DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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

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WARNING LETTER
Via Federal Express

MAR 17 2003

Timothy M. Talbert, M.D.
2205 McCallie Avenue
Chattanooga, Tennessee 37404

Dear Dr. Talbert:

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 May 6 - May 16, 2002, and was conducted by Ms. Pamela M. Thomas, an investigator from FDA's New Orleans District Office. The purpose of the inspection was to determine if your activities as a clinical investigator in [redacted] comply with applicable FDA regulations. These catheters 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, 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 Mr. Howard Lewis, Nashville Branch Director, New Orleans District Office, dated June 10, 2002. 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 sponsor and to the reviewing IRB. [21 CFR 812.150(a)(1)]

You failed to report to the sponsor or the reviewing IRB, within the required time period, the occurrence of pneumothorax requiring placement of a chest tube, atrial fibrillation requiring cardioversion, and subsequently, death of subject [redacted]. You also failed to report in a timely manner that subject [redacted] required placement of a pacemaker to treat ventricular tachycardia. 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. Furthermore, the Investigational Plan for the study indicates that all serious and/or unanticipated adverse events and patient deaths must be reported to the sponsor (by phone) within 24 hours of the receipt of information by the investigational site and faxed to the sponsor within five working days of the event.

Failure to obtain signed and dated study informed consent documents from all study subjects prior to participation in the study. (21 CFR 812.100, 50.20, and 50.27)

Several study subjects signed and/or dated the informed consent document after undergoing [redacted] echocardiograms. As stated in 21 CFR 812.100, an investigator is responsible for ensuring that informed consent is obtained in accordance with 21 CFR Part 50. According to 21 CFR 50.20, no investigator may involve a human being in an investigational study unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. Moreover, 21 CFR 50.27 requires that informed consent be documented by the use of a written consent form approved by the institutional review board (IRB) and signed and dated by the subject or the subject's legally authorized representative.

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

Follow-up examinations were to have been conducted at [redacted] again at [redacted] after the [redacted] procedure. Several follow-up examinations were outside the prescribed time frames (examples include subjects [redacted], and the FDA investigator found no documented evidence that attempts were made to contact the subjects. Monitoring of subjects was to have been for six months post [redacted] with hand-held telemetry, and with 24-hour Holter monitoring at the end of six months. Monitoring was not performed on all subjects (for example, subjects [redacted] and [redacted] did not receive the Holter monitor, and subject [redacted] did not receive the hand-held telemetry device).

Failure to maintain accurate, complete, and current subject records. [21 CFR 812.140(a)(3)]

Several case report forms (CRFs) reviewed were lacking required information and a number of discrepancies were noted between source documents and data recorded on the CRFs. Examples included, but were not limited to: 1) Case report form for subject [redacted] echocardiogram indicates that a pericardial effusion was present, yet the echocardiogram report dated [redacted] source data) states that no pericardial effusion was identified. The case report form for this subject's post-procedure echocardiogram indicates that a pericardial effusion was present, but the echocardiogram report dated [redacted] (source data) states that no pericardial effusion was present. 2) For subject [redacted], the Symptomatic and Monthly Transtelephonic Transmissions page of the CRF does not include documentation of a [redacted] transmission by the subject. 3) Holter monitor results on [redacted] for subject [redacted] document that the subject went into ventricular tachycardia, but the six month follow-up examination portion of the CRF indicates no new arrhythmias.

Failure to maintain accurate, complete, and current device accountability records. [21 CFR 812.140(a)(2)]

The Device Accountability Log supplied by you during the inspection did not accurately reflect the number of investigational devices received from the sponsor, as well as their use or disposition. A participating investigator is required to maintain accurate, complete, and current records of the receipt and use or disposition of all investigational devices.

The deviations listed above 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 ensure that an investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations.

Your June 10 response addresses each of the FDA 483 items and 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. In general, your letter indicates a lack of understanding of the regulatory requirements that clinical investigators must meet and includes few corrective actions taken or planned, with regard to the deviations noted during the inspection. 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, 54, 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 54, Financial Disclosure by Clinical Investigators, includes information regarding your regulatory responsibilities with regard to any financial interest you might have in the outcome of studies in which you participate. Part 56, Institutional 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, 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 II (HFZ-312), 2098 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 New Orleans District Office, 6600 Plaza Drive, Suite 400, New Orleans, Louisiana 70127. 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

cc:

[redacted] (purged)

William C. Jacobs, Chair (purged)
Western Institutional Review Board
3535 7th Ave. S.W.
Olympia, WA 98502-5010