From: Woollen, Stan - OC
Sent: Thursday, February 27, 2003 7:58 AM
To: [Redacted]
Subject: RE: And more

[Redacted],

In answer to your first question I would punt this back to the IRB regarding what their expectations are. I suspect the only reason they assign an expiration date is to ensure the investigator comes back to them within a year for continuing review of the study. FDA certainly has no requirement for approval dates or expiration dates on the ICF. This is an IRB procedure. I would say that if the IRB required no new information to be provided to the subjects, there would be no need to obtain a new consent form.

The second question about the 1572 is could probably be answered either way. One needs to consider the intent of the 1572. In my opinion, the 1572 or ?Statement of Investigator? is principally a means for the sponsor to obtain and document information about a site where they will be shipping and investigational product for study, as well as a means of obtaining and documenting the investigator's commitment to fulfill all of his/her responsibilities under the regulations (see block 9). The sponsor must obtain this information and investigator's commitment before they can ship the investigational drug. In the scenario you describe the sponsor appears to have selected a central radiology center to serve all of the sites in the study. Obviously the sponsor already has this information therefore listing it on the 1572 would not serve the purpose of communicating this to the sponsor. From this perspective documenting this information in the protocol or other regulatory documentation could probably suffice.

Now for the other answer, one could also argue that the form 1572 could serve to document agreement between the sponsor and the investigator as to who will be doing what. If this is the view of the sponsor, they may wish to have central labs and reading facilities listed on the 1572 to ensure the investigator understands this. We certainly have seen cases where a CI has sent samples to a lab not authorized by the Sponsor. Of course, this information could also be communicated in the protocol as well or by other means as well.

OK, pick the answer you like best and go with it.

Stan

-----Original Message-----
From: [Redacted]
Sent: Wednesday, February 26, 2003 9:49 AM
To: Woollen, Stan - OC
Subject: Re: And more

Thank you Stan- You be it is. Two other questions came up this week (I'm beginning to feel like I am a wealth of information- good thing).

1. We discovered at two different institutions that the IRB provided both an approval and an expiration date to the ICF, I.e. 12/02/01 through 12/01/02 and then again with annual re-approval- 12/02/02 through 12/01/03. Our opinions differ on how to handle this. Some of us feel that subjects active at the time of the re-approval should sign the second ICF because the original document is no longer valid. Others of us feel the subjects do not have to sign the second ICF because nothing substantial has changed about the study and the subjects were consented once. Getting your view on this situation will be greatly appreciated also.

2. I relayed the info about having the radiology centers where study related procedures are filmed recorded on section 4 of the 1572. Another question followed: If the films are being sent to a central reader who is

identified in the Sponsor's regulatory documentation), is it necessary to add the radiology centers to the 1572? I said yes, but was asked to swing this one by you again.

Thank you Stan!!
Best regards,
[Redacted]
----- Original Message -----
From: Woollen, Stan - OC

To: [Redacted]
Sent: Tuesday, February 25, 2003 7:18 AM
Subject: RE: And more

[Redacted]
I cannot comment on specific incidents without knowing the full details of the case. That said, I'll respond generally to the issue of who should be listed in section 6. For drugs and biological products, according to the regulations, a clinical investigator means the individual(s) who actually conduct(s) and take(s) responsibility for an investigation, i.e. under whose immediate direction the drug or biologic is administered or dispensed to a subject or who is directly involved in the evaluation of research subjects. Where an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. Subinvestigator includes any other individual member of that team (see 21 CFR 312.3(b). You may also want to refer to the E6 Consolidated Guideline on GCP http://www.fda.gov/oc/gcp/guidance.html for guidance regarding the definition and responsibility of study investigator. Hospital staff, including nurses, residents, or fellows and office staff who provide ancillary or intermittent care but who do not make direct and significant contribution to the data are generally not meant to be listed in box 6. A general statement regarding the participation of staff residents on rotation can be included in section 6.
This question does arise quite frequently and there really in no one answer that fits every case. It always comes down to how significantly do the individuals participate in the study conduct. Perhaps the closest thing we have to official guidance on the topic is found in our guidance on financial disclosure for clinical investigators http://www.fda.gov/oc/guidance/financialdis.html . Specifically, question 12 talks about who should be listed in the context of part 54. As you know, this became a much hotter topic when the Financial Disclosure rule required reporting by subinvestigators listed in section 6. I hope this information is helpful.
Stan
HI Stan,

Another question for you. One of my clients just called to report that one of their sites was cited on a 483 for not documenting the Study Coordinator in section 6 of the 1572. They are checking into it to see why, but I suggested I ask you.....Is it necessary to enter the SC on the 1572 if she/he is not conducting PEs or other clinical evaluations? If the SC is taking HX, vitals, blood samples, etc. We have been entering PA-Cs and NPs as sub-investigators, but not necessarily RNs. Do you have a spin on this one?

Thanks very much,
[Redacted]