DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407) 475-4700 Fax:(407) 475-4768 Industry Information: www.fda.gov/oc/industry	04/12/2010 - 05/24/2010* FEI NUMBER 3008127817

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Rajiv Chandra, M.D., Clinical Investigator

FIRM NAME	STREET ADDRESS
Rajiv Chandra, M.D., Clinical Investigator	20 East Melbourne Ave
CITY, STATE, ZIP CODE, COUNTRY Melbourne, FL 32901	TYPE ESTABLISHMENT INSPECTED Clinical Investigator

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

An investigation was not conducted in accordance with the signed statement of investigator and investigational plan.

Specifically,

1. You did not adequately supervise the conduct of the (b) (4) study by ensuring that study subject's informed consent was obtained by an authorized individual per the delegation of authority log. The informed consent however, was obtained by (b) (7)(C). with assigned duties of code (b) (4) clerical coordination activities only. This individual obtained informed consent for all (b) (4) subjects in the (b) (4) study.

2. You did not ensure that all associates, colleagues and employees assisting in the investigation were informed about their obligations in following the investigational plan as evidenced by:

(a) The inclusion/exclusion criteria was assessed by (b) (7)(C). for Subjects (b) (7)(C), and (b) (7)(C) (b) (7)(C) was not authorized to assess inclusion/exclusion criteria per the delegation of authority log.

(b) The inclusion/exclusion criteria was assessed by (b) (7)(C). for Subject (b) (7)(C). However, (b) (7)(C) is not authorized to assess inclusion/exclusion criteria per the delegation of authority log.

(c) Subjects (b) (7)(C), and #(b) (7)(C) source documents reflect that (b) (7)(C). assessed adverse events. However, (b) (7)(C). is not authorized to assess adverse events per the delegation of authority log. This individual did not consistently assess if the patient denies congestive heart failure "CHF" symptoms and intermittent claudication since previous visit as noted on the CRF. The delegation of authority log does not specify what "other" clinical assessments (b) (7)(C). is authorized to perform.

(d) Subjects #(b) (7)(C) and #(b) (7)(C) source documentation reflected that sections of the CRF, for documenting assessments of Interval Cardiovascular events, were pre-filled by (b) (7)(C). prior to the subject arriving for their study related visit. (b) (7)(C). is not authorized per the delegation of authority log to perform assessments of study subjects.

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(e) Subjects #(b) (7)(C) (visit #40) and #(b) (7)(C) (visits #19, 27, and 31) source documentation reflected that (b) (7)(C) signed the CRF- Infusion Visit Worksheet in the spot designated for the study staff members that performed the physical assessments, assessed adverse events, and administered the investigational study drug. However, per the delegation of authority log (b) (7)(C). is not authorized to perform these duties.

(f) (b) (7)(C) made trial-related medical decisions for the adverse bleeding event reported 9/22/2009 for Subject (b) (7)(C) in the Appraise-2 study (b) (7)(C) classified the intensity of the event as mild, and not related to the study drug. (b) (7)(C). is not authorized to make trial-related medical decisions per the delegation of authority log.

(g) You did not list all Sub-Investigators on the Form FDA 1572. (b) (7)(C) is not listed on the Form FDA 1572, however his curriculum vitae and email correspondence reflect serving in this capacity since joining the site.

3. IRB correspondence, dated 11/5/09, to the site specifies that all current enrollees and all new enrollees should sign the revised informed consent (version date 8/26/09). However, documentation provided reflects that only (b) (4) subjects signed this consent as required by the IRB.

OBSERVATION 2

Failure to report promptly to the IRB all unanticipated problems involving risk to human subjects or others.

Specifically,

1). You did not report the death of subject (b) (7)(C) in accordance with the designated IRB requirements that specified all serious and unexpected adverse events that occur at your site must be reported within 10 business days of the Investigator's knowledge of the event and all fatal or life threatening events should be reported immediately. Subject #(b) (7)(C) received an intravenous infusion of the investigational drug on 7/19/2006 and died on 7/21/2006. Documentation provided during inspection reflects you became aware of this death on or about 7/31/2006. However, no documentation was provided to show that this death had been reported to the IRB.

2. You did not report the deaths of subjects #(b) (7)(C), and (b) (7)(C) in accordance with the designated IRB requirements, as evidenced by:

(a) Subject (b) (7)(C) died on 11/1/2007. Documentation provided during inspection reflects you became aware of this death on or about 11/5/2007, however you reported the death of this subject to the IRB on 11/13/2007.

