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SUMMARY

For Cause inspection of this Clinical Investigator, initiated at the request of the Division of Scientific Investigations, Good Clinical Practices Branch I, HFD-45 (FACTS #1205141), was conducted in accordance with CP 7348.811, Clinical Investigators and Sponsor-Investigators Program and Assignment Memo dated 09/13/10, (DSI Complaint #2814).

Current inspection covered one study: Protocol 7 U01-HL-092607, Trial to Assess Chelation Therapy (TACT).

Current inspection noted deficiencies in the following areas; adherence to protocol, reporting of SAEs to the IRB, informed consent, continuing IRB review, and maintenance of case histories.

An FDA 483, Inspectional Observations Form, was issued to and discussed with Carol L. Roberts, MD, Principal Investigator. An amended FDA 483 was issued to Dr. Roberts on 12/16/10 due to the fact that the hospitalization referenced in Observation 2.a occurred after the deadline for the reporting of adverse events per the protocol so it did not need to be reported. Dr. Roberts promised corrections and a written response.

No samples were collected and there were no refusals.

ADMINISTRATIVE DATA

Inspected firm:	Carol Roberts
Location:	1209 Lakeside Drive Wellness Works Brandon, FL 33510-4109
Phone:	813-661-3662
FAX:	813-661-0515
Mailing address:	1209 Lakeside Drive Wellness Works Brandon, FL 33510-4109
Dates of inspection:	12/1/2010, 12/2/2010, 12/6/2010, 12/7/2010, 12/8/2010, 12/9/2010, 12/16/2010
Days in the facility:	7
Participants:	Gene R. Gunn, Investigator Jennifer A. Robinson, Investigator

On 11/30/10, I phoned the firm, Wellness Works, to speak with Dr. Roberts and pre-announce the inspection. She was not available so I spoke with her coordinator, (b) (6) . I asked (b) (6) about the availability of the study records. She stated that they were currently in the office and could be available as early as the next day. I told her that the next day would be fine and we scheduled the inspection to begin on 12/01/10.

On 12/01/10, I arrived at the firm with Investigator Jennifer A. Robinson. Upon arriving we were greeted by (b) (6) to whom we presented our credentials. (b) (6) showed us to an office area where we then met with Carol L. Roberts, MD. Investigator Robinson and I once again presented our credentials and I issued an FDA 482, Notice of Inspection to Dr. Roberts. We then briefly discussed the scope and nature of the inspection. (b) (6) was available throughout the inspection and provided us with copies of all requested documents.

On 12/09/10, an FDA 483, Inspectional Observations Form was issued to and discussed with Dr. Roberts. An amended FDA 483 was issued to Dr. Roberts on 12/16/10 due to an error found while writing this EIR. Investigator Gunn returned to the site alone as Investigator Robinson was busy with another assignment and unable to sign the amended FDA 483 or accompany Investigator Gunn.

Investigator Gene R. Gunn Jr. was solely responsible for writing this EIR.

HISTORY

Dr. Roberts has been the Medical Director of Wellness Works, Inc. since it's inception in 1994. The study being inspected, Trial to Assess Chelation Therapy is the only trial she has worked on as an Investigator. Her CV is included **(Exhibit 1)**, as is that of Sub-Investigator, (b)(6) **(Exhibit 2)**.

All correspondence should be sent to:

Carol L. Roberts, MD
1209 Lakeside Drive
Brandon, FL 33510

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

According to the FDA 1572, Statement of Investigator **(Exhibit 3)**, **Carol L. Roberts, MD** is the PI for this site. She has listed one Sub-I, (b)(6) . (b)(6) works for Dr. Roberts as a coordinator for the study. (b)(6) provided us with documentation and copies throughout the course of the inspection. Several other people are listed on the Site Responsibility and Signature Log **(Exhibit 4)** as having worked on the study in the past. The majority of who are no longer employed by the firm.

Ms. Ana C. Mon, Project Manager, Mt. Sinai Medical Center, provided us with copies of the letters to and from OHRP as well as the IND application and acknowledgement letter.

