



DEC 10 2004

WARNING LETTER
Via Federal Express

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

Tyrone J. Collins, M.D.
Cardiovascular Intervention at Ochsner
Clinic Foundation
1514 Jefferson Highway
New Orleans, LA 70121-2429

Dear Dr. Collins:

This purpose of this Warning Letter is to inform you of the objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site. This letter also discusses your written response, dated September 23, 2004, to the noted violations and requests that you implement prompt corrective actions. Ms. Traci Armand, an investigator from the FDA's New Orleans District Office, conducted the inspection from August 16-20, 2004. The purpose of the inspection was to determine if your activities and procedures relating to your participation in the clinical study entitled [REDACTED] complied with applicable FDA regulations. The [REDACTED] is a device defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. 321(h)].

The FDA conducted the inspection 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. The program also ensures 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 problems in the conduct of the trial and your role as a "Clinical Investigator." **Please note that this is not an Investigational Drug trial, it is an Investigational Device trial and is governed under the device regulations.** The regulations governing device clinical trials are found at Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions, and Part 50 - Protection of Human Subjects. You received a Form FDA 483, "Inspectional Observations," at the conclusion of the inspection that listed the deviations noted and discussed with you. The deviations noted on the Form FDA 483 and our subsequent review of the inspection report are discussed below:

Failure to conduct the investigation according to the investigation plan and conditions of approval imposed by an Institutional Review Board (IRB) [21 CFR 812.110(b)].

FDA regulations 21 CFR 812.110(b), require you to conduct your clinical investigation in accordance with the signed agreement, investigational plan, and applicable FDA regulations. Deviations from the investigational plan include:

A) Required testing for the study endpoint assessments from baseline to 9 months post procedure for clinical efficacy and hemodynamic patency were not conducted as required by the protocol. Examples include:

- The baseline [REDACTED] was not determined for subject [REDACTED]
- The [REDACTED] was not conducted at the 9 month follow up visit for [REDACTED]
- The resting [REDACTED] were not conducted at the 9 month follow up visit for subjects [REDACTED] and [REDACTED]
- The [REDACTED] was not conducted at discharge for subjects [REDACTED] and [REDACTED]
- No [REDACTED] was conducted, and incomplete laboratory data was recorded at the 9 month follow up visit for subject [REDACTED]

B) Other required testing and study activities were not conducted as required by the protocol through the course of the investigational study as evidenced by the following:

- Complete laboratory data was not collected at discharge for subject [REDACTED] and [REDACTED]
- Complete study testing was not conducted at various nonscheduled study visits for subjects [REDACTED], [REDACTED], and [REDACTED]

C) You failed to submit complete and accurate reports to the reviewing IRB and sponsor for serious adverse device effects (SAEs) that occurred during the investigation within the time constraints set forth by the reviewing IRB and stated in the investigational plan [21CFR 812.110 (b)]. Some SAEs were reported 6 months after you became aware of the events. Examples include but are not limited to:

- 1/30/2004 SAE for subject [REDACTED] was identified as being “possibly related” to the study device, but was not reported to the IRB until 8/8/04.
- 2/25/2004 SAE for subject [REDACTED] was identified as being “possibly related” to the study device, but was not reported to the IRB until 8/5/04.
- 2/9/2004 and 5/13/2004 SAEs for subject [REDACTED] were identified as being “possibly related” to the study device but were not reported to the IRB until 6/24/2004 and 8/10/2004 respectively.

- 12/2/2003 SAE for subject [REDACTED] was identified as being “definitely related” to the study device, but was not reported to the IRB until 12/30/2003.

In your response you describe some changes implemented to address these problems. Developing a binder for each study and including follow up instructions for each follow up visit and using standardized physician ordering sheets will assist with scheduled visits. These interventions do not address the issues related to testing and evaluation at unscheduled visit intervals. **Please provide us with procedures you have or plan to implement to address the issues related to unscheduled visits.** In addition, reporting of SAEs is an essential component of patient safety. Your reported plan of providing an e-mail report of subject’s admissions to your Emergency Department or your Institution should assist in ensuring you are notified of these unplanned admissions. Please provide us with the written procedures that are being implemented or planned to be implemented to ensure timely assessment and reporting of all SAEs.

Failure to obtain proper informed consent for 3 of [REDACTED] study subjects [21 CFR 50.20, 812.100, and 812.140(a)(3)(i)].

Investigators are responsible for ensuring that informed consent is obtained and that records of informed consent are kept in accordance with FDA regulations 21 CFR 50.20, 812.100, and 812.140.(a)(3)(i). This includes obtaining new consent for subjects when the IRB approves changes in the consent document. In addition, clinical investigators must include in each subject’s case history, documents evidencing informed consent and that such consent was obtained.

You failed to obtain revised versions of the informed consent form for 3 of [REDACTED] subjects. Examples include but are not limited to:

- Subject [REDACTED] did not sign the 3/9/03 approved version.
- Subject [REDACTED] and [REDACTED] did not sign the 7/10/03 approved version.

In your response you note that in the future when consents are revised the new version will be placed on the subjects CRF binder so it is seen when follow-up is performed. This should ensure that subjects are informed as needed. Please note that there may be a need to inform the subjects of the new information prior to a scheduled visit in case there is new information pertinent to the safety and welfare of the subjects.

Failure to maintain records of device receipt, use, and disposition [21 CFR 812.140(a)(2)].

Pursuant to 21 CFR 812.140(a)(2), an investigator is responsible for maintaining records of the names of all person who received, used, or disposed of each device, as well as records relating to why and how many units of the device have been returned to the

sponsor, repaired, or otherwise disposed of. Your device accountability records do not record the receipt of 17 of [REDACTED] devices received during the course of the study.

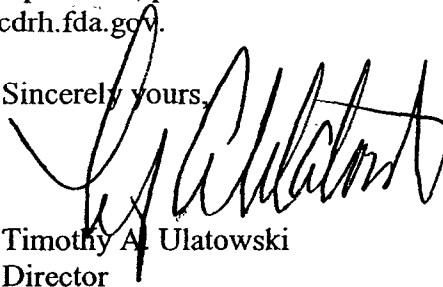
In your response you stated, "This trial used a commercially available device for an off-label use under an Investigational Device Exemption (IDE)." The [REDACTED] is not commercially available for the use under investigation and may only be shipped for that investigational use in accordance with the terms of the IDE. These terms include maintenance of records of device receipt, use and disposition. Please provide a copy of the written procedures you have implemented or plan to implement to ensure accurate tracking of investigational devices.

This is not intended to be an all-inclusive list of deficiencies at your site. It is your responsibility to ensure that you follow FDA regulations.

Within 15 working days after receiving this letter please provide written documentation of the specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations in current and future studies. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. In addition, please provide a list of your current investigational studies and include the name of the study sponsor and the date of IRB approval. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action including initiation of disqualification procedures, without further notice. Please send your response to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch (HFZ-312), 2094 Gaither Road, Rockville, Maryland 20850, Attention: Viola Sellman, Chief, Program Enforcement Branch

We are also sending a copy of this letter to FDA New Orleans District Office, 6600 Plaza Drive, Suite 400, New Orleans, LA 70127. We request that a copy of your response also be sent to that office. If you have any questions, please contact Ms. Sellman by phone at (240) 276-0125, or by email at vxS@cdrh.fda.gov.

Sincerely yours,



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