From: OC GCP Questions
To: [redacted] OC GCP Questions
Cc: [redacted]
Subject: RE: question
Date: Thursday, October 06, 2016 10:00:29 AM
Attachments: [redacted]

Hello, [redacted],

The term "protocol deviation" is not defined in FDA's regulations; however, in FDA's Compliance Program Guidance Manual (CPGM) chapter on clinical investigator inspections (www.fda.gov/ICECI/EnforcementActions/BioresearchMonitoring/ucm133569.htm), protocol deviation is described as generally being "*an unplanned excursion from the protocol that is not implemented or intended as a systematic change. A protocol deviation could be a limited prospective exception to the protocol (e.g., agreement between sponsor and investigator to enroll a single subject who does not meet all inclusion/exclusion criteria)*." Like protocol amendments, deviations initiated by the clinical investigator must be reviewed and approved by the IRB and the sponsor prior to implementation, unless the change is necessary to eliminate apparent immediate hazards to the human subjects (21 CFR 312.66), or to protect the life or physical well-being of the subject (21 CFR 812.35(a)(2)). Analogous language on protocol deviations can be found in "ICH E6 Good Clinical Practice: Consolidated Guidance" (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf), which is considered FDA guidance (see section 4.5.2). Additional discussion about protocol deviations and what inspectors evaluate during an inspection is described in the Clinical Investigator CPGM.

Although the FDA regulations require changes to the protocol to be reviewed by an IRB before they are initiated (unless necessary to eliminate an immediate hazard), FDA guidance does allow minor changes to be reviewed through an expedited review procedure. Please see question 20 in FDA guidance "Institutional Review Boards Frequently Asked Questions – Information Sheet" (http://www.fda.gov/RegulatoryInformation/Guidances/ucm126420 htm) for more details. Similarly, the situation you describe appears to be a good example of why building a lit bit of flexibility into a protocol is often a good thing to do whenever it is possible.

I hope this information is helpful to you. If further assistance is needed, please feel free to contact us once again at the official GCP mailbox, gcp.questions@fda.hhs.gov.

Thanks,

Kevin

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From: [redacted]

Sent: Tuesday, October 04, 2016 8:23 AM
To: OC GCP Questions; Prohaska, Kevin
Cc: [redacted]
Subject: question

Hello

I am writing to obtain clarification with regard to FDA regulatory requirements for obtaining prospective IRB approval of minor protocol deviations. Typically, we have not required the investigator to obtain prospective IRB approval for minor deviations that have no impact on participant safety or the scientific conduct of the study. For example, a follow up scan that was required by the protocol to take place on a certain date, but due to that day falling on a holiday, was performed slightly out of window. There were no safety implications with this deviation. We would like to confirm that a minor deviation such as this would not require prospective IRB approval.

Thank you

[redacted]

[redacted]