REGULATORY DOCUMENT REVIEW

The investigation product being evaluated in this study is edetate disodium **(Exhibit 5)**. I included a copy of Version 3 of the protocol **(Exhibit 6)** as this is the protocol under which the majority of the subjects at this site were randomized. This study is sponsored by the National Institutes of Health (NIH), specifically the National Heart, Lung, and Blood Institute (NHBLI) and the National Center for Complementary and Alternative Medicine (NCCAM). It is also being conducted under an IND (#66,743) **(Exhibit 7)** that is held by Gervasio A. Lamas, MD, 4300 Alton Road, Suite 207A, Miami Beach, FL 33140, who is the PI for the entire study.

Several IRBs are listed as overseeing the trial study-wide. They are Mt. Sinai Medical Center IRB, (b)(4) IRB, Duke University Health System IRB, and Sterling IRB. The IRB of record for Dr. Roberts' site is Sterling IRB, 6300 Powers Ferry Rd., Suite 600-351, Atlanta, GA

30339. Sally P. Green, MD is the chairperson of the IRB **(Exhibit 8)**. See Table 1 for an IRB approval timeline.

Laboratory Analysis is done by (b) (4) . The Laboratory Director is (b) (6) . The regulatory binder contained current CLIA and CAP certificates for the lab.

Table 1.

IRB Action	Date
Initial Approval of ICF (v1) **(Exhibit 9)**, Protocol (v2), & Ads **(Exhibit 10)**	04/21/04
Approval of Amended ICF (v2) **(Exhibit 11)** & Protocol (v3)	04/29/04
Continuing Review	03/23/05
Continuing Review	03/08/06
Approval of Amended ICF (v3) **(Exhibit 12)** & Protocol (v4)	07/27/06
Continuing Review	02/21/07
Continuing Review	02/07/08
Study-wide Suspension of Accrual	08/29/08
Lifting of Suspension and Approval of Amended ICF (v4) **(Exhibit 13)**	12/24/08
Continuing Review	06/04/09
Approval of Amended ICF (v5) **(Exhibit 14)**	11/05/09
Study-wide Suspension of All Study Related Activities	12/04/09
Lifting of Suspension	12/11/09
Site Suspension of Accrual	04/19/10
Continuing Review	06/01/10
End of Enrollment	07/14/10
Approval of Amended ICF (v6)	09/14/10

Monitoring of the study was done by Duke Clinical Research Institute (DCRI). The Site Visit Log shows that the monitor for the site visited one day each year **(Exhibit 15)**. I have included samples of the monitor's letters **(Exhibit 16)**.

Dr. Roberts completed training for the study at the Investigator and Coordinator Meeting held on 03/25-28/04. Dr. Roberts also completed the NIH Human Participant Protections Education for Research Teams internet training on 12/05/03.

STUDY SUSPENSIONS

Enrollment into the study was suspended by the PI **(Exhibit 17)**, and subsequently by Sterling IRB **(Exhibit 18)**, in response to a letter from the Office for Human Research Protections (OHRP), dated (b) (4) **(Exhibit 19)**. This letter was sent in response to allegations from a source outside of the study citing problems with the information provided on the Informed Consent Form (ICF), as well as issues with the selection of co-investigators. A response letter was sent to OHRP on 11/05/08 in which the concerns were addressed **(Exhibit 20)**. OHRP responded on 05/27/09, asking for clarification on some issues and further corrective actions on others **(Exhibit 21)**. This was done in a letter dated 07/31/09 **(Exhibit 22)**. On 10/30/09, OHRP sent another letter providing some final clarification about their concerns and ceasing their involvement in the matter **(Exhibit 23)**. Sterling IRB lifted the suspension on 12/24/08 **(Exhibit 24)**.

A study-wide suspension of all study related activities was instituted by Sterling IRB on 12/03/09 due to the fact that the study's (b) (4)
infusion bags without first getting approval from the IRB **(Exhibit 25)**. The suspension was lifted a week later on 12/10/09 **(Exhibit 26)**.

