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SUMMARY

The current high priority data audit was initiated by CDER Assignment Memorandum titled, FY 2014 – High Priority CDER For-Cause Inspection Clinical Investigator Data Validation Inspection using the Bioresearch Monitoring Compliance Program (CP 7348.811), dated 05/21/2014; FACTS # 8772341, OP ID 7394654: OSI Complaint # 4006. Target completion date: 07/21/2014. The Assignment memo requested the data audit of:

- Clinical Investigator: Dr. Nicole A. Shonka
- IND# (b) (4)
- Sponsor: (b) (4)
- Drug: (b) (4)
- Protocol: "A Randomized Phase (b) (4) Study of (b) (4) in Combination with (b) (4)

The current inspection was conducted under CP 7348.811 Clinical Investigators, PAC 48811F Human and Animal Drugs; Human – Investigational.

This is the first inspection of Dr. Nicole A. Shonka, *Clinical Investigator*.

The current inspection was pre-announced by phone call to Dr. Nicole A. Shonka, *Clinical Investigator*, on 06/09/2014.

The current inspection found Dr. Shonka practices as a physician at The University of Nebraska Medical Center, as well as a Clinical Investigator for Human Clinical Trials and she identified herself as such.

The directed study for review, (b) (4) OSI Complaint #4006, was conducted two years ago, from the first patient consent signed on 04/13/2012 to the last patient discontinuation on 06/22/2012. Dr. Shonka selected patients under her care to screen for participation in said trial, which was initiated at The University of Nebraska Medical Center.

An additional clinical study was reviewed in order to confirm Dr. Shonka's compliance with federal regulations. The study titled, "(b) (4) r (b) (4) ", IRB# (b) (4), was reviewed in accordance with CP 7348.811 Clinical Investigators, PAC 48811F Human and Animal Drugs; Human – Investigational.

This inspection covered: protocol review, amendments, deviations, appendices, patient consent forms, patient screening, financial disclosures, FDA 1572s, blinding procedures, IRB review, dosing records, lab reports, verification of overdosing, clinical staff and investigator interviews, test article accountability, and death documents. All copies of documents were obtained per the assignment memo. The documents were well organized, there was no obliterated data, and all changes were initialed. I did not find any information that was contrary to the background assignment data.

The closing discussion was conducted on 06/20/2014 with Dr. Shonka and her staff. During the current inspection I did not encounter any refusals, I did not collect any samples, I did not find any objectionable conditions, and I did not issue a list of observations. There were no voluntary corrections.

Dr. Shonka was warned of her responsibility to be in compliance with the Food, Drug, and Cosmetic Act.

ADMINISTRATIVE DATA

Inspected firm:	Shonka, Dr Nicole A.
Location:	987680 Nebraska Medical Center University of Nebraska Omaha, NE 68198-7680
Phone:	402-559-3848
FAX:	
Mailing address:	987680 Nebraska Medical Center University of Nebraska Omaha, NE 68198-7680
Dates of inspection:	6/17/2014, 6/18/2014, 6/19/2014, 6/20/2014
Days in the facility:	4
Participants:	Jason R. Caballero, Investigator

The current inspection was pre-announced by phone call to Dr. Nicole A. Shonka's, *Clinical Investigator*, office on 06/09/2014. During the preannouncement, I did not divulge the study I would be reviewing.

The inspection began on the eighth floor of the Lead Transplant building, in the oncology department. Mrs. Julie L. Ehlers, *Clinical Manager of Trials Oncology*, scheduled the appointment with Dr. Shonka on 06/17/2014, on said date I presented my credentials to Dr. Shonka and gave Mrs. Ehlers, Mrs. (b) (7) (C) ; (b) (6), *Clinical Research Nurse for Oncology*, Mrs. (b) (7) (C) ; (b) (6), *Research Coordinator Radiation Oncology*, a business card. An FDA 482 Notice of Inspection was issued to Dr. Shonka.

Mrs. (b) (7) (C) ; (b) and Mrs. (b) (7) (C) ; (b) (6) were directed to photocopy the information I requested. On 06/20/2014, immediately before the closing discussion, I performed a page count on the documents obtained during the inspection and found all page numbers in sequence and inclusive of first to last pages.

