

Khosla, Ranjan PH/US

From: Christopher Jones [Christopher.Jones@rtp.ppd.com]
Sent: Monday, January 21, 2002 1:27 PM
To: Catherine Ross
Cc: Melinda Edwards; Ann Marie Cisneros; Tammye Morgan; Jackie
Subject: Re: Dr. Garner

I have deactivated this site.

Chris

Catherine Ross wrote:

Chris,

Please shut off Site 0881 / Dr. Garner from enrolling any more subjects within the IVR. Apparently, has enrolled at least one subject today already. I also left a message on the IVR Hotline.

Thank you for your prompt attention to this request.

Sincerely,
Catherine

Melinda Edwards wrote:

Dr. Garner/NY (site 0881)

This site was monitored on Thursday, 1/17/02. The site had significant issues which were discussed with Nadine during the Aventis call on Friday. Nadine agreed that this site needed to be shut off in the IVRS.

Summary of issues:

- enrolled 86 subjects
- indicates that has Phase II, III, IV research experience
- several subjects were enrolled prior to signing the revised consent. The subjects signed the revised consent and back dated the consent. The originals were thrown in the trash.
- PI signed the revised consent and photocopied each with his signature. Many have a copy of the PI signature and many are not dated by the PI.
- PI enrolled himself in the study
- No source docs on many subjects.
- consent forms were missing for 4 subjects
- unreported adverse events

There were some other issues as well, but these were discussed with Nadine who agreed that we should stop the site from enrolling any additional subjects.

Melinda

Khosla, Ranjan PH/US

From: Ann Marie Cisneros [annmarie.cisneros@rtp.ppd.com]
To: Khosla, Ranjan PH/US
Cc: Melinda Edwards; Jessica Lasley; Catherine Ross; Mary Ann Russo
Subject: Re: Problems at Dr. Terpstra's site: TREAT Study

Ranjan-
Thanks for your reply. This site has been closed in the IVRS and follow up regarding the issues you outlined will be a joint effort between the site management CRA and the field monitor. I will forward you the follow up letter and trip report for Dr. Garner's site in addition to Dr. Terpstra's as you requested.

Kind Regards,
Ann Marie

Ranjan.Khosla@aventis.com wrote:

- > Dear Ann Marie,
- >
- > Thank you very much for informing us about the GCP Issues at the site of
- > Dr. Terpstra's site. I discussed the information provided by you with
- > Gerard Marini, Head of GCP NA Operations Center. Following are our
- > commendations:
- >
- > 1. Please close the IVRS to this site immediately so that no new subjects
- > are enrolled before we have ensured that site has resolved all outstanding
- > issues.
- >
- > 2. Please send a Certified Letter to the site requesting the site to create
- > an action plan to resolve all outstanding issues. Please ensure that all
- > issues are addressed in the Certified letter and the following
- > recommendations provided to the site:
- > A. For subjects 089, 092, 093, and 095-160 in whose ICFs one of the phone
- > numbers had been marked out with black marker, the site should have the
- > subjects sign a new ICF with current date, generate a Memo to File and
- > notify the IRB.
- > B. For subjects 001-160 the ICF indicated that the subjects would not be
- > receiving compensation; however, the PI was compensating subjects \$35 if
- > they completed the study. The PI is not required to pay the subjects as the
- > IRB approved ICF does not require that. However if he wants to pay the
- > subjects he should have a transparent process of paying all the subjects
- > regardless of whether the subjects completed the study. This is to ensure
- > that there is no element of coercion involved.
- > C. Please remind the site to follow the protocol diligently. The site should
- > document all protocol violations in Memos to File and report them to the
- > IRB.
- > D. The site need to document due diligence in having the subjects come in
- > for visit 2 by making phone calls and if that fails then by sending
- > Certified Letters to the subjects.

