitant Medications sheets were noted to be blank or with less entries than the case report form Adverse Event sheets; source document Wound Evaluations were blank or stated "N/A" while case report forms noted entries; abnormal laboratory findings were not always documented; and data was not always recorded concurrently with work performed.
- b) You failed to adequately document device accountability in that invoices lacked date, protocol number, and other identifying information to assure proper accountability of the investigational devices.

3. Failure to obtain and provide informed consent in accordance with 21 CFR 50.20.

On 4/8/98, study [REDACTED] was given an "old" version of the informed consent. We note that an attempt was made, via mail, to obtain the subject's signature on the revised form but the subject did not return the form and no further attempt was made to follow-up with the subject.

We acknowledge receipt of the June 9, 1999, letter from David P. Shingleton, MS, MBA, Manager, Office of Clinical Trials, which serves as the cover letter for your letter dated June 8, 1999, in response to the inspectional observations. In your letter, you stated that new "SOP's" and training were implemented and that you do not feel that any patient was placed at any risk by utilization of the device or by participation in the study. Regardless, as a clinical investigator, it is your responsibility to ensure that your investigation is conducted in accordance with the signed agreement, the investigational plan, and applicable FDA regulations.

Please advise this office, in writing, within 15 working days of receipt of this letter, of the additional steps you have taken or will be taking to prevent recurrence in future studies of violations similar to those listed above. Please send 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: Pamela Reynolds. A copy of this letter has been forwarded to our Dallas District Office, 3310 Live Oak Street, Dallas, Texas 75204. We request that a copy of your request be sent to that office.

If you have any questions you may contact Ms. Pamela Reynolds at (301) 594-4720, ext. 155.

Sincerely yours,



for

Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosure

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cc: Dennis P. Shingleton, MS, MBA
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