ABBREVIATED REPORT

This CDRH PMA-Based High Priority Directed, Clinical Investigator Data Validation Inspection was conducted at the request of HFZ-312 and Dallas District FACTS Assignment #1028621. This inspection was conducted in accordance with the instructions found in CP7348.811, Clinical Investigators. EIR under Turbo ew200615.

The previous inspection of this investigator was conducted in 8/2006 as an IDE Probability Sampling Surveillance Inspection, and was classified NAI.

This current inspection of this investigator covered the clinical study protocol under **PMA #P060040** entitled: **" The Evaluation of the HeartMate II Left Ventricular Assist System – Destination Therapy Protocol"** The sponsor of the audited study is Thoratec Corporation, Burlington, MA 01803.

This data audit revealed the site enrolled (b)(4) subjects into this arm of the study. I audited records for all (b)(4) subjects. This inspection revealed minor deficiencies that were discussed with the Investigator. No FDA-483, Inspectional Observations, was issued. No sample was collected.

Post-Inspectional Correspondence may be sent to: O. Howard Frazier, M.D., Clinical Investigator, Texas Heart Institute of St. Lukes Hospital, 1101 Bates Street, MC 2-144A Ste C-38, Houston, TX 77030. (832) 355-3000 Fax (832) 280-2597.

ADMINISTRATIVE DATA

Inspected firm:	Oscar "Howard" Frazier
Location:	6770 Bertner Ave. MC 2-114A Houston, TX 77030
Phone:	832-355-3000
FAX:	(832)355-6798
Mailing address:	6770 Bertner Ave. MC 2-114A Houston, TX 77030
Dates of inspection:	6/2/2009, 6/3/2009, 6/4/2009, 6/8/2009, 6/9/2009, 6/10/2009,

	6/11/2009, 6/17/2009, 6/18/2009
Days in the facility:	9
Participants:	Andrea A Branche, Investigator

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

On 06/02/2009, I (CSO Andrea Branche) presented my credentials and an FDA-482, Notice of Inspection, to O. Howard Frazier, M.D./ Clinical Investigator. This inspection was preannounced. According to Dr. Frazier he has been instrumental in pioneering cardiac assist devices. Dr. Frazier stated he has been working/researching (b) (4) (b) (4) since his college years, and started experimental work (clinical) in 1982. Dr. Frazier stated he is responsible for developing this type of device under study and was most responsible for developing this protocol. According to Dr. Frazier he is most responsible for this study, however, the entire cardiac team confers on the best course of action for the patient. Dr. Frazier stated he was very involved in every aspect of each subject's care during this study, and he maintained control of this study as follows: by conferring with the Sub-Investigators, making eligibility determinations, performing surgeries, and clinical observations. Exhibit 1 contains a copy of the Investigator's Agreement signed by Dr. Frazier. Exhibit 2 contains a copy of Dr. Frazier's current Curriculum Vitae that lists his professional qualifications.

Also present at the start of this inspection was Mrs. Kathy Vershave, RN, Assistant Director. Ms. Vershave is responsible for the overall coordination of clinical studies within the cardiac transplant department, and directs the research coordinators. Ms. Vershave introduced (b) (6), (b) (7)(C), Research Coordinator. According to (b) (6), (b) (7)(C), he has been the coordinator for this study since 2007. (b) (6), (b) (7)(C) was assisted by (b) (6), (b) (7)(C) (b) (6), (b) (7)(C), Research Coordinator. (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C) assisted me throughout this inspection and provided requested copies and information as needed. According to (b) (6), (b) (7)(C), the Sponsor provided training for all the staff on this protocol. (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C) (b) (6), (b) (7)(C) stated their responsibilities included: consent of subjects, performing (b) (6), (b) (7)(C) assessments, administrative correspondence with IRB and Sponsor, CRF completion/data entry data collection, and making study related appointments. Exhibit 3 contains a copy of the site responsibility log completed in June 2009.

IRB HISTORY

The Institutional Review Board for this study is the (b) (4) (b) (4). The IRB Chairman is (b) (4) M.D. Exhibit 4 contains a copy of the IRB Roster for 2007. Exhibit 5 contains copies of the IRB approval/request history for this study as follows:

