From: OC GCP Questions
To: [redacted]
Subject: RE: FDA 1572 Question
Date: Thursday, September 17, 2015 10:34:00 AM

Dear [Redacted]-

Thank you for your question. I remember meeting some [Redacted] staff at a conference this past Spring and I'm glad they suggested you contact FDA.

FDA's IND regulations at 21 CFR 312.3(b) define an investigator: "*Investigator means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event 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."*

21 CFR 312.53(c)(1)(viii) requires the sponsor to obtain information from the investigator, including *"a list of the names of the subinvestigators (e.g., research fellows, residents) who will be* ***assisting the investigator in the conduct of the investigation(s)*** *." [emphasis added]*

The 1572 is a form the sponsor is responsible for obtaining (refer to 21 CFR 312.53(c)) and is meant to supply the study sponsor with pertinent information about a site who is conducting a particular study. The 1572 also serves as an agreement by the investigator, once signed, to comply with the investigational plan/protocol and pertinent regulations. For studies being conducted under an IND, the sponsor is required to submit information on investigators participating in a study to their IND (refer to 21 CFR 312.23(a)(6)(iii)(b) and 312.30(c)). Since the information required to be submitted to the IND is the same information collected on the 1572, sponsors usually submit copies of 1572s to FDA to fulfill this requirement because it provides a convenient means of supplying the required information.

As you know, the regulations do not specifically address how to complete the Form FDA 1572. When the regulations are silent investigators, institutions, sponsors, and IRBs are free to develop their own procedures and practices as long as applicable regulatory requirements are met.

Thanks for mentioning that you have already reviewed FDA's guidance on the Form FDA 1572 found at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf. Section VII of the document, and question #s 31-35 are meant to provide guidance on who should be listed as a subinvestigator on the 1572. As you mentioned, the guidance recommends that the decision to list an individual in Section #6 depends on his/her level of responsibility (i.e., whether he/she is performing significant clinical investigation-related duties). As the guidance suggests, the decision about who to include on the 1572 is a matter of judgment and is dependent upon the contribution that the individual makes to the study.

The guidance is meant to provide flexibility in how to determine on a study-by-study basis, who should be included on the 1572. While I realize your struggle with determining the meaning of the phrase "*performing significant clinical investigation-related duties*", I also recognize that the meaning of "*significant clinical investigation-related duties*" can vary from study to study, so it is difficult to be any more prescriptive in guidance about how to interpret this – one size does not seem to fit all study scenarios. However, the FDA guidance does go on to say, "*In general,* ***if an individual is directly involved in the performance of procedures required by the protocol, and the collection of data, that person should be listed on the 1572****. [emphasis added] For example, if the protocol notes that each subject needs to visit a specified internist who will perform a full physical to qualify subjects for the clinical investigation, that internist should be listed in Section #6."*

In considering the internal suggestions you shared (i.e., including the names of the biostatisticians in box #6, or including all Pediatric Nurse Practitioners), you will want to think through whether the biostatisticians or all of the Pediatric Nurse Practitioners are assisting the investigator in the conduct of the investigation, performing critical study functions, and making direct and significant contributions to the data.

Since the Form FDA 1572 is a sponsor form/responsibility, I suggest you discuss the expectations for box #6 with any sponsors you are working directly with on any given study, as they may have suggestions and/or expectations that you need to be aware of.

However, if you are working with/assisting investigators at your institution who are functioning as sponsor-investigators, I suggest that you discuss the 1572 form and the guidance with the various investigators and the appropriate institutional officials to determine whether there is any site or institutional expectations for completing the 1572 form. You may want to discuss setting expectations that best suit the studies in question and your specific business practices.

I also wanted to share with you that FDA's Office of Good Clinical Practice (OGCP), which is the group that I work in, has a central public mailbox where we welcome GCP questions (gcp.questions@fda.hhs.gov). You can find information about OGCP and the public mailbox address at the following web location http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm134476.htm. I am responding to your question through the OGCP mailbox address. We find that it is best to ask the public to send questions to the public mailbox instead of to a particular staff member because the mailbox is monitored Monday through Friday each week. Sending a question directly to a specific staff member may result in a delay if that staff member is out of the office, so please feel free to use the public mailbox for future questions. Also, simply for your reference, FDA posts "*Replies to Inquiries to FDA on Good Clinical Practice*", which is a compilation of previous GCP questions from the public and our responses. The questions are redacted and are followed by the OGCP office response. Questions and responses are categorized by topic and filed in folders by year (years 2002 to 2014). You can see the redacted questions and responses at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm .

I hope this information is useful. If you need further information and/or have additional questions, please feel free to contact us at the official GCP mailbox, gcp.questions@fda.hhs.gov. As mentioned above, you may also find it useful to access the set of redacted GCP e-mails found at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm since we find that many questions and concerns are repeated over time.

Best Regards,

Janet

Janet Donnelly, RAC, CIP
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Office of Special Medical Programs, Food and Drug Administration

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From: [redacted]
Sent: Monday, September 14, 2015 10:53 AM
To: Donnelly, Janet
Subject: FDA 1572 Question

Dear Mrs. Donnelly,

I am working with investigators at [redacted] on new and existing IND applications.
There seems to be a fair amount of confusion regarding the 1572 and who should be listed. A coworker who attended one of your talks recommended that I reach out for more specific guidance. Judging from the amount of information on the web relating to this, I do not feel alone in my confusion.

I am familiar with the below information from the FDA and have seen several questions of a similar nature. We find ourselves struggling with the definition of "performing significant clinical investigation-related duties." For example, we received the suggestion to add statisticians to section 6, but do not see how their role impacts clinical care. We have also received the internal suggestion to include all Pediatric Nurse Practitioners, which would add a dozen plus individuals.

If you have any suggestions on how we can most effectively complete the form while maintaining compliance, we would be most appreciative.

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf

Thank you very much for your time,
[redacted]