CAPA in Clinical Research at SCCR - REDCap CAPA Tool

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BACKGROUND

Corrective and Preventive Action (CAPA) program is an integral part of an organization's Quality Management System (QMS) including Manufacturing and Clinical Operations. It is not restricted to any particular industry or sector, and is a widely accepted concept, basic to any QMS. CAPA can be most powerful to improve quality of Clinical Research.

Regulations and standards such as US Food & Drug Administration (FDA) 21CFR820, ISO13485:2016, ICH E6(R2) mandate the implementation of CAPA for issues and nonconformances (NC). In Clinical Research, issues arising due to deviations from protocol are very common. Further, audit program, another key component of QMS proactively reveals NCs during internal audits and/or monitoring activities. CAPA can be used as a tool to effectively address and close all issues and nonconformances.

Using the existing resources at Stanford University School of Medicine, we have developed an electronic CAPA tool using REDCap system. We describe here the configured tool for CAPA. The tool underwent thorough validation testing per general requirements of CAPA workflow listed under METHODS. User Manual has been developed. Training slides are ready to train SCCR personnel that are likely Owners of CAPA observation(s).

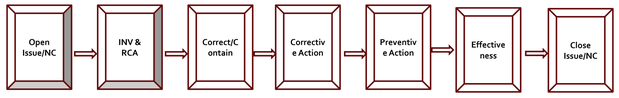
All Clinical Research-related issues/ nonconformities must be closed to avoid any 483s or warning letters by regulatory agencies. See Table 2 in RESULTS section for sample of Warning Letters issued. Such deficiencies can be addressed through CAPA.

Our CAPA tool conforms to 21CFR Part 11 requirements.

METHODS

- REDCap system is configurable

- We configured REDCap for the CAPA Workflow below:



- Login to the system
- Create project (My Projects)
- Use in-built Designed tool to design the workflow consisting of:
  - CAPA Admin Info
  - CAPA Details
  - CAPA Close out
- System was tested to meet requirements of SCCR CAPA
- System deployed to Production for use in July 2019

RESULTS

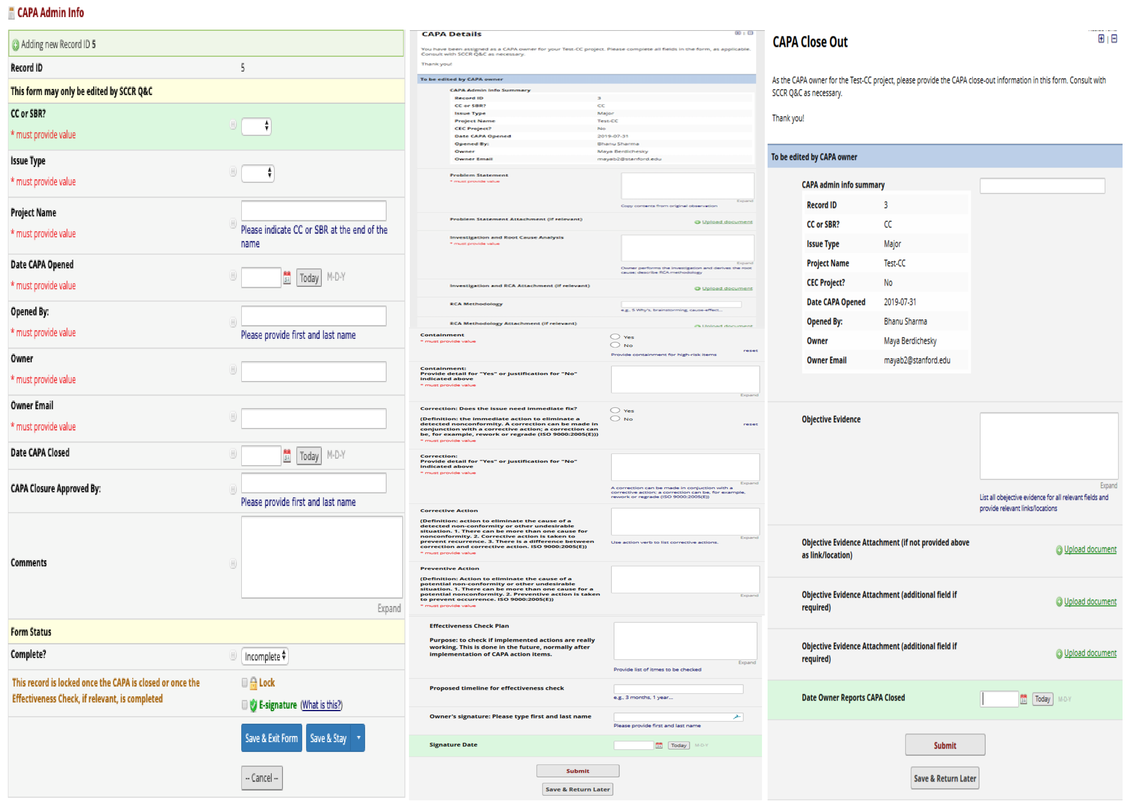
- CAPA Tool Forms and Survey
- Part 11 Compliance tool
  - Validation testing (see Table 1)
  - User Manual
  - Training
- Warning Letters on clinical nonconformance (see Table 2)

