When there is an assessment of “Unacceptable” or “Acceptable, Needs Follow-up” in any of the three components of a SWOG Institution’s Quality Assurance Audit Report, a response is required, usually within 21 days. The focus of the response must be on documenting the institution’s actions taken to correct the deficiencies found, and also on the Corrective and Preventive Action (CAPA) that will be implemented to prevent future occurrences of these deficiencies.

The following information is provided to help guide the institution through the CAPA process. A template is provided to document the response & to assure that all identified deficiencies are addressed, that the response is adequate, and that the required supporting documentation is both present and organized. The template is a Microsoft Word document in which the institution’s data and responses can be entered. Use of this particular document is not mandatory; however, organizing the response in this way will expedite review and completion of the audit process.

**What is Corrective and Preventative Action (CAPA)?**

“A corrective and preventive action (CAPA) plan is a series of actions taken to resolve a compliance issue, and most importantly, to prevent further recurrence” (Bishany & Gorkun, 2019) (available at <https://www.socra.org/blog/corrective-and-preventative-action/> )

Although CAPAs are not specifically addressed in the FDA regulations related to clinical trials the CAPAs origin
stems from Good Manufacturing Practices (GMP) and are addressed specifically in 21CFR part 820 Quality
System Regulations. SWOG requires CAPAs when major findings of non-compliance occur. The following are some of the FDA guidance documents that discuss requirements for components of the CAPA:

* “Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects” (<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.”
* “Oversight of Clinical Investigations - A Risk-Based Approach to Monitoring” guidance (available at
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf> ) , discusses 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
<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”
* “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.”

**What are the Essential Components of a CAPA?**

* **Corrective Action:** this component of the CAPA addresses any immediate action needed to resolve or correct the specific deficiency identified or a problem that has occurred. Special attention should be given to participant safety issues.
* **Preventative Action:** Actions taken, after a route-cause analysis is performed, to prevent the specified deficiency identified from occurring again. The preventative action may also include a plan to identify problems prior to them becoming a deficiency.
* **Root Cause Analysis:** This is the method used to identify the cause of the specific problem or deficiency. The root cause is the factor that contributed to the problem or deficiency and needs to be addressed to prevent this from happening again. (ASQ, 2019) <https://asq.org/quality-resources/root-cause-analysis>
* **Evaluation:** A description of the plan or procedure to evaluate the implementation and completion, timeframe of the preventative actions. The evaluation is critical to ensure that changes to prevent the identified deficiency have the desired effect. The evaluation should be specific, including what will be evaluated, how it will be evaluated, who will be responsible for the evaluation, and when the evaluation will be completed. Regulatory authorities hold study team accountable for the evaluation of preventative actions, therefore be sure to make the plan and timeline realistic.

**How do I complete a Root Cause Analysis?**
There are various tools available to assist in conducting a root cause analysis. Regardless of the tool used, the
goals of using the root cause analysis for identified deficiencies is to determine :

* What happened?
* Why and how did it happen?
* Actions for preventing the deficiency from happening again.

Each of the following causes should be explored:

* Human (staffing issues)
* Physical (there was construction or freezer malfunction)
* Organizational (no standards).

The following tool is useful when exploring these factors.

* **“The 5 Whys”:** This technique is based on drilling down to find the root cause of the problem by asking
a succession of “whys”. The first step is to identify the problem and ask why it occurred. Continue to
ask why until you have reached the root cause of the problem. Do not stop when it is assumed the
root cause is reached. Be sure you the answers are grounded in factual information about what
happened and not assumptions or “easy outs”. “
* **“The 5 Whys” Example:**
Problem: *The urine sample for the urinalysis has been missed on the last three research participants at
the screening visit.*

**#1 Ask Why?** – Why was the urine sample missed on the last three research participants at the screen?
Answer- The research assistant forgot to collect it
**#2 Ask Why?** – Why did the research assistant forget to collect it?
Answer – The research assistant did not know that it was needed
**#3 Ask Why?** – Why did the research assistant not know that it was needed?
Answer – The Urine was not included on the study source flow sheet or CRF
**#4 Ask Why?** – Why was the urine not included in the study flow sheet or CRF
Answer – the CRC who developed the Flow Sheet / CRF left it off in error
**#5 Ask Why?** – Why did the CRC who developed the Flow Sheet / CRF leave it off
Answer – there was no quality control mechanism to double check the flow sheet represented
the protocol accurately.

**What do I do with the CAPA once complete?**

* The principal investigator needs to agree and sign the document.
* Be sure to report the CAPA to the IRB and sponsor.
* Always be sure to complete all action items identified in the CAPA and document completion.
* Remember the CAPA may have addressed departmental issues that need to be addressed and are not only applicable to the current study.
* Train staff and document any new procedures.
* Evaluate the success of the CAPA in a timely fashion. If it does not resolve the problem, a new plan needs to be implemented.