Enrollment into the study was also suspended at the site on 04/19/10 because of a Hepatitis C outbreak that was found to have occurred at Dr. Roberts' site.

HEPATITIS C OUTBREAK

Sterling IRB suspended enrollment into the study at Dr. Roberts' site on 04/13/10 due to an outbreak of Hepatitis C **(Exhibit 27)**. The IRB notified OHRP in a letter dated 04/19/10 **(Exhibit 28)**. The outbreak was found to have occurred because an RN that prepared infusion bags contaminated a (b) (4) with the virus. According to a response letter from Dr. Roberts' office manager dated 04/20/10, the RN involved was terminated and the site has stopped using (b) (4) and started using (b) (4) or (b) (4) **(Exhibit 29)**. Sterling IRB sent another letter to the site on 04/24/10 inquiring about the status of subject notification and testing regarding the outbreak **(Exhibit 30)**. According to the response letter from the site, the subjects in the TACT trial were at no risk of exposure or contamination so they were left out of the testing. According to the letter, this decision was made by Roger Sanderson, Head of Epidemiology for the Florida Department of Health **(Exhibit 31)**.

SUBJECT RECORD REVIEW

During the course of the study 28 potential subjects were screened and signed an Informed Consent Form (ICF). Of the 28 subjects screened, four screen failed and 24 were enrolled into the study and given study drug **(Exhibit 32)**. I have included the signed and dated copy of the most recent version

of the ICF **(Exhibit 33)**. Of the 24 subjects randomized into the trial 15 completed the trial or are still currently in follow-up, five subjects withdrew their consent, three subjects died, and one subject was lost to follow-up.

Over the course of the inspection Investigator Robinson and I reviewed 100% of the subject records and ICFs. The subject records were held in manila folders. Many of the records did not contain medical histories that were thorough enough to document whether subjects met the inclusion/exclusion criteria. (b) (6) was able to find the missing paperwork and provide it to us in all cases. The subject numbers used to reference the observations on the FDA 483 and in this EIR are the screening numbers (257-90xx) that were used to identify subjects. Some of the exhibits may reference the randomization number (257-0xx).

During our review of the subject records we made the following observations: the investigation was not conducted in accordance with the signed statement of investigator and investigational plan, failure to report promptly to the IRB all unanticipated problems involving risk to human subjects, failure to obtain informed consent, failure to assure continuing IRB review of the study, and failure to maintain adequate case histories and informed consent.

Failure to Follow Signed Statement of Investigator (FDA 483, Observation 1)

a. Commitment to Follow the Protocol

1. Subject (b) (6) was enrolled into the study on 04/26/05. On 02/17/05 the subject was seen by a physician at the (b) (4) for shortness of breath due to underlying COPD **(Exhibit 34)**. On page 129 of the subject's medical record (page 6 of the exhibit), the physician states the patient is expected "to be very sensitive to even slight fluid overload." According to the protocol (exclusion bullet 16), potential subjects that are unable to tolerate the weekly fluid load (b) (4) of fluid) are not eligible for the study **(FDA 483, Observation 1.a.1)**. This subject died on (b) (4) due to complications from his COPD.

2. Four subjects received infusions in less than the protocol specified (b) (4) hour time period **(FDA 483, Observation 1.a.2).**

(b) (6) – Received infusion (b) (4) from 0840 – 1130 and infusion (b) (4) from 1015 – 1300 **(Exhibit 35).**

(b) (6) – Received infusion (b) (4) from 0940 – 1230 and infusion (b) (4) from 1045 – 1335 **(Exhibit 36).**

(b) (6) – Received infusion (b) (4) from 1350 – 1645 and infusion (b) (4) from 1320 – 1605 **(Exhibit 37).**

(b) (6) – Received infusion (b) (4) from 0945 – 1215 and infusion (b) (4) from 0950 – 1245 **(Exhibit 38).**

3. Four subjects had laboratory values that required a delay of subsequent infusions and/or laboratory follow-up that did not occur **(FDA 483, Observation 1.a.3)**. According to page 45 of the protocol if the hematocrit falls below the lower limits of normal the next infusion will be delayed by two weeks and the levels will be checked with each infusion for the next two weeks. The same procedures should be followed if the subjects liver enzymes double.

