Contractual versus regulatory obligationsFrom: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Friday, September 30, 2005 3:06 PM
To: [purged]
Subject: RE: Contractual versus regulatory obligations

Dear Ms. [purged]:

Your question about completing the Form FDA 1572 (1572) was forwarded to me for a response.

The short answer to your question is: the investigator at each of the sites should sign his/her own 1572, and the investigators at sites #2 and #3 should not be listed as "sub-investigators" on the 1572 for site #1. I say this for the following reasons:

FDA regulations use the terms "investigator" and "sub-investigator":

> "Investigator means an individual(s) who actually conduct(s) a clinical investigation (i.e., under whose immediate direction the drug or biologic 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." (See 21 CFR 312.3.)

For IND studies, sponsors are required to obtain a 1572 from each investigator before permitting the investigator to begin participation in an investigation. On the 1572, the investigator is required to list, in block #3, the names and addresses of the facility or facilities that he/she will use to carry out the study. He/She is required to list in block #6, the names of the "subinvestigators (e.g., research fellows, residents, associates) who will be assisting the investigator in the conduct of the investigation(s)." (See 21CFR 312.53(c)(1)(viii).)

The prefix "sub-" in "sub-investigator" implies that the "sub-investigator" is subordinate to (i.e., reports to) the investigator who is responsible for the conduct of the study. Indeed, it is not possible to delegate clinical investigator responsibilities under the regulations --- only tasks can be delegated, as appropriate, to individuals qualified to conduct them, based on their education, training, and experience; thus, the investigator remains responsible under the regulations for personally conducting or supervising all aspects of the study at the sites that have been identified.

FDA's official guidance, the ICH E-6 Good Clinical Practice: Consolidated

Guideline, contains the following definition for "Investigator" in section 1.34:
"A person responsible for the conduct of the clinical trial at a trial site.
If a trial is conducted by a team of individuals at a trial site, the
investigator is the responsible leader of the team and may be called the
'principal investigator'." Thus, the ICH guideline supports the position that
there should be a responsible individual at a trial site who is responsible for
the conduct of the clinical trial at that site.

In your e-mail, you stated that personnel from site #1 will not be performing
any study related duties at sites #2 or #3 and vice versa. This further
supports the need to ensure that each site has its own investigator, and that
each investigator sign his/her own 1572.

If the investigators for sites #2 and #3 are listed as sub-investigators on the
1572 for site #1, this will only cause confusion as to who is responsible for
carrying out the study related functions at sites #2 and #3. Likewise, the
1572 for site #1 should only list personnel who are actually at site #1.

I hope this helps to clear up any confusion.

Sincerely,
Carolyn Hommel
Consumer Safety Officer
Good Clinical Practice Program
Office of Science and Health Coordination
Office of the Commissioner
U.S. Food and Drug Administration (HF-34)
5600 Fishers Lane, Room 9C24
Rockville, MD 20857
Phone: 301/827-3340
Fax: 301/827-1169
This communication does not constitute a written advisory opinion under 21 CFR
10.85, but rather is an informal communication under 21 CFR 10.85(k) which
represents the best judgment of the employee providing it. This information
does not necessarily represent the formal position of FDA, and does not bind or
otherwise obligate or commit the agency to the views expressed.

-----Original Message-----
From: [purged]
Sent: Thursday, September 15, 2005 1:14 PM
To: gcpquestions@oc.fda.gov
Subject: Contractual versus regulatory obligations

This question involves 3 clinical trial sites for a federally-funded clinical study.
Because this is a federally-funded study, additional sites were added under the contract for an existing site, rather than contracting with these sites as independent sites. The contractual obligations with the federal agency require the PI at site 1 to oversee sites 2 and 3; however, sites 2 and 3 each have their own PI, both of whom have signed an FDA-1572. Although sites 2 and 3 have their own FDA-1572, the FDA-1572 from site 1 lists all the personnel at sites 2 and 3 as sub-investigators, even though none of the personnel from sites 2 and 3 work at the site 1 clinic. Personnel (including the PI) from site 1 do not treat any subjects from sites 2 and 3. It appears as though there has been some confusion between the contractual obligations and regulatory obligations with these sites and we would appreciate your feedback on the following questions. Should the personnel from sites 2 and 3 be listed on the FDA-1572 form site 1? If yes, is it necessary for site 1 to maintain a set of duplicate regulatory documents for sites 2 and 3? It would seem that the FDA-1572 from site 1 should just list the personnel working on the study at site 1. Do you agree?
[purged]