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> E. TRAINING: Please retrain the site about the proper informed consent
> procedure as noted in ICH GCP Guidelines section 4.8 and in the 21 CFR Part
> 50. Also retrain the site about proper source documentation practices as
> described in the ICH 1.51, 1.52 and 4.9. Please document all the training
> provided to the site. Please reeducate the site about the protocol inclusion
> and exclusion criteria.

> F. Please request the site to complete the CRFs and logs in a timely manner.

> 3. Please ensure that the site creates and implements an action plan to
> resolve the QA issues and please assess compliance in a future monitoring
> visit. If the site is found to be compliant in the next monitoring visit,
> then they should be allowed to enroll more subjects. If the site does not
> comply to the above mentioned recommendations, please close the site.

> Please feel free to call/ email if you have any questions.

> Thanks and regards

> Ranjan Khosla, MBBS, MD, CQA

> Senior GCP/QA Specialist

> GCP NA Operations Center

> Aventis Pharmaceuticals

> Mail Code: EM-B1A

> Route 202-206, P.O. Box 6800

> Bridgewater, NJ 08807-0800

> Phone: 908 541 5476

>-----Original Message-----

> From: Ann Marie Cisneros [mailto:annmarie.cisneros@rtp.ppd.com]

> Sent: Tuesday, January 22, 2002 9:45 PM

> To: Khosla, Ranjan PH/US; jessica.lasley@rtp.ppd.com;

> melinda.edwards@rtp.ppd.com

> Subject: Problems at Dr. Terpstra's site

> I am forwarding an e-mail in regards to Dr. Terpstra's site. The
> monitor recommends the site be shut down in the IVRS and have a
> re-visit. The IRB has been notified of the ICF changes.

> Please advise-

> Ann Marie Cisneros

> Subject: Problems at Dr. Terpstra's site

> Date: Tue, 22 Jan 2002 20:40:00 -0600

> From: MaryAnn.Russo@wilm.ppd.com

> To: annmarie.cisneros@rtp.ppd.com

> Ann Marie,

> I wanted to give you a summary of Dr. Terpstra's site. Please forward
> this e-mail to those involved.

> The following items cause concern and I think it would be in our best
> interest to close enrollment overall at this site.

> All ICF had been altered in some way
> A. For subjects 089, 092, 093, and 095-160 one of the phone numbers
> had been marked out with black marker
> B. For subjects 001-160 the ICF indicated that the subjects would
> not be receiving compensation; however, the PI was compensating subjects
> \$35 if they completed the study. Subject that did not complete the
> study did not receive any compensation.
> The PI was unaware of GCP guidelines and IRB procedures. When I
> discussed these with the PI he was argumentative about compiling with
> the guidelines and the IRB. The PI did not seem interested in learning
> about GCP guideline or in following the guidelines.

> 2. Over 20 protocol violations were documented with the ICFs (this is
> not including the previously mentioned PVs). For example, several ICFs
> were not dated by the PI and consentor, one of the ICFs could not be
> located, and several ICFs did not have corresponding signature dates
> between the PI and subject.

> 3. A cursory look at CRFs and source documents indicated that many
> subjects had visit 1 but had not come back for visit 2. Usually one
> phone call was being made and no other follow up was made to have the
> subjects return to the office.

> I was only able to look at 3 subjects; however, 2 of the 3 were
> enrolled with allergies to beta-lactam antibiotics. When I discussed
> this with the PI he questioned this exclusion criteria and when I showed
> him the criteria in the protocol he indicated he wasn't aware of this
> until I showed him. The PI continued to question this exclusion
> criteria.

> 5. CRFs and logs are not legible and they are incomplete.

> The PI does not have a SC or SI assisting him with the study. He is
> doing all the work himself and with 160 subjects it appears to be too
> much. Of more concern, the PI does not seem interested in correcting or
> learning from these errors.

> Please let me know if you have any questions about this site.

> Thanks

> Mary Ann

> * Mary Ann Russo <maryann.russo@wilm.ppd.com>

> Clinical Research Associate II

> PPD Development

> Wilmington TCC

> Mary Ann Russo