(b) (6) – The subject had a hematocrit level of 38.3% on 01/27/05 which is below the lower limit of normal of 38.5% **(Exhibit 39)**. The next infusion should have been delayed two weeks. It wasn't, it was done the next week on 02/02/05 **(Exhibit 40)**. Labs should have been drawn at the next two infusions. This was not done.

(b) (6) – The subject had a hematocrit level of 37.9% on 02/01/06 which is below the lower limit of normal of 38.5% **(Exhibit 41)**. Labs should have been drawn at the next two infusions. This was not done.

(b) (6) – The subject had a hematocrit level of 35.6% on 03/22/07 which is below the lower limit of normal of 38.5% **(Exhibit 42)**. The next infusion should have been delayed two weeks. It wasn't, it was done the next week on 03/29/07 **(Exhibit 43)**. Labs should have been drawn at the next two infusions. This was not done.

The subject had a hematocrit level of 34.8% on 05/31/07 which is below the lower limit of normal of 38.5% **(Exhibit 44)**. The next infusion should have been delayed two weeks. It wasn't, it was done the next week on 06/07/07 **(Exhibit 43)**. Labs should have been drawn at the next two infusions. This was not done.

(b) (6) – The subject's liver enzymes (AST) went from 17 U/L on 03/25/10 **(Exhibit 45)** to 74 U/L on 05/06/10 **(Exhibit 46)**. They were tested again the next week on 05/11/10 as per the protocol and found to be back to normal levels. However, they were not tested the next week as per the protocol. They were tested again at the regular interval on 06/09/10 **(Exhibit 47)**. Even though the AST levels were found to back to normal prior to the next scheduled infusion, according to the protocol, the infusion should have been delayed two weeks. It was not delayed, but was given the next week on 05/13/10 **(Exhibit 48)**.

4. Subject (b) (6) received an infusion that was meant for another subject **(FDA 483, Observation 1.a.4) (Exhibit 49)**. Once the error was discovered, the site notified the subject and the IRB **(Exhibit 50)** and instituted corrective actions **(Exhibit 51)**.

5. Subject (b) (6) (257-010) received infusion (b) (4) on 06/09/06 **(Exhibit 52)**. The infusion was made on 06/05/09 **(Exhibit 53)**. According to the protocol, the study drug shall be infused (b) (4) hours of it being made. The site notified the IRB **(Exhibit 54) (FDA 483, Observation 1.a.5)**.

b. Obtaining Ongoing Informed Consent

1. Subjects (b) (6) were not re-consented with version 3 **(Exhibit 12)** of the ICF as required by the IRB **(FDA 483, Observation 1.b.1)**. Changes to this version of the ICF include:

- A change in the number of participants,
- Removal of "(b) (4) " at the end of the sentence "Chelation therapy has been practiced in the community for many years." on page 2 of the ICF,
- Added information concerning the possibility of retaining fluid on page 8, and
- Changed the vitamin supplier

2. Subjects (b) (6) , & (b) (6) were not re-consented with version 4 **(Exhibit 13)** of the ICF as required by the IRB **(FDA 483, Observation 1.b.2)**. Changes to this version of the ICF include:

- Change in the protocol number,
- Removed sentence stating "The Food and Drug Administration (FDA) has approved chelation therapy for the treatment of lead poisoning, but not as a treatment for heart disease." on page 2 of the ICF,
- Changed the vitamin supplier,
- Changed "EDTA, or ethylenediamine tetraacetate is in the chelation solution." to "EDTA, or Edetate Disodium is in the chelation solution." on page 7,
- Added "Death is a rare complication of EDTA infusions." on page 7