The closing discussion was conducted with Dr. Shonka, Mrs. Ehlers, Mrs. (b) (7) (C) ; (b), and Mrs. (b) (7) (C) ; (b) (b) (7) (C) ; (b) on 06/20/2014. No FDA 483 was issued.

HISTORY

Dr. Nicole A. Shonka, *Clinical Investigator*, has been employed as a physician and clinical investigator with the University of Nebraska Medical Center for four years. Prior to working in her

current position, she participated in a Neuro-oncology fellowship at the (b) (7) (C) (b) (7) (C). She received her Doctor of Medicine degree from the University of Nebraska Medical Center, Omaha, Nebraska.

JURISDICTION

This Clinical Investigator conducts Human Clinical Trials in support of FDA-regulated products submitted in research/marketing permits and applications.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

Dr. Nicole A. Shonka, *Clinical Investigator*, is the most responsible individual for the clinical trials reviewed during this inspection. Dr. Shonka is responsible for clinical enrollment screening, clinical care, and patient eligibility criteria review. She stated most of the patients in her studies are previously under her immediate care and she then inquires if they would like to participate in a clinical trial. Dr. Shonka was present during the entire inspection and provided information contained in this report. She does not possess direct hire and fire privileges.

Mrs. Julie L. Ehlers, *Clinical Manager of Trials Oncology*, is the replacement manager for clinical trials for Mrs. Ishna Petal, who (b) (7) (C) ; (b) (6) and could not be in attendance during the inspection. Mrs. Ehlers has been employed under her current title for approximately 2 years. She did not partake in any of the clinical trials reviewed during this inspection. She currently provides logistics and data support for the oncology clinical trials. Prior to her employment at the University of Nebraska Medical Center, she (b) (7) (C) ; (b) (6). She does not possess direct hire and fire privileges. Mrs. Ehlers was present during the entire inspection and provided information contained in this report.

Mrs. (b) (7) (C) ; (b) (6), *Clinical Research Nurse for Oncology*, is responsible for direct patient medical care. She has worked under her current title for (b) (7) (C) ; (b) (6) years. She also administers chemotherapy medication infusions in the patient treatment facility. She does not possess direct hire and fire privileges. Mrs. (b) (7) (C) ; (b) was present during the entire inspection and provided information contained in this report.

Mrs. (b) (7) (C) ; (b) (6) *Research Coordinator Radiation Oncology*, is responsible for IRB regulation correspondence, data entry for the clinical studies, and has been employed under her title for (b) (7) (C) years. She does not possess any direct hire and fire privileges and previously worked at (b) (7) (C) ; (b) (6).

SPECIFIC ASSIGNMENT INFORMATION REQUESTED IN MEMORANDUM DATED 05/21/2014, FACTS #8772341, OSI COMPLAINT #4006

This section includes information collected for the clinical study titled:

"A Randomized Phase (b) (4) Study of (b) (4) in Combination with (b) (4) t (b) (4) .

General Instructions:

1. Please review 1/3-1/2 total number of records for subjects, if less than 25 review all. Total number of subjects for the study was (b) (4) patients. All records pertaining to said subjects were reviewed in their entirety.

2. Please verify if informed consent was appropriately obtained for each subject. All informed consents were appropriately obtained for each subject in this study and all informed consent forms did comply with 21 CFR 50.25, *Elements of informed consents.* There was no evidence of signature forgery on any of the informed consent forms.

3. Please obtain a signed and dated copy of the most recent IRB/Ethics Committee approved version of the informed consent form used in the study with your EIR. Please refer to Exhibit #1, pages 1-19, for the most recent IRB approved version of the informed consent form for (on file for subject (b) (7) (the study titled, "A Randomized Phase (b) (4) Study of (b) (4) in Combination with (b) (4) t- (b) (4) ".

4. Please verify if all subjects met study eligibility criteria. I did verify that all subjects did meet the eligibility criteria in this study. Concerning the clinical study titled, "A Randomized Phase (b) (4) Study of (b) (4) in Combination with (b) (4) t (b) (4) ', all eligibility criteria was reviewed for Subject (b) (6) – Patient ID # (b) (6) t t.

