From: Toth-Allen, Jean
Sent: Tuesday, December 12, 2006 2:40 PM
To: [Redacted]
Subject: RE: Protocol signatures

Dear [Redacted]:

Thank you for your inquiry regarding the signing of study protocols.

There is a mention in the ICH GCP guidance (available at http://www.fda.gov/cder/guidance/959fnl.pdf), a guidance document with which FDA concurs, that states

"The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement." (4.5.1)

However, FDA cannot and does not enforce guidance, but only regulation, and there is no requirement in FDA regulations that the protocol be signed. Assuming that the study in question is FDA-regulated, FDA regulations do require a signed Form FDA-1572 for pharmaceutical studies (Title 21, Code of Federal Regulations - 21 CFR - 312.53(c)(1)) or a signed investigator agreement for device studies (21 CFR 812.43(c)). These documents would qualify as the "alternate contract" spoken of in the GCP guidance citation above. If a site has sent a study to an IRB for review and approval, it would seem that the 1572/investigator agreement would need to be in place beforehand, signaling an agreement between the site/clinical investigator and the sponsor. I am hoping that the audit you are referring to was one requested and paid for by your firm and not an FDA inspection of your study, since guidance does not impose requirements, as stated above.

Hope this information is useful. If you need further information and/or have additional questions, please submit them once again to the official GCP mailbox, gcp.questions@fda.hhs.gov, in lieu of responding to my personal e-mail address.

Sincerely yours,

Jean Toth-Allen, Ph.D.
Good Clinical Practice Program
OSHC, Office of the Commissioner, US FDA

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.

From: [Redacted]
Sent: Monday, December 11, 2006 5:39 PM
To: OC GCP Questions
Subject: Protocol signatures
Importance: High

A recent audit resulted in the following observation:

"Since the GCPs require that the protocol be signed to be considered final, it is implied that it be signed and dated prior to IRB approval. It is unclear whether it is [Redacted] responsibility to assure that the protocol has been signed, but it appears prudent that [Redacted] review a signed copy, as until it is signed, it is considered a draft, not a final."

Can you direct me to the regulation that supports this observation?

We have approximately 20 days to respond to this observation.

Your prompt attention is appreciated.

Regards,

[Redacted]