3. Subjects (b) (6) were not re-consented with version 5 **(Exhibit 14)** of the ICF as required by the IRB **(FDA 483, Observation 1.b.3)**. Changes to this version of the ICF include:

- Added "treating hardening of the arteries" to sentence 1 of Introduction,
- Added "treating hardening of the arteries" to sentence 1 of Purpose of the Study,
- Added "The drug under use in this study, disodium EDTA, is not the same drug approved by the FDA for use in cases of lead poisoning. The use of disodium EDTA as treatment for heart disease or hardening of the arteries in patients that have suffered a heart attack has never been an approved indication of the drug." to Background on page 2,

c. Informing Subjects of the Investigational Status of Drug

1. The last paragraph on the PATIENT GENERAL CONSENT states the following **(Exhibit 55)**:

"I understand that some of the treatments suggested for me are as of yet unproven and experimental, however, I have been informed of this, and I am willing to accept the risks on the basis of the information provided to me. I will have the opportunity to ask questions and to research any treatment suggested before I agree to do it. I understand that the doctors have done their research as well, including (in most cases) having taken these treatments themselves." **(FDA 483, Observation 1.c.a).**

I informed Dr. Roberts that the statement, in most cases the doctors have taken these treatments themselves, could mislead a potential subject into believing that drug is safe and effective when this may not be the case.

2. On 11/02/09 Subject (b) (4) asked via phone message if the IV is FDA approved. The response on the phone message is "Yes!" **(Exhibit 56)**. The study drug, edetate disodium, was not approved for any indication at this time as the NDAs and ANDAs were withdrawn on 05/15/08 as was published in the Federal Register **(Exhibit 57)**. Edetate disodium was never approved for the indication being studied and was being evaluated under an IND **(FDA 483, Observation 1.c.b).**

I informed Dr. Roberts of the drug's current status. She did not know that the edetate disodium had been removed from the FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" or "Orange Book". She stated that she had been using the drug in her practice off-label. I informed her that the movement of this product in interstate commerce without an approved application is illegal and that since it is no longer approved it can't be used off-label. The product can be used in the trial only because it is covered under an Investigational New Drug Application and since the New Drug Applications had been removed it should no longer be used.

Failure to Promptly Report SAEs to the IRB (FDA 483, Observation 2)

a. This observation was removed from the FDA 483. While writing this EIR I discovered that the hospitalization referenced in this example occurred after the deadline for the reporting of adverse events per the protocol. This example was recorded on the FDA 483 as Observation 2.a.

b. Subject (b) (6) was hospitalized from (b) (4) for weakness, chest pain, and transient ischemic attack **(Exhibit 58)**. These conditions were reported to the sponsor as adverse events **(Exhibit 59)** but since the subject was hospitalized for over 24 hours, they should have been reported as Serious Adverse Events to both the sponsor and to the IRB **(FDA 483, Observation 2.b).**

c. Subject (b) (6) died on (b)(6) This SAE was reported to the site on 06/02/05. It was reported to the IRB on 05/23/08 **(Exhibit 60) (FDA 483, Observation 2.c).**

d. Subject (b) (6) died on (b)(6) . This SAE was reported to the site on 11/18/05. It was reported to the IRB on 05/23/08 **(Exhibit 61) (FDA 483, Observation 2.d).**

Failure to Obtain Consent Prior to Conducting Study Related Tests (FDA 483, Observation 3)

Subject (b) (6) was consented into the study on (b) (4) **(Exhibit 62).** According to a progress note dated (b) (4) **(Exhibit 63),** the subject was evaluated **(Exhibit 64)** and instructed to stop taking his current regimen of vitamin and mineral supplements. The subject also had labs drawn on 09/06/05 **(Exhibit 65).**

Failure to Ensure Continuing IRB Review and Approval (FDA 483, Observation 4)

Continuing review of the study lapsed between 02/07/09 – 06/03/09. Continuing review was approved on 02/07/08 **(Exhibit 66).** The site prepared its Site Continuing Review Status Report on 04/21/09 **(Exhibit 67)** and it was approved by the IRB on 06/04/09, nearly 16 months after the approval on 02/07/08. A progress note, dated 04/22/09 **(Exhibit 68),** in which the coordinator left a message for a subject to pick up his vitamins **(Exhibit 69)** and an Infusion Record Sheet **(Exhibit 70)** recording an infusion given on 02/26/09 show that study related procedures were still taking place.

