From: OC GCP Questions
To: [redacted]
Subject: FDA access to CAPAs
Date: Wednesday, September 23, 2015 6:14:26 AM

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).

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 http://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 http://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- "Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring" draft guidance (available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf), when discussing possible components of a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 http://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."

These guidance documents indicate that FDA review of records may include CAPA plans specific to a problem that occurred during a trial and CAPA plans that are part of trial monitoring or quality assurance. If an establishment has a GCP CAPA plan that is separate from the ongoing monitoring and quality assurance programs, it would seem unlikely that FDA would review those records. If, however, the establishment references those plans as a means of addressing problems found during an FDA inspections, than I believe the CAPA plans would be subject to FDA review.

I hope this information is useful to you. If you need further information and/or have additional questions, please feel free to contact us at gcp.questions@fda.hhs.gov.

Kind regards,

Doreen M. Kezer, MSN

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Office of Good Clinical Practice
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From: [redacted]
Sent: Tuesday, September 22, 2015 2:32 PM
To: OC GCP Questions
Subject: FDA access to CAPAs

Dear Staff:

I recently was asked if FDA accesses CAPA (Corrective and Preventative Action) during clinical investigator/site BIMO inspections? Please advise.

Thanks in advance for your time and attention to this question.

With best regards,
[redacted]