5. Please verify if test article accountability/disposition was adequately documented. Dr. (b) (7) (C) ; (b) (6), *Clinical Pharmacist,* stated he is responsible for investigational drug agents and he stored the test articles in a secured location with IRB number identification. Dr. (b) (7) (C) ; (was responsible for both clinical studies reviewed test articles. Each sponsor ships directly to him and specifies temperature monitoring and requires a log of inventory and dispensing. Dr. (b) (7) (C) ; (separates each set of study supplies with patient name and sponsor labeled on each prescription bottle. We reviewed his drug inventory and concluded all test

articles were accounted for. All unused drugs were returned from the patients enrolled in this clinical study reviewed during the inspection.

6. Please verify if protocol specified blinding/randomization procedures were followed. This clinical study did not utilize any blinding/ randomization procedures.

7. Please verify if all FDA 1572s were signed and appropriately completed (please submit copies of all 1572s with the EIR). Please refer to Exhibit #3, pages 1-11, for Dr. Shonka's submitted FDA 1572 and Curriculum Vitae to the sponsor.

8. Please verify if the clinical investigator and subinvestigators who were/are directly involved in the treatment or evaluation of study subjects completed financial disclosures and provided them to the sponsor of the study. Please refer to Exhibit #4, pages 1-1, for Dr. Shonka's submitted financial disclosure to the sponsor.

Specific Instructions:

1. Obtain a list of all studies conducted by the clinical investigator. On this list, please note (a) the IND # for each study; (b) the sponsor of each study; and (c) the Institutional Review Board (IRB) providing oversight for each study. Please refer to Exhibit #5, pages 1-14, for a complete list and descriptions of all studies conducted by Dr. Shonka. All of Dr. Shonka's studies are reviewed by the University of Nebraska Medical Center IRB. The submitted list and detailed descriptions includes each study's IRB assigned number, given after each review.

2. Expand your inspection, as needed, to include an audit of one other study that was conducted under an IND to determine the clinical investigator's general compliance with applicable regulations. If you feel that further expansion is warranted, please contact Headquarters and obtain Headquarters' concurrence before expanding the inspection further. An additional clinical study was reviewed in order to confirm Dr. Shonka's compliance with federal regulations. The study titled, "(b) (4) of (b) (4)", IRB# (b) (4). Please refer to the immediately following section for more information concerning this clinical study.

3. Review all of the records for subjects (b) (7) (C) ; (b) (6) referenced in the allegation, and verify and document the IRB's allegations as noted above. All records for patients (b) (7) (C) ; (b) (6) were reviewed in their entirety. Please refer to Exhibit #6, pages 1-4, for the IRB's review of the allegations made and the purposed corrective actions.

4. Please review the dosing records, the laboratory reports for Subject (b) (7) (C) ; (b) (6) to verify the overdosing and, please review any records that document the death of subject and document you findings in the EIR. Please refer to Exhibit #7, pages 1-4, for patient prescriptions and study drug assignments. This illustrates the confusion/error between the two dosage arms of the clinical study.

   The laboratory reports for Subject recorded signs of (b) (7) (C) ; (b) (6) and stopped all medication (b) (4) while subject was subjected to the overdosing of (b) (4)). Subject (b) (7) (C) ; (b) (6) count went from (b) (7) (C) ; (b) (6) after his removal from the clinical trial. Both patients were considered to be at stage (b) (7) (C) ; (b) (6).

   Subject 's lab results showed (b) (7) (C) ; (b) (6) the overdosing of (b) (4) occurred. Prior to the clinical study, on (b) (7) (C) ; (b) (6) and after the clinical trial her white blood count was (b) (7) (C) ; (b) (6).

   Subject expired on (b) (7) (C) ; (b) (6). Attending physician (b) (7) (C) ; (b) (6), made a patient diagnosis describing (b) (7) (C) ; (b) (6) in the setting of (b) (7) (C) ; (b) (6) (b) (7) (C) ; (b) (6). Dr. (b) (7) (C) ; (b) (6) noted other conditions such as (b) (7) (C) ; (b) (6), probable (b) (7) (C) ; (b) (6), questionable (b) (7) (C) ; (b) (6) known history of (b) (7) (C) ; (b) (6).