Failure to Maintain Adequate Case Histories and Consent (FDA 483, Observation 5)

Subject (b) (6) did not have source documentation or original consents available for review. According to (b) (6) the file was lost. She produced copies of the consent form and print-outs of the data submitted to the sponsor for us to review.

INVESTIGATIONAL PRODUCT ACCOUNTABILITY

The Investigational Product is prepared specifically for each subject by a Accu-Care Services Pharmacy, 18812 South Dixie Highway, Miami, FL 33157. The infusions are made after the site requests them and should be infused within (b)(4) hours of the infusion being made. The bags and two

syringes are temporarily stored in a refrigerator in the pharmacy area. I inspected the temperature logs for the refrigerator. The temperatures were all within the recommended range.

When I asked (b) (6) to show me where the IP is stored she took me to the pharmacy area. The door to the pharmacy was unlocked at this time and throughout the inspection. I informed (b) (6) that the IP needed to be stored in an area with limited access. She assured me that they would start locking the door during business hours. I also observed a bottle of study related vitamins sitting on a shelf at the receptionist's desk. I asked (b) (6) why they were there and she replied that they were expecting a study subject to come and pick them up. I informed her that they should be kept locked in the pharmacy.

The fact that the infusions are made to order made it difficult to reconcile the study drug as the used infusion bags are not kept. Investigator Robinson and I reviewed the shipping records and compared them with the subject records. We found no discrepancies. The vitamins used in the study are destroyed at the site once the subject returns them so we again compared shipping and subjects records. We found no discrepancies.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

OBSERVATION 1

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

Specifically,

a. Commitment to follow the protocol.

1. Subject (b) (6) met exclusion criterion #16 "Inability to tolerate the weekly fluid load (500cc of fluids)" due to underlying lung disease that left the subject "very sensitive to even slight fluid overload" according to a physician that assessed him two months prior to the subject enrolling into the study.

2. Subjects (b) (6) , and (b) (6) received their infusions of study drug in less than the three hours required by the protocol.

3. Subjects (b) (6) , and (b) (6) had laboratory values that required delay of subsequent infusions and increased laboratory follow-up per the protocol that did not occur.

4. Subject(b) (6) received an infusion that was meant for another subject.

5. Subject(b) (6) received an infusion that was prepared outside of the [redacted] hour window specified by the protocol.

b. Obtaining informed consent

1. Subjects(b) (6) were not re-consented with version 3 of the ICF as required by the IRB.

2. Subjects(b) (6) were not re-consented with version 4 of the ICF as required by the IRB.

3. Subjects(b) (6) &(b) (6) were not re-consented with version 5 of the ICF as required by the IRB.

c. Informing subjects of investigational status of drug

a. The last paragraph on the PATIENT GENERAL CONSENT states the following:

"I understand that some of the treatments suggested for me are as of yet unproven and experimental, however, I have been informed of this, and I am willing to accept the risks on the basis of the information provided to me. I will have the opportunity to ask questions and to research any treatment suggested before I agree to do it. I understand that the doctors have done their research as well, including (in most cases) having taken these treatments themselves."

b. On 11/02/09 Subject(b) (6) asked via phone message if the IV is FDA approved. The reponse on the phone message is "Yes!". The study drug, edetate disodium, was not approved for any indication at this time as the NDAs and ANDAs were withdrawn on 05/15/08 as was published in the Federal Register. Edetate disodium was never approved for the indication being studied and was being evaluated under an IND.