(b) Subject (b) (7)(C) died 2/12/2006. Documentation provided during inspection reflects you became aware of this death on or about 2/24/2006, however you reported the death of this subject to the IRB on 6/13/2006.

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(c) Subject (b) (7)(C) died 4/5/2006. Documentation provided during the inspection reflects you became aware of this death on or about 4/7/2006. You reported the death of this subject to the IRB on 6/13/2006.

(d) Subject (b) (7)(C) died 7/2/2008. Documentation provided during the inspection reflects you became aware of this death on or about 7/10/2008. You reported the death of this subject to the IRB on 7/25/2008.

3. Subject (b) (7)(C) was hospitalized from 11/26-27/2004 for ventricular fibrillation (V-Fib). Subject last received intravenous study drug on 5/5/2005. An adverse event was entered into (b) (4) by (b) (7)(C) for medical condition of (V-Fib) on 12/1/2004. Adverse event was noted to be serious on 3/8/2005. No serious adverse event was filed.

4. Subject (b) (7)(C) was hospitalized on 11/3/2005 with shortness of breath rule out myocardial infarction. Subject last received intravenous study drug on 10/20/2005. No adverse event was entered into (b) (4) for medical condition of shortness of breath.

5. Subject #(b) (7)(C) was hospitalized on 3/24/2006 with altered mental status rule out myocardial infarction. History of the present illness reflects that the family of the subject reported subject had a change in mental status which started approximately 6 weeks before the 3/24/2006 hospital admission. No adverse event was entered into (b) (4) for medical condition of altered mental status.

OBSERVATION 3

Failure to prepare or maintain adequate case histories with respect to observations and data pertinent to the investigation.

Specifically,

1. Source records revealed inadequate documentation of who actually performed study related activities in accordance with delegation of authority log as evidenced by:

(a) Subjects (b) (7)(C) urinalysis results do not reflect the "clarity" of the specimen, did not identify who performed the test, does not identify all urinalysis test results by study subject number, nor are the out of reference range laboratory results deemed to be clinically significant or not clinically significant.

(b) Source documentation for Subjects (b) (7)(C) did not adequately identify the study staff members that completed in-clinic assessments, concomitant medication assessments, vitamin accountability, or weight assessments.

(c) Subject (b) (7)(C) Appraise-2 bleeding event source documents do not identify the staff member that recorded the positive

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fecal occult result during hospitalization.

2. Documentation was not made available at the site to show that the intravenous investigational study drug, with a volume of (b) (4) was infused at an administration rate of (b) (4) as specified in the Protocol and Study Manual. The site used a medical device, a Rate Flow Regulator IV Set, with incremental settings of ***"OFF***App.ml/h***5***10***15***20***25***30***40***50***60***80***100***125***150***200***250*** OPEN"*** for administration of the study drug and the dial on the device was was set between (b) (4) and (b) (4).

3. Source documentation of adverse events that were reported in the iCRF were not made available for review during the inspection.

OBSERVATION 4

Investigational drug disposition records are not adequate with respect to dates, quantity, and use by subjects.

Specifically,

1. Source documentation for Subjects (b) (7)(C) doe not show the date and quantity of vitamins dispensed or returned by the subjects throughout the study. However, the (b) (4) Study Manual indicates that the number of study drug vitamins returned/or unaccounted for should be recorded on the visit record and in the iCRF on the vitamin accountability screen. Study drug accountability was only recorded in the iCRF vitamin accountability screen.

2. Delivery Packing Slips for the receipt and packaging integrity of (b) (4) study drugs was not maintained in accordance with the Sponsors directions.

OBSERVATION 5

Unused supplies of an investigational drug were not disposed of in accordance with sponsor instructions.

Specifically,

1. Source documentation for Subjects #(b) (7)(C) was inadequate and did not show the final disposition or disposal of study supplements. However, the (b) (4) Study Manual, May 2005, the Alpha-Medical/TruMed Ed Site Policy and Procedure for the Disposal of Unused, Expired or Returned Medications/Study Drugs, and Monitoring correspondence dated 2/5/2009 reflect that this should be recorded on the appropriate log - in this case

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the vitamin accountability log.

*** DATES OF INSPECTION:**
04/12/2010(Mon), 04/13/2010(Tue), 04/14/2010(Wed), 04/16/2010(Fri), 04/19/2010(Mon), 04/20/2010(Tue), 04/23/2010(Fri), 04/26/2010(Mon), 04/27/2010(Tue), 04/28/2010(Wed), 04/29/2010(Thu), 05/03/2010(Mon), 05/04/2010(Tue), 05/05/2010(Wed), 05/18/2010(Tue), 05/24/2010(Mon)

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