5. Also, please visit the investigational pharmacy to determine how the drugs were dispensed to the study subjects and document your findings in the EIR. (b) (7) (C) ; (b) (6), *clinical pharmacist,* stated he is responsible for investigational drug agents and he stored the test articles in a secured location with IRB number identification. Each sponsor ships directly to him and specifies temperature monitoring and requires a log of inventory and dispensing. Before dispensing an investigational article, Dr. separates each set of study supplies with patient name and sponsor labeled on each prescription bottle. His records reflected each amount of drug dispensed to each patient on a specific date/time during the clinical study.

6. Dr. Shonka developed a corrective action plan as identified in the June 13, 2012 letter from the IRB, please review and determine if the corrective action plan was put into place and document your findings in the EIR. Dr. Shonka and Mrs. confirmed that only Dr. Shonka can now write out electronic signatures for patient prescriptions and dispensing medication amounts. Please refer to Exhibit #8, pages 1-2, for the corrective action submission to the IRB. The corrective action was approved by the IRB and is now utilized in all oncology clinical studies when dispensing chemotherapy medication to participating patients.

7. For each study inspected, collect a copy of:
   i. Original protocol: Please refer to Exhibit #9, pages 1-109
   ii. Protocol in effect: Please refer to Exhibit #10, pages 1-69
   iii. Protocol amendments in effect at the site while the study is/ was ongoing: Please refer to Exhibit #11, pages 1-25
   iv. Protocol appendices: Please refer to Exhibit #10, pages 36-69
   v. All protocol specific manuals and any other protocol-specific materials and instructions provided by the sponsor as part of the investigational plan. The sponsor provided the protocol to the clinical investigator, which was submitted with this report.
   vi. All versions of the informed consent documents: Please refer to Exhibit #10, pages 36-48
   vii. All IRB approved notices that informed the site when the protocol amendments, if any, were approved: Please refer to Exhibit #8, pages 1-2

8. If protocol violations are found and included on the FDA 483, collect the version of each protocol that was in effect at the time the violations occurred. No protocol violations were recorded during this inspection.

9. Review any available source documents used to meet the requirements of the study. Document in the EIR any missing documents, and obtain copies of all relevant documents that are available. All available source documents were reviewed and there was no missing documentation during the inspection. I obtained copies of all relevant source documents.

10. Interview Dr. Shonka and study staff, if any, to obtain information on the conduct of the study, enrollment of subjects, staff responsibilities, and Dr. Shonka's involvement in the study. Please document these findings in the EIR.

Dr. Nicole A. Shonka's interview: She stated she was responsible for standard care for patients suffering from (b) (4) growths. She stated she was particularly interested in her specific clinical studies because of the allowance of patients to enroll with previous (b) (4), "which renders MRIs hard to read". She stated herself, Mrs. (b) (7) (C) ; (b) (6) and Mrs. (b) (7) (C) ; (b) emailed the principal investigator of the study, (b) (4), concerning issues with the protocol prior to initiating the study involved with the patient overdosing. Dr. Shonka stated the protocol was not clear; particularly the dosage/duration arms were easily confused with each other.

Subjects (b) (7) (C) ; (b) (6) were issued a paper prescription for (b) (4) and Dr. Shonka would write in intended dose. She stated Mrs. (b) (7) (C) ; (b) would handwrite in the drug dispensing amounts. Dr. Shonka stated from her past experience of writing prescriptions, she knows not to dispense (b) (4) days. She stated she would leave it blank for

Mrs. (b) (7) (C) ; (b) to complete, which is no longer a practice, thanks to the electronic prescription corrective action currently in place. Once Dr. Shonka noticed the dosage error, she immediately contacted both subject (b) (7) (C) ; (b) (6), while Mrs. (b) (7) (C) ; (b) and Mrs. (b) (7) (C) ; (b) (6) emailed the principal investigator.