Reference: 21 CFR 312.60

OBSERVATION 2

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

Specifically,

~~a. Subject(b) (6) was hospitalized from(b) (4) for atrial fibrillation and angina. This event was not reported by the site as an SAE to the IRB.~~

b. Subject(b) (6) was hospitalized from(b) (4) for weakness, chest pain, and transient ischemic attack. These events were not reported by the site as SAEs to the IRB.

c. Subject (b) (6) died on (b) (4) . This SAE was reported to the site on 06/02/05. It was reported to the IRB on 05/23/08.

d. Subject (b) (6) died on (b) (4) . This SAE was reported to the site on 11/18/05. It was reported to the IRB on 05/23/08.

Reference: 21 CFR 312.66

OBSERVATION 3

Failure to obtain informed consent in accordance with 21 CFR Part 50 from each human subject prior to conducting study-related tests .

Specifically,

Subject (b) (6) was screened for the trial on (b) (4) and had study related laboratory tests done on 09/06/05. The subject did not sign the Informed Consent Form until (b) (4) .

Reference: 21 CFR 312.60

OBSERVATION 4

Failure to assure that an IRB complying with applicable regulatory requirements was responsible for the initial and continuing review and approval of a clinical study.

Specifically,

Continuing review of the study was approved for 12 months by the IRB on 02/07/08. It was approved again 16 months later on 06/04/09, four months past the IRB imposed deadline.

Reference: 21 CFR 312.66

OBSERVATION 5

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

Specifically,

Subject(b)(6) 's original source documentation and consent forms were not available for review.

Reference: 21 CFR 312.62(b)

REFUSALS

There were no refusals.

FINAL DISCUSSION WITH MANAGEMENT

Investigator Robinson and I held a close-out meeting with Dr. Roberts in which we discussed the observations on the FDA 483. I informed her of the possibility and types of action the FDA may take in response to the findings of this inspection and that they may be initiated without further notice. I also informed Dr. Roberts that the observations listed on the FDA 483, in my judgment, rose to the level of reportable observations but that this did not represent final Agency determination of their compliance with the regulations. I informed her that higher authorities would make that determination. I informed Dr. Roberts that if she wished to respond to the observations listed on the FDA 483 she should submit her response in writing within 15 business days. Dr. Roberts stated that she would be submitting a response letter. I provided her with the name of our District Director and the address to which she should send her written response. We then read over the FDA 483 and discussed each observation. Dr. Roberts had no further comment about any of the observations.

On 12/16/10 I returned to Wellness Works to issue to Dr. Roberts an amended FDA 483 due to an error found while writing this EIR. I issued the amended FDA 483 to Dr. Roberts and explained to her that the hospitalization referenced in Observation 2.a occurred after the deadline for the reporting of adverse events per the protocol so it did not need to be reported. She expressed understanding of the situation and had no further questions.

SAMPLES COLLECTED

No samples were collected.

