Guidance on Corrective and Preventive Action Plans

The term "Corrective And Preventive Action" (CAPA) plan has been in use for years and actually originated from FDA regulations regarding device manufacturing (21 CFR 820.100, Subpart J Corrective and Preventive Action). While much of the research overseen by the University of South Florida (USF) Institutional Review Board (IRB) is not FDA-regulated, the IRB is tasked with reviewing activities and events, under 45 CFR 46.108(4)(i). To do so, a CAPA plan may be required to provide enough information.

At USF, we typically hear about CAPAs when the IRB requires study teams to submit one. This usually occurs as part of a Reportable New Information (RNI) (previously called Reportable Events) for protocol deviations or non-compliance as defined in HRP-001 and HRP-103 (located in the BullsIRB library). This Guidance is designed to help study teams develop, document, implement, and evaluate effective CAPAs.

A Stepwise Approach to Developing a Corrective and Preventive Action Plan

Step 1: Corrections. Once a deviation occurs, immediate actions must be taken to protect the rights, safety, and welfare of the subject(s). These immediate actions are typically called "corrections" and must be differentiated from "corrective actions." Corrections are what we do in response to an error. Corrective actions are implemented after the root cause has been identified and are intended to *prevent* more significant deviations and/or serious non-compliance from occurring in the future.

The PI and study team should document and discuss the deviation, the reason it occurred, and any immediate corrections. Consider the reporting requirements of the sponsor, IRB, and any regulatory agencies and report the deviation appropriately. If subjects beyond those involved in the deviation need to be notified, the IRB will provide guidance on how to notify those subjects. Immediate corrections should be focused on protecting the rights, safety, and welfare of subjects and reporting the event. If there is a potential serious risk to several subjects, call the IRB for guidance before contacting subjects, unless a delay may result in harm.

Step 2: Evaluate Risk. After immediate corrections have been made, the PI evaluates the risk of the deviation regarding seriousness and frequency.

The USF IRB considers events that adversely affect the rights, welfare, and/or safety of subjects to be a serious risk. Events that pose a serious risk are considered serious events and must be reported to the USF IRB within 5 business days, as set forth in HRP-103 INVESTIGATOR MANUAL (located in BullsIRB Library). Events that do not pose a serious risk can usually be reported at the time of Continuing Review. If you are uncertain about how to classify an event, contact the IRB for guidance or report promptly to err on the side of caution. You can reach the IRB at rsch-IRB@usf.edu.

To evaluate frequency, consider the history of past occurrences and the potential for problems to occur again. For the past assessment, review the protocol deviation log(s) for other occurrences of the event. On occasion, you may need to review deviation logs for several protocols to determine frequency. For the future assessment, consider the risk of the event recurring in the same subject or other subjects in the study. If you notice a pattern on the deviation log(s) or if you identify a risk of the problem recurring in the future, there is a risk of frequency.

If the deviation is considered serious and frequency is ongoing or has a pattern, you must continue to investigate the problem through root cause analysis (RCA). If there is no risk of seriousness or frequency, the corrections should resolve the problem. Lastly, document the deviation, corrections, and risk assessment and continue to monitor the protocol deviation log for patterns.

Step 3: Conduct a Root Cause Analysis. A root cause analysis (RCA) is the process of identifying and documenting the root cause and the downstream effect on the causal chain. Root cause analysis should focus on identifying underlying problems that may have contributed to an error rather than on mistakes made by individuals.

When a serious deviation or non-compliance occurs in research, it is important to identify the cause(s) of the problem so that it can be resolved and prevent further non-compliance. There can be multiple causes that contribute to one single deviation or non-compliance event. The root cause is the initiating and most basic cause of a problem, which may lead to other problems. Eliminating the root cause should prevent recurrence of the problem(s).