Dr. Shonka stated four out of the (b) (4) patients enrolled in the study were previously under her care and she would suggest their participation in her clinical trials. She stated she would review the eligibility checklist with each patient, which Mrs. (b) (7) (C) ; (b) (6) provide. When directly asked if Dr. Shonka had any personal conflicts with any of her patients, she stated she never had personal conflicts even though there was personal rapport with patients. She particularly had a close relationship with subject (b) (7), who expired (b) (7) (C) ; (b) (6). She stated she was curious as to why Dr (b) (7) (C) ; (b) (6), *clinical pharmacist*, never brought up the issue with the dosage amounts of (b) (4) She stated subject (b) (7) lived for (b) (7) (C) ; (b) (6); (b) (7) (C) ; (b) (6) until he too expired at the (b) (7) (C) ; (b) (6). She stated she did not note any evidence of document falsification or attempts to cover up the overdosing. She recalls calling the family of the subjects (b) (7) (C) ; (b) (6) immediately.

Dr. Shonka stated her, Mrs. (b) (7) (C) ; (b), and Mrs. (b) (7) (C) ; (b) (6) would draft correspondences to IRB together. Mrs. (b) (7) (C) ; (b) (6) would write the IRB seeking approvals and all three ladies wrote the corrective action (electronic signatures for prescriptions) which is now implemented. She stated only doctors can input dosage amounts and prescriptions in the new computer system. She stated there is no possible way Mr. (b) (7) (C) ; (b) could repeat the dosage dispensed mistake now.

(b) (7) ***interview***: Mrs. (b) (7) (C) ; (b) (6) stated her responsibilities include clinical research coordination, obtaining IRB approval, and reviewing study protocols. She stated Dr. Shonka would evaluate her patients and if they were eligible she ask them to consider enrolling in her clinical trials. Mrs. (b) (7) (C) ; (b) (6) stated Dr. Shonka and herself would obtain patient consents. She stated the protocol was approved by the (b) (4), (b) (4) y group. She stated the IRB reviewed all clinical studies in real-time, met (b) (4) n, and would immediately address study amendments.

Mrs. (b) (7) (C) ; (b) (6) stated the protocol was not written clearly, "I wouldn't write it that way" and the overdosing of subjects (b) (7) (C) ; (b) (6) was just an honest error. Mrs. (b) (7) (C) ; (b) (6) stated Dr. Shonka strictly adheres to all protocols. She stated (b) (4) mg of (b) (4) is usually given for (b) (4) days, (b) (4) mg dosages would be dispensed for (b) (4) days. She stated Dr. Shonka was responsible for dosages, so she believed it was an honest mistake on the part of the clinical investigator. She did not note any falsification of documents from those involved in the clinical study titled, "A Randomized Phase (b) (4) Study of (b) (4) in Combination with (b) (4) (b) (4) (b) (4))". She stated all patients were 19 years of age and above.

(b) (7) (C) ; (b) (6) *v:* When questioned about her responsibilities during the clinical trial, she stated she provides help managing patient screening, completes patient eligibilities, provides study background information to families, and reviews the informed consent with patients and family. She stated the trial was executed in a very serious manner. She stated when a patient would start the trial she would meet with the new subject in a clinical setting and formulate a drug diary calendar to schedule appointments and dosing. She stated she was a aware of the overdosing situation with patient (b) (7) (C) ; (b) (6) during the study titled, "A Randomized Phase (b) (4) Study of (b) (4) in Combination with (b) (4) ((b) (4) " Mrs. (b) (7) (C) ; (b) stated the study was meant to (b) (4) in a phase (b) (4) environment. She stated the dose was not defined clearly, "it was a bit of a grey area".

Mrs. (b) (7) (C) ; (b) stated Dr. Shonka singed patient prescriptions and the two arms were mixed up ((b) (4) mg and (b) (4) mg (b) (4) dosing). She stated it is not usual to see a (b) (4) mg (b) (4) dosage for (b) (4) days duration. She stated the (b) (4) co-administration attacked the cancer from other pharmacological avenues. She stated she did not document any drug-drug interactions, she just noted the exacerbated decrease in white cell count. She stated there were no defined responsibilities documented for the clinical trial. She stated there were no attempts to falsify documents and she contacted patients as soon as the overdosing situation came to the forefront. During a second interview, on 06/18/2014 at 8:50 a.m., Mrs. (b) (7) (C) ; (b) admitted to writing the wrong amount of (b) (4) to be dispensed to subjects (b) (7) (b) (7) (C) ; (b) (6) She stated Dr. Shonka signed the prescription but she (Mrs. (b) (7) (C) ; (b)) wrote the amount to be dispensed and this practice has been eliminated when the corrective action (electronic prescription signatures) was put into effect.

