From: OC GCP Questions
To: [redacted]
Subject: Protocol Deviations/CAPAs
Date: Tuesday, February 27, 2018 11:12:00 AM
Attachments: [redacted]

Good morning –

Corrective and preventive action (CAPA) programs are not a specific regulatory requirement in FDA's regulations related to clinical trials (21 CFR parts 50, 56, 312 and 812) but are discussed in the quality system regulation for medical devices (21 CFR part 820). Additionally, FDA does not have a CAPA template.

I can offer you the following general information on CAPA plans. FDA would expect an investigator, the investigational site and/or the sponsor to take corrective actions when issues arise during a clinical investigation and to document the actions taken. Several FDA guidance documents indicate this. See for example:

- "Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects" (available at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf) includes as a possible element for an investigator's plan to supervise and oversee a clinical trial "A procedure for the timely correction and documentation of problems identified by study personnel, outside monitors or auditors, or other parties involved in the conduct of a study."

- "IRB Continuing Review after Clinical Investigation Approval" (available at www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf) indicates that, when an IRB notes a pattern of non-compliance with the requirements for continuing review, "the IRB should determine the reasons for the non-compliance and take appropriate corrective actions."

- "Oversight of Clinical Investigations - A Risk-Based Approach to Monitoring" draft guidance (available at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf), when discussing possible components of a monitoring plan to address management of noncompliance, "Processes to ensure that root cause analyses are conducted where important deviations are 456 discovered and that appropriate corrective and preventive actions are implemented to address issues identified by monitoring."

- "FDA Inspections of Clinical Investigators" (available at www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126553.pdf) indicates that an FDA investigator may inspect records to ascertain "corrective actions in response to previous FDA inspections, if any"; that if significant violations of FDA regulations are found, a warning letter may be issued and "include a request for correction and a written response to the agency"; and that "If, in response to the NIDPOE (notice of initiation of disqualification proceedings and opportunity to explain), the investigator provides an explanation that is accepted by the agency and the disqualification is not warranted, alternatives such as a detailed corrective action plan may be considered."

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov if you have additional questions.

Kind regards,

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From: [redacted]
Sent: Monday, February 26, 2018 4:06 PM
To: OC GCP Questions <gcp.questions@fda.hhs.gov>
Subject: Protocol Deviations/CAPAs

Hello,
Is there any guidance on when to implement a CAPA after a review of protocol deviations? For example, a CAPA would be needed after the discovery of a single critical deviation, but only after a certain number of repeat offenses for minor deviations.
Thank you,

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