**From:** OC GCP Questions
**To:** [redacted]
**Subject:** RE: Corrective and Preventive Actions
**Date:** Friday, July 24, 2015 10:41:00 AM

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[redacted],

Thank you for your inquiry. Corrective and preventive action (CAPA) programs are not specifically addressed 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).
For GCPs 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" 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 discovered and that appropriate corrective and preventive actions (e.g., additional training on a study or study site level) 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."

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. Compliance Program Guidance Manuals (CPGMs) were developed to provide uniform guidance and specific instructions to the FDA field investigators for conducting inspections of Clinical Investigators (CP 7348.811), Sponsors (CP 7348.810), In-Vivo Bioequivalence facilities (CP 7348.001), Institutional Review Boards (CP 7348.809), and Nonclinical Laboratories (CP 7348.808). FDA makes these documents available to the public at http://www.fda.gov/ICECI/ComplianceManuals/ComplianceProgramManual/ucm255614.htm. Specifically, the CPGM for Sponsors (CP 7348.810) and Clinical Investigators (CP 7348.811) each discuss corrective actions and what investigators will look for with regard to corrective actions during an inspection.

Also, the definitions that have been referenced for Corrective Action and Preventive Action in presentations made by FDA staff (which can be found on the FDA website, see link below) are from ISO 9000:2005.

- Corrective Action (CA): Action to eliminate the cause of a detected nonconformity or other undesirable situation in order to prevent recurrence. There can be more than one cause of a nonconformity.

- Preventive Action (PA): Action to eliminate the cause of a potential nonconformity or other undesirable potential situation in order to prevent occurrence. There can be more than one cause for a potential nonconformity.

http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm337109.pdf

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

additional questions.

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**From:** [redacted]
**Sent:** Monday, July 20, 2015 4:11 PM
**To:** OC GCP Questions
**Subject:** Corrective and Preventive Actions

Dear FDA,
Can you define FDA's expectations for preventive actions? Currently our Quality System within our company defines preventive actions as per GMP definitions in that Preventive Actions are to prevent a quality issue or event from occurring.

In the GCP space we implement Preventive Actions in response to quality issues or events that have already occurred, have an corrective action implemented if possible and implement a preventive action to prevent it from reoccurring.

What is FDA's definition of a Preventive Action in the GCP space?
Thank you,
[redacted]