



WARNING LETTER
Via Federal Express

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 19 2003

Frank J. Criado, M.D.
Union Memorial Hospital
3333 North Calvert Street, Suite 570
Baltimore, Maryland 21218

Dear Dr. Criado:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site, to discuss your written response to the deviations noted, and to request a prompt reply informing us of your corrective actions. The inspection took place during the period of February 13, 2003 – March 14, 2003, and was conducted by Ms. Stephanie Shapley, an investigator from FDA's Baltimore District Office. The purpose of the inspection was to determine if your activities as a clinical investigator in your clinical studies of [REDACTED] [REDACTED] comply with applicable FDA regulations. These grafts are devices, 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 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 prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions and Part 50 - Protection of Human Subjects, and Section 520(g) of the Act. You received a Form FDA-483, "Inspectional Observations," at the conclusion of the inspection that listed the deviations noted and discussed with you. We acknowledge receipt of a copy of your response to Ms. Shapely, dated March 18, 2003. The deviations noted on the FDA-483, our subsequent review of the inspection report, and your responses to the FDA-483 items are discussed below. The deviations noted include:

Failure to report unanticipated adverse device effects or deaths in a timely manner to the reviewing IRB. [21 CFR 812.150(a)(1)]

You failed to report to the reviewing IRB, within the required time period, the occurrence of renal complications, acute renal failure and thrombocytopenia in subject [REDACTED] and respiratory insufficiency, myocardial infarction, and renal complications in subject [REDACTED]

An investigator is required to report to the sponsor and to the reviewing IRB any unanticipated adverse device effects as soon as possible, but in no event later than ten working days after the investigator first learns of the effect.

Failure to obtain IRB approval before allowing any subjects to participate. (21 CFR 812.110 (a))

You implanted the investigational device in subjects [REDACTED] in the [REDACTED] study, during a period in which the study did not have IRB approval, from March 25, 2000 through August 29, 2000. In addition, it could not be determined if the [REDACTED] study received IRB approval for continuing review, as there was no approval letter in the regulatory binder for the study. Study personnel indicated that an approval letter for another study included approval of the [REDACTED] study, during the period of March 25, 1999 to March 25, 2000. Subjects [REDACTED] received the [REDACTED] investigational device during the period for which it could not be determined if the study had IRB approval.

Failure to conduct the study in accordance with the investigational plan. (21 CFR 812.100 and 812.110(b))

You failed to perform protocol-required procedures for 11 of 11 subjects reviewed in the [REDACTED] study. You failed to perform protocol-required procedures for four of five subjects reviewed in the [REDACTED] study. You failed to perform protocol-required procedures for seven of seven subjects reviewed in the [REDACTED] study. These subjects had missing laboratory tests, X-rays, ankle brachial pressure indices, physical examinations, CAT scans, and/or quality of life surveys at the required intervals.

The deviations listed above are not intended to be an all-inclusive list of deficiencies that may exist in your clinical studies. It is your responsibility as a clinical investigator to ensure that an investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations.

Your March 18 response addresses each of the FDA 483 items and in several places it states that steps have been implemented to prevent future occurrences, but in most cases, it does not specify what these steps are or how they will prevent future deviations. It is important for a clinical investigator to understand that unless the physical safety of a subject demands otherwise, treatment of study subjects must adhere to the requirements of the investigational plan.

Enclosed to assist you in better understanding your responsibilities as a clinical investigator are copies of 21 CFR Parts 50, 56, and 812. These documents also are available electronically at www.access.gpo.gov/nara/cfr. Part 812 describes your responsibilities as a clinical investigator of an investigational medical device and Part 50 includes what is required to protect the welfare of study subjects. Part 56, Institutional

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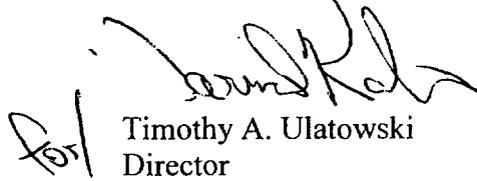
Review Boards, covers the responsibilities of IRBs and what an IRB expects from you as a clinical investigator, as well as their responsibilities to you.

Please inform us in writing, within 15 working days of receipt of this letter, of the additional corrective actions you have taken or plan to take with regard to the deviations noted. Please send this information to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch I (HFZ-312), 2094 Gaither Road, Rockville, Maryland 20850, Attention: Rachel Solomon. Failure to respond could result in regulatory action without further notice.

A copy of this letter has been sent to FDA's Baltimore District Office, 6000 Metro Drive, Suite 101, Baltimore, Maryland 21215. We request that a copy of your response also be sent to that office.

If you have any questions, feel free to contact Rachel Solomon at (301) 594-4723, ext. 123.

Sincerely yours,


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

Enclosures