

**Walsky, Philip**

**From:** Vermillion, Terry  
**Sent:** Thursday, March 06, 2003 11:24 PM  
**To:** Bourne, David; Aspinwall, Greg; Niemiec, Michael  
**Subject:** RE: As I promised

This guy is world class. My hats off to him

Terry

-----Original Message-----

**From:** West, Robert  
**Sent:** Thursday, March 06, 2003 9:46 PM  
**To:** Vermillion, Terry  
**Cc:** Bourne, David; Aspinwall, Greg; Niemiec, Michael  
**Subject:** As I promised

Dr. Anne Kirkman Campbell  
Case Number 03-NEL-707-0040

**Case Overview:**

During October 2002, the Birmingham Resident Post was issued a notice to inspect Campbell site since she was one of the PIs involved in the conduct of the clinical trial for the pharmaceutical company Aventis. Prior to inspecting Campbell, CSO Patricia Smith was not aware of the protocol violations uncovered by the monitor PPD Development. This indicates to me that CDER was also not aware of any discrepancies uncovered by PPD and provided to the sponsor. Based on FDA's site inspection, it was determined that Campbell enrolled 407 study subjects for either Acute Sinusitis or Acute Exacerbation of Chronic Bronchitis. Campbell enrolled these study subjects between November 2001 and the beginning of February 2002. It should be understood that Campbell practices medicine in Gadsden, AL, which is not a major metropolitan city. FDA, during the inspection, uncovered numerous regulatory violations involving the consent forms, case report forms etc. Based on these discrepancies, CSO Smith contacted several of the study subjects and determined that they did not fully participate in the clinical trial. Campbell has submitted a document which indicates that 407 study subjects enrolled and 407 completed the clinical trial. CSO immediately contacted OCI and referred these issues since it appeared that Campbell submitted false documents through the sponsor to the FDA.

**OCI Investigation:**

Prior to going to North Carolina to interview PPD personnel, I interviewed several of the study subjects which resulted in the following:

- Study Subjects never received study medication
- Study Subjects were not sick
- Study Subjects did sign consent form and did provide initial blood sample
- Study Subjects did not return to the clinic for the required 2<sup>nd</sup> Visit which means they did not provide 2<sup>nd</sup> blood sample
- Study subjects were not contacted as required for the 3<sup>rd</sup> visit
- Study subjects did not have a history of chronic bronchitis

I also interviewed 3 employees of Campbell. All three have told me that over half and maybe 3/4 of the study subjects were not sick when Campbell enrolled them in the study. All the employees have told me that Blood was split meaning that extra blood was drawn from either study subjects or regular patients and assigned to those study subjects that never returned for the 2<sup>nd</sup> visit which required a blood draw.

5/25/2006

They also informed me that Campbell changed dates and added fictitious diagnosis into patient medical records. 1 employee has admitted that she was told by Campbell to forge subject's names on consent forms. They have also told me that 1 study subject was fictitiously produced (Study subject 26-Manda Burwell). This was confirmed based on the SSN which was assigned to the patient. This SSN, based on SSA-OIG, belongs to a black male. They also told me that Campbell attempted and was rather successful in enrolling almost everyone that entered her clinic whether that person was sick or not. This includes pharmaceutical reps, staff, friends, ex-husband, underage patients (you have to be 18) and those individuals that brought people to the clinic for some reason. She also enrolled several patients with Alzheimer's.

#### PPD Interviews:

I interviewed several PPD personnel who informed me that during their monitoring, they uncovered a tremendous number of protocol violations. They suspected based on these discrepancies that Campbell might be falsifying documents. They also discovered that dates were being changed, the signatures appeared to be different handwriting, and that she was inserting dates into medical records. Dr. John Reynolds, a contract employee for PPD, undertook a statistical analysis of the blood values for Campbell's site. Based on his analysis, he felt that Campbell had split blood samples for a majority of the blood draws for the 2<sup>nd</sup> visit. He looked at times of collection, dates of collection, and blood values. All of the discrepancies, protocol violations, and Reynolds's analysis were provided to Aventis. 1 of the employees of PPD (Beth Heding) told me that Nadine, project manager for Aventis, made the following comment, "I don't care if the patients take the medication for the indication as long as they take the medication". She said that she felt that Nadine did not care about the results as long as some type of data was collected.

#### Aventis Interviews:

I interviewed several individuals including Nadine. All of them acknowledged that they were told of the protocol violations or discrepancies uncovered by PPD. This also included Reynolds's report. They all told me that these discrepancies and protocol violations were discussed verbally or in writing with Campbell and that she provided them with a "Plausible Explanation". These employees continuously used these buzz words throughout the interview. They also informed me that their Statistician conducted his own analysis and that he did not find that Campbell's site was any different than any other high enrollee site. I interviewed Nadine who admitted to making the aforementioned comment; however, she said the comment was taken out of context. She explained that after making this comment, she told PPD personnel that this study was mainly for safety and that the safety data was the only data analyzed. She explained that she felt that since the efficacy data was not being analyzed, the indications (Sinusitis or Chronic Bronchitis) were not as important as the safety data which is obtained from blood analysis.

I believe that CDER has conducted several other inspections but unless you personally interview study subjects, no one will ever know whether the documents have been falsified. I think it is great that CDER is looking into the clinical trial but they will never uncover fraud unless the subjects are contacted. Even though there are protocol violations or other discrepancies, patient interviews are a must. The average study subject population for this large trial was 50 or so. I think any PI who enrolled a larger number of patients, should be closely examined. I know that there are restrictions or the lack of man power to inspect all PIs (over 1800 in this study) (Around 25,000 subjects), but I think FDA needs to take the initiative to at least examine the monitoring reports, case reports etc. I also think that an analysis should be conducted on blood values for other sites similar to what was done with Campbell's site. (Not the way Aventis conducted the analysis)

It is my belief that Aventis took the "Plausible Explanations" from Campbell, disregarded Dr. Reynolds's report and submitted the NDA. I think they had their fingers crossed with hopes that FDA would not inspect any of the sites. I think they miscalculated and that is the reason we are at this point in time.

The End