11. Submit a copy of any screening and enrollment logs with subject identification (ID), and confirm on-site that the number of subjects on these logs accurately reflects the number of subjects screened/enrolled. Please refer to Exhibit #12, 1 page, for the enrollment log pertaining to this clinical study. All subjects on this log do accurately reflect the number of subjects enrolled in the study. This log includes patient ID, informed consent form version, informed consent signature date, subject enrollment, any reasons for screening failure, date of patient discontinuation, and reason for patient discontinuation of the clinical study.

12. If falsification is found, attempt to determine the following, and collect any available evidence to show that the clinical investigator submitted falsified information to the FDA or the sponsor. During this current inspection, I did not record any evidence of falsification.

This section includes information collected for clinical study titled:

(b) (4)

1. Please review 1/3-1/2 total number of records for subjects, if less than 25 review all. Total number of subjects for the study was (b) (4) patients. All records pertaining to said subjects were reviewed in their entirety.

2. Please verify if informed consent was appropriately obtained for each subject. All informed consents were appropriately obtained for each subject in this clinical study and all informed consent forms did comply with 21 CFR 50.25, *Elements of informed consents.* There was no evidence of signature forgery on any of the informed consent forms.

3. Please obtain a signed and dated copy of the most recent IRB/Ethics Committee approved version of the informed consent form used in the study with your EIR. Please refer to Exhibit #13 pages, 1-25, for the most recent IRB approved version of the informed consent form for the study titled, "(b) (4) r (b) (4) .

4. Please verify if all subjects met study eligibility criteria. Concerning the clinical study titled, (b) (4) . All eligibility criteria was reviewed and met for patient ID numbers (b) (7) (C) ; (b) (6) , (b) (7) (C) ; (b) (6) . Patient ID number (b) (7) (C) ; (b) (6) failed to meet eligibility criteria due to patient's insurance denying patient's enrollment in clinical trial. Patient ID number (b) (7) (C) ; (b) (6) failed to meet eligibility criteria due to elevated Bilirubin blood levels exceeding the maximum threshold for participation. Patient ID number (b) (7) (C) ; (b) (6) failed to meet eligibility criteria due to advanced disease progression and neurologic findings. Patient ID number (b) (7) (C) ; (b) (6) was instructed to start standard care immediately.

5. Please verify if test article accountability/disposition was adequately documented. Dr. (b) (7) (C) ; (b) (6), *Clinical Pharmacist,* stated he is responsible for investigational drug agents and he stored the test articles in a secured location with IRB number identification. Dr. (b) (7) (C) ; (b) was responsible for both clinical trials' test articles. Each sponsor ships directly to him and specifies temperature monitoring and requires a log of inventory and dispensing. Dr. (b) (7) (C) ; (b) separates each set of study supplies with patient name and sponsor labeled on each prescription bottle. We reviewed his drug inventory and concluded all test articles were accounted for. All unused drugs were returned from the patients enrolled in this clinical study.

6. Please verify if protocol specified blinding/randomization procedures were followed. This study did utilize a double blinded procedure described in the protocol and all procedures were successfully executed.

Description of blinding procedure:

(b) (4)

The data manager, nurse, or pharmacist will then contact the registration office for a (b) (4) was recorded by Dr. (b) (7) (C) ; (b) (6), *Clinical Pharmacist*. The registration office will (b) (4) . Please refer to Exhibit #16, page 27, for a complete description of the blinding procedures followed during the clinical study.

7. Submit a copy of any screening and enrollment logs with subject identification (ID), and confirm on-site that the number of subjects on these logs accurately reflects the number of subjects screened/enrolled. Please refer to Exhibit #14, Pages 1-2, for the enrollment log submitted by Mrs. (b) (7) (C) ; (b) during the inspection.