DATE	ACTION
10/03/03	Initial IRB Approval of Protocol (pp.1-2)
06/07/04	CI Submission of Protocol Amend (p. 3)
06/10/04	IRB Approval of Amend. and Revised IC (p.4)
10/12/04	C.I. Report of Compassionate Use (Note: not a Destination Therapy Arm Subject) (p.5)
11/10/04	IRB denial of Compassionate Use (p. 6)
12/22/04	IRB Continuation Approval (p. 7)
08/29/05	CI Renewal Application (p. 8)
01/20/06	IRB Continuation Approval (p. 9)
08/28/06	CI Renewal Application (pp. 10-11)
09/13/06	CI Report of Protocol Deviation (pp 12-16)
10/06/06	IRB Continuation Approval (p. 17)
02/02/07	CI Report of Outside UADE (pp. 18-19)
09/14/07	CI Renewal and Sponsor Annual Report (pp. 20-22)
10/05/07	IRB Continuation Approval (p. 23)
04/18/08	C.I. Report of Protocol Deviations (p. 24-25)
05/12/08	IRB Response to Protocol Deviations Requiring CI Staff to complete in house "Human Participant Protection Education for Research Team" (Note: Certificates of Completion for staff are attached) (pp. 26-32).
08/13/08	C.I. Renewal App and Annual Report (pp. 33-36)
09/22/08	IRB Approval of Continuation (p. 39)
01/08/09	C.I. Report to IRB of Device Correction Report from Sponsor (pp. 40-42)
03/20/09	IRB Receipt of Emergency Use (pp. 43-44)
04/06/09	IRB Approval of Compassionate Use (p. 45)
05/11/09	IRB Approval of Continuation/Increase Subjects (p. 46)

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INSPECTIONAL FINDINGS:

(b) (6), (b) (7)(C) presented study binders and "shadow" study charts for each subject enrolled. The hospital records for each subject are now maintained electronically. I visited electronic records near the end of the inspection and compared several of the records I obtained from the shadow charts as well as adverse event reporting to the source documents. I compared the records sent from HFZ-312 and data summaries from the sponsor to the information contained in the investigator's records and patient files. I observed the following source data for each subject: Patient Randomization Confirmation, Physician's Consultation/Medical Histories, Surgical Reports, Echocardiography Labs, (b) (4) Assessment Forms, Quality of Life Questionnaires, and Adverse Event Reports. I observed each subject had a signed consent form. Exhibit 6 contains a copy of two consent forms approved by the IRB, as found in the subject's records. The regulatory documents, patient records, and study files I reviewed indicated the study was well controlled and documented. I did not observe any unreported adverse events for any of the subjects enrolled.

The sponsor monitored this site approximately (b) (4) Exhibit 7 contains a copy of the monitoring log. Exhibit 8 contains a copy of the several site monitoring reports. The device accountability for this study was controlled by the study coordinators. Exhibit 9 contains copies of Device Accountability Log. I did not observe any significant discrepancies.

GENERAL DISCUSSION WITH MANAGEMENT

Before concluding this inspection on 06/18/2009 I held a close-out meeting with Dr. Frazier, Mr. Vershave, (b) (6), (b) (7)(C) and (b) (6), (b) (7)(C). I informed Dr. Frazier that persons at the Center for Devices and Radiological Health would further review my findings however, I would not issue an FDA 483 at this time. I discussed the following deficiencies: Subject #(b) (4) Should have been excluded due to placement of a (b) (4) device just prior to the study device. Exhibit 10 contains a copy of the Surgeon's Note and Protocol Deviation Form. This deviation was reported to the IRB in 09/2006 (Exhibit 5 pp. 12-16). The IRB subsequently required additional training of C.I. and his staff. Dr. Frazier stated the sponsor has attempted to revise the study protocol, as this ((b) (4) (b) (4) was not available when the protocol was written.

Also, I discussed the sites device accountability records did not fully document the receipt of each study device. The site maintained the delivery note from the sponsor (Exhibit 11), however, there is no check, initial, date, etc on the Delivery Notes to say when, and who received the study devices. Additionally, the surgery reports did not include a copy of the labeling from the study devices to include in the study file. Exhibit 12 contains a copy of the Implant form for study.

Lastly, I explained to Dr. Frazier that each protocol deviation, such as missed labs, incomplete on-study evaluation could all be considered for inclusion on the FDA 483, however, according to many of the missed evaluations the subject was too ill, or refused. Therefore, I did not include them on a 483. I concluded the inspection.

Attachment:

a. FDA Form 482, Notice of Inspection

Exhibits:

1. Copy of Form FDA 1572
2. Copy of Dr. Frazier's C.V.
3. Copy of Site delegation Log
4. Copy of IRB
5. Copy of IRB Approval/Request History
6. Copy of (2) Consent Forms
7.. " " Monitoring Log
8. " " Monitoring Reports
9. Device Accountability Records
10. Protocol Deviation Report, Surgery Notes
11. Study Device Shipping Notes
12. Implant Form/Surgery Report

Andrea A Branche, Investigator