EXHIBITS COLLECTED

1. CV of Carol L. Roberts, MD, 5 pages
2. CV of(b) (6) , dated 07/18/06, 1 page
3. Form FDA 1572, dated 02/05/04, 2 pages
4. Site Responsibility and Signature Log, 2 pages
5. Edetate disodium Investigator's Brochure, dated 02/25/06, 29 pages
6. TACT Trial Protocol, dated 02/17/04, 95 pages
7. Edetate sodium IND Acknowledgement, 2 pages
8. Sterling IRB Roster, 1 page
9. Informed Consent Form (version 1), dated 10/29/03, 12 pages
10. Study Advertising, 3 pages
11. Informed Consent Form (version 2), dated 04/19/04, 12 pages
12. Informed Consent Form (version 3), dated 05/05/06, 13 pages
13. Informed Consent Form (version 4), dated 12/16/08, 13 pages
14. Informed Consent Form (version 5), dated 08/26/09, 12 pages
15. Site Visit Log, 1 page
16. Monitor Letters, 7 pages
17. Dear Participant Letter from Gervasio Lamas, MD, dated 09/10/08, 1 page
18. Sterling IRB Suspension Letter, dated 08/29/08, 1 page
19. OHRP Letter #1, dated 08/25/08, 4 pages
20. Response to OHRP Letter, dated 11/05/08, 17 pages
21. OHRP Letter #2, dated 05/27/09, 8 pages
22. Response to OHRP Letter #2, dated 07/31/09, 17 pages
23. OHRP Letter #3, dated 10/30/09, 4 pages
24. Sterling IRB Letter Lifting Suspension, dated 12/24/08, 1 page
25. Sterling IRB Suspension Letter #2, dated 12/04/09, 1 page
26. Sterling IRB Letter Lifting Suspension #2, dated 12/11/09, 1 page
27. Sterling IRB Suspension Letter #3, dated 04/19/10, 1 page
28. Sterling IRB Letter to OHRP, dated 04/19/10, 1 page
29. Wellness Works Letter to Sterling IRB, dated 04/20/10, 1 page
30. Sterling IRB Letter in Response to Site Corrective Action, dated 04/24/10, 1 page
31. Wellness Works Letter to Sterling IRB #2, dated 04/28/10, 1 page
32. Subject Screening/Enrollment Log, 2 pages
33. Signed/Dated Copy of Most Recent ICF, dated 08/26/09, 13 pages
34. Progress Note, dated 04/12/05, 6 pages
35. Infusion Records, dated 08/12/04 & 09/03/04, 2 pages

36. Infusion Records, 2 pages
37. Infusion Record, 1 page
38. Infusion Record, 1 page
39. Lab Results, dated 01/27/05, 1 page
40. Infusion Record, 1 page
41. Lab Results, dated 02/01/06, 1 page
42. Lab Results, dated 03/22/07, 1 page
43. Infusion Record, 1 page
44. Lab Results, dated 05/31/07, 1 page
45. Lab Results, dated 03/25/10, 1 page
46. Lab Results, dated 05/06/10, 1 page
47. Lab Results, dated 06/09/10, 1 page
48. Infusion Records, dated 05/06/10 & 05/13/10, 2 pages
49. Progress Note, dated 04/15/05, 1 page
50. Protocol Deviation Report, dated 04/15/05, 1 page
51. Corrective Action Plan, 1 page
52. Delivery Packing Slip, dated 06/05/06, 1 page
53. Infusion Record, dated 05/10/10, 3 pages
54. Protocol Deviation Report, dated 06/28/06, 1 page
55. Wellness Works-Patient General Consent, dated 04/12/05, 1 page
56. Phone Message Form, dated 11/02/09, 1 page
57. Federal Register, dated 06/12/08, 2 pages
58. Progress Note, 1 page
59. Adverse Event Report, 6 pages
60. SAE Report (Subject 257-9009), dated 05/23/08, 2 pages
61. SAE Report (Subject 257-9018), dated 05/23/08, 2 pages
62. ICF Signature Page, dated 09/16/05, 1 page
63. Progress Note, 1 page
64. TACT Trial Screening Worksheet, dated 09/13/05, 2 pages
65. Lab Results, dated 09/06/05, 1 page
66. Sterling IRB Annual Renewal, dated 02/07/08, 1 page
67. Continuing Review Status Report, dated 04/21/09, 3 pages
68. Sterling IRB Annual Renewal, dated 06/04/09, 1 page
69. Progress Note, 1 page
70. Infusion Record, 1 page

ATTACHMENTS

- FDA Form 482, Notice of Inspection issued to Carol L. Roberts, MD, dated 12/01/10, 1 page
- FDA Form 483, Inspectional Observations issued to Carol L. Roberts, dated 12/09/10, 3 pages
- FDA Form 483, Inspectional Observations, Amendment 1 issued to Carol L. Roberts, dated 12/16/10, 4 pages
- Assignment Memo, dated 09/13/10, 5 pages

Gene R. Gunn, Investigator

Jennifer A. Robinson, Investigator