

Alguacil, Maribel PH/US

From: Jessica Lasley [jessica.lasley@rtp.ppd.com]
Sent: Wednesday, February 27, 2002 3:15 PM
To: Grethe, Nadine I. PH/US; Khosla, Ranjan PH/US
Cc: McCormick Robert; Cathy Tropmann; Teresa Dunlap; Melinda Edwards; Ann Marie Cisneros; John Reynolds; Price Mary
Subject: Teleconference to discuss findings from monitoring Kirkman-Campbell
Importance: High



Ketek Findings at Dr
Campbell b...

Hi, Nadine and Ranjan,

The PPD team met with Robert McCormick, VP Quality Management Systems at PPD, yesterday to review some of the information regarding TREAT study site 1129, Dr. Kirkman-Campbell. We would like to hold a teleconference with you to review some of the information that is of concern to us. Some of the items that we reviewed with Robert and he agreed were of concern include:

- * proper diagnosis of an appropriate medical condition to warrant study entry was lacking
- * medical charts were very limited
- * time of randomization in the IVRS (large numbers of patients in a short increment of time and most occur when the office is closed for lunch and not seeing patients)
- * consent form anomalies including date modifications and patient signature inconsistencies
- * analysis of lab values for multiple patients suspiciously similar

Ann Marie and John have assembled some examples of this information that we can share with you. Let us know when it would be possible to discuss this with you. We have attached a summary of Ann Marie's findings during her visit. We also have some examples of findings that we could fax to you in advance of our teleconference that might be helpful. Many thanks, Jessica

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Findings at Dr. Anne Kirkman-Campbell's site (copies of consents and charts were obtained):

Informed Consent Issues:

Subject VGS Informed Consent signature for the Subject does not resemble the signature in the Subject's medical chart, however, does match the study coordinators handwriting. This appears to be a forged signature.

Subject 361/SMD- Initials on each Informed Consent page differ and do not resemble the Subject's signature.

Subject 388/DLB- Initials on each Informed Consent page differ and do not resemble the Subject's signature.

Subject 335/FSC- Initials on each Informed Consent page differ and do not resemble the Subject's signature.

Subject 333/BLW- Initials on each Informed Consent page differ from the subjects. The date of signature was changed from 1/17/02 to 1/18/02 and 'verified' by the subject, however, the initials do not match the subject's signature.

Subject 077 is 89 years old, has Alzheimer's disease, and appears to be living in a nursing home. This subject signed, but did not date her own consent.

Source Document Issues:

Subject 361/SMD- The Subject's medical chart consisted of 3 total pages. One page had the Visit 1 and 2 dates the subject was seen for the TREAT study, another page had the study drug given to the subject and one page was totally blank. (this chart is included in the packet)

Subject 333/BLW- the day of Visit 1 was changed from 1/17/02 to 01/18/02 on only one page of the 2 page medical chart. The subject was being seen for follow up on hypertension. In different ink "sinus congestion x2 days" was added. (See informed consent issue for this subject above)

Subject 272/JW- Subject was randomized in the IVRS and the day of Visit 1 on the CRF occurred on 1/16/02, however the consent was signed and blood sent in on 01/09/02. The subject's medical chart does not indicate a visit on 1/9/02, however the subject had labs drawn (not study related) on 01/08/02. In the medical chart there is documentation of a visit occurring on 01/08/02, however that date was changed to 1/16/02. It is apparent the subject did not date their signature on page 6 of the ICF. The lab results from 01/08/02 are similar to those sent in to Covance on 01/09/02. Labs were not sent in on 1/16/02.

Subject 077/RLY-Subject was seen on 11/30/01 for feet and ankle swelling. In a different pen, "chest congestion x3days" was marked on the form and Acute Exacerbation of Chronic Bronchitis indicated. The subject's physical exam, respiratory section, respiration were even and unlabored, clear/equal sounds bilaterally, lung fields no flatness, dullness or hyperresonance. The subject does not have a history of bronchitis.

Subject 405/NCG- the day of Visit 1 was the first day the subject was seen in the office. Chief complaint was back pain, in different ink in the middle of the medical history page, "chest congestion 2-3 days" was written in. The subject did not have a history of Chronic Bronchitis, or any respiratory problems.

Subjects 312, 361, 344, 355, 300, 263, 223, 196, 359, 407, 405, 393, 188, 161, 135, 077, 063 were diagnosed with AECB, however had no history or limited history of bronchitis.

General Issues noted: (copies not obtained)

- Dating changes were made via write-overs throughout the medical charts. They were mostly changing the date that was originally documented to the day of Visit 1.
- The majority of the consents were not dated by the subjects.
- Subjects with diagnoses of AECB had no physical symptoms indicated, i.e., lungs were clear, etc.
- The office is closed from noon-2 p.m. every day. This was confirmed by me on the 3 days I monitored at the site. The site does not see patients between this time period. An analysis of the dates and times patients were registered in the IVRS at this site indicates that many patients were entered in the IVRS during this time frame. (See IVRS analysis).
- The study coordinators would not talk to me and whispered to the PI anytime that I was within listening distance.
- I am concerned about confidentiality with this PI as she gave me an informed consent for a different study to copy.
- Out of 407 subjects there were 0 SAE's
- Out of 407 subjects there were 4 AESI's, all hepatic lab events that were captured by John Reynolds, MD.
- No CAP subjects were randomized.
- Out of 407 subjects, there were maybe a dozen AE's reported.
- Out of 354 subjects, 85 of them were randomized with AECB. Once AS was closed in the IVRS, the site enrolled 52 AECB subjects within a week.

Prepared by Ann Marie Cisneros, Sr CRA, PPD Development February 27, 2002

