From: OC GCP Questions
To: [redacted]
Subject: GCP Question - Noncompliant Sites
Date: Thursday, April 13, 2017 6:15:00 AM
Attachments: [redacted]

Good morning –

As you are probably aware "promptly" is mentioned numerous times in FDA regulations. However, I don't believe it has been formally defined by FDA.

The scenario you describe in your second paragraph may not conflict with FDA regulations. All sites should have standard operating procedures in place to deal with non-compliance including those that pose a risk to subjects.

Kind regards,

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From: [redacted]
Sent: Wednesday, April 12, 2017 1:52 PM
To: OC GCP Questions
Subject: GCP Question - Noncompliant Sites

Hello and thanks for a very helpful section on the web site. I am a former ORA employee (23 years in FDA) who began doing bi-mo inspections way back in 1974. I presently consult on GCP compliance issues with a variety of clients.

Recently someone asked the meaning of the word "promptly" within 21 CFR 312.56(b), e.g., "A sponsor who discovers that an investigator is not complying with the signed agreement (Form FDA-1572), the general investigational plan, or the requirements of this part or other applicable parts shall promptly either secure compliance or discontinue shipments of the investigational new drug to the investigator and end the investigator's participation in the investigation." (A parallel requirement can be found in ICH E6 at Section 5.20.2.)

My answer was that "promptly" within the meaning of this section was a relative term at best and would be a judgment call based on the specific circumstances. I advised that if there was sound justification, documented, that could establish an (1) an ongoing effort to work with the site to

secure compliance, (2) continuous progress toward that end on the part of the site, (3) assurance, including the imposition of interim controls if necessary, to assure that patient safety, human subjects' rights (informed consent), data integrity and investigational product accountability were under control, and deliberate wrongful conduct was not involved, that should preclude an immediate need to close the site and report to the agency. If there was slippage in one of those critical factors then escalation to closure and reporting would be warranted. I further suggested that the sort of interim controls that would be helpful might include an enrollment suspension pending correction of issues, increased frequency and depth of monitoring, escalation of response from the CRO or sponsor (such as peer to peer discussion between the PI and medical monitor) or other similar steps.

Does this sound reasonable? Has the agency ever spoken officially as to the meaning of "promptly" within this section of the regulations? I want to make sure I am guiding clients in the right direction on this.

Thanks.