8. For each study inspected, collect a copy of:
   i. Original protocol: Please refer to Exhibit #15, pages 1-132
   ii. Protocol in effect: Please refer to Exhibit #16, pages 1-114
   iii. Protocol amendments in effect at the site while the study is/ was ongoing: Please refer to Exhibit #17, pages 1-9
   iv. Protocol appendices: Please refer to Exhibit #15, pages 87-132
   v. All protocol specific manuals and any other protocol-specific materials and instructions provided by the sponsor as part of the investigational plan: The sponsor provided the protocol to the clinical investigator, which was submitted with this report.
   vi. All versions of the informed consent documents: Please refer to Exhibit #18, pages 1-22
   vii. All IRB approved notices that informed the site when the protocol amendments, if any, were approved: Please refer to Exhibit #19, pages 1-3

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

I did not note any objectionable conditions.

REFUSALS

There were no refusals. Management was cordial and provided all requested information.

GENERAL DISCUSSION WITH MANAGEMENT

Dr. Shonka, Mrs. Ehlers, Mrs. (b) (7) (C) ; (b), and Mrs. (b) (7) (C) ; (b) (6) were present during the close-out discussion on 06/20/2014. I did not have any FDA-483 items, nor did I have any discussion items. I informed Dr. Shonka of her responsibilities under the FD&C Act.

SAMPLES COLLECTED

I did not collect any samples.

EXHIBITS COLLECTED

Exhibit 1: Most recent IRB approved version of the informed consent form, IRB #(b) (4), 19 pages

Exhibit 2: Copy of subjec(b) (7) (C) ; (bs eligibility checklist, 4 pages

Exhibit 3: Dr. Shonka's submitted FDA 1572 and Curriculum Vitae, 11 pages

Exhibit 4: Dr. Shonka's submitted financial disclosure, 1 page

Exhibit 5: List and descriptions of all clinical studies conducted by Dr. Shonka, 14 pages

Exhibit 6: IRB's review of the allegations made and the purposed corrective actions, 4 pages

Exhibit 7: Patient (b) (7) (C) ; (b) (6) 's prescriptions and study drug assignments, 4 pages

Exhibit 8: Corrective action submission to the IRB, 2 pages

Exhibit 9: Original protocol, IRB #(b) (4), 104 pages

Exhibit 10: Protocol in effect, IRB #(b) (4) 69 pages

Exhibit 11: Protocol amendments, IRB (b) (4) , 25 pages

Exhibit 12: Enrollment log, IRB #(b) (4), 1 page

Exhibit 13: Most recent IRB approved version of the informed consent form, IRB# (b) (4), 25 pages

Exhibit 14: Patient enrollment log, IRB# (b) (4), 2 pages

Exhibit 15: Original protocol, IRB# (b) (4), 132 pages

Exhibit 16: Protocol in effect, IRB# (b) (4), 114 pages

Exhibit 17: Protocol amendments in effect, IRB# (b) (4), 9 pages

Exhibit 18: All versions of informed consent documents, IRB# (b) (4) 22 pages

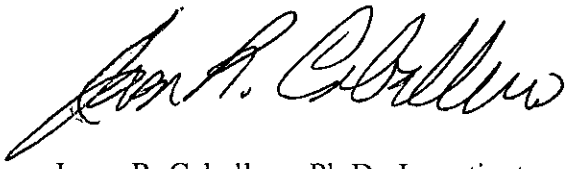
Exhibit 19: All IRB approved notices that informed site of protocol amendments, 3 pages

ATTACHMENTS

FDA 482, Notice of inspection, issued on 06/17/2014 to Dr. Nicole A. Shonka, Clinical Investigator, 1 page

FACTS Assignment Sheet, WAID: 8772341, OP ID: 7394654, 2 pages

CDER Assignment Memorandum titled, FY 2014 – High Priority CDER For-Cause Inspection Clinical Investigator Data Validation Inspection using the Bioresearch Monitoring Compliance Program (CP 7348.811), dated 05/21/2014; FACTS # 8772341, OP ID 7394654: OSI Complaint # 4006, 7 pages



Jason R. Caballero, Ph.D., Investigator