Finding the root cause of an issue is not always easy. Sometimes it will require talking to many different people and departments to understand what went wrong. Often it will require asking questions that people tend to skip, thinking the answers are obvious. Finding the root cause may require writing the facts down in a systematic manner so the less obvious causes can become more visible. Consider contacting the institution's risk management or compliance department for assistance with conducting your root cause analysis.

Step 4: Develop and Implement Your CAPA. There are two main reasons for a CAPA plan. One is to acknowledge and correct the existing errors that have already occurred. The other is to prevent the same or similar errors from occurring in the future. A CAPA plan can be protocol specific or more broadly applicable to a departmental or institutional process. The type of CAPA plan will largely depend on the error and result of the root cause analysis.

During this phase, any changes to processes should be reviewed by the impacted departments and managers. Something that positively impacts your workflow could have a major negative impact on another's or result in non-compliance with other policies or procedures.

Below is a list of questions to ask while developing and implementing your CAPA plan:

1. Who
    a. Who is going to make the change?
    b. Who is impacted by this change?
    c. Is the Principal Investigator involved in the change?
    d. Who is going to teach/implement the change?
    e. Who is going to track the changes?
2. What
    a. What specific events, failures, deviations, exceptions, or non-compliance occurred that resulted in the need for this CAPA plan?
    b. What is the root cause of each problem?
    c. What is going to change?
    d. What is the corrective action that will be taken?

    e. What is the preventive action that will be taken?
3. Where
    a. Where are the changes being made?
4. How
    a. How is the change proposed by the CAPA plan going to occur?
    b. How will those affected by the proposed change be educated? Is education/reeducation part of the plan? What type of education will be used?
    c. How will the implementation of the CAPA plan be tracked (objective and measurable)?
    d. How does this plan correct the event, failure, deviation, exception, and noncompliance?
    e. How does this plan prevent the event, failure, deviation, exception, or noncompliance from occurring again?
5. When
    a. When is the CAPA plan going to be taught?
    b. When is the CAPA plan going to be implemented?
    c. When is the CAPA plan going to be evaluated?
    d. When does the USF IRB require an update on the results of this CAPA plan (if applicable)?

Step 5: Evaluate (monitor) your CAPA plan. Your CAPA plan should be monitored to ensure effectiveness. If your CAPA plan is applicable to a departmental process, consider whether this ongoing monitoring should occur at the departmental level or at an individual study level. You should maintain documentation of your ongoing evaluation of the effectiveness of your CAPA plan (See Appendices 1 & 2). If your evaluation demonstrates that the CAPA plan is not effective, you should amend your CAPA plan and begin the cycle of training, implementing, and evaluating again (See Appendix 3). It is important to remember that the primary goal of a CAPA plan is to protect the rights, safety and welfare of study participants.

Appendix 1 **Note-to-File formatting example for CAPA plan**

Delete Blue Guidance Text

Date CAPA finalized:

Protocol/IRB#:

Investigator:

Subject ID (if applicable):

Date subject enrolled (consent/randomized, if applicable):

Date of study procedure or product started (if applicable):

Issue:

Immediate remedy/ assessing risk: (Steps 1 & 2)

Root cause: (Step 3)

CAPA plan: (Step 4- Include if study specific or departmental change, SOP changes when applicable, training/ communication to study team etc.)

Plan to evaluate if CAPA plan is effective: (Step 5- Include objective ways to measure and timeline for completion)

Investigator Signature: _____ Date: _____

(Adding a signature or digital equivalent to demonstrate PI responsibility is ideal for regulatory file but the IRB usually accepts a copy without.)

Coordinator Signature: _____ Date: _____

☐ Attached: documentation after the evaluation plan was completed.

Appendix 2 **Table formatting Example for CAPA Plan**

Subject ID	Date deviation occurred	Description	Corrective Action & Preventative Plan	Serious / Non-serious	Date study team aware	Date IRB notified

*Deviation log templates can be found under Investigator Tools on USF QA web page

Appendix 3

CAPA Flow Chart