Table 1: Testing REDCap Functionality (example only)

Test ID#	Functionality/ Steps	Pass (P)/ Fail (F)	Result	Comments
1	Login to REDCap System	P	Login successful	
2	Choose My Project	P	Able to choose My Project	
3	Add/ Edit record , Select/ add New Record	P	New Record ID 10 created	
4	Choose CAPA Admin Info, complete first 7 fields, and leave form status incomplete	P	Able to enter all info in the form	
5	Press Save and Exit	P	Record saved. Exited from Admin info	

Table 2: US FDA Warning Letters on clinical CAPA
(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3043366/)

1. Submission of false information, fabricated/altered/concealed study records to FDA or the sponsor; missing records/evidence records that have been deliberately destroyed or discarded; information changed after the subject had completed the study up to 2 years postcompletion
2. Repeated or deliberate failure to comply with regulations. Administration of study drug to subjects not authorized to receive it; subjects overdosed due to lack of dose adjustments based on weight/toxicity; no or inadequate records of receipt, preparation, use and/or disposition of study drug; records of study medication storage conditions not maintained to confirm the integrity of the investigational product; use of prohibited concomitant medications; numerous inaccuracies noted in the source documents and CRFs such that integrity of data collected at site cannot be verified
3. Inadequate human subject protection. Issues include nondisclosure of right to refuse to participate in study, denial of withdrawal from study, repeated or deliberate failure to provide study information in language understandable to subject or legally authorized representative; failure to appropriately delegate duties to qualified personnel (e.g., physical exams, SAE evaluation) with resultant exposure of subjects to unreasonable and significant risk or injury, …. subjects started on treatment before checking safety/baseline reports; failure to assure that IRB has reviewed/approved changes in research; enrollment of subjects before IRB approval; subjects not consented before enrolment, not (timely) reconsented on updated safety information; enrollment of ineligible subjects; failure to (timely) report serious or life-threatening events to sponsor



CONCLUSIONS

- CAPA is an integral part of an organization's QMS
- It is a continuous improvement tool for QMS
- CAPA is opened for internal and external audit observations, monitoring activities, and management initiatives for improvement of procedures and processes
- CAPA workflow includes: issue identification, investigation and root cause analysis, containment of the issue if required, correction & corrective actions, preventive action, effectiveness of implementation, and closure
- Development of CAPA tool using REDCap is described. Features include:
  - Three forms for both Admin and Owner
  - Autonotifications
  - Review/ approval, authentication, audit trail, conversion of completed CAPA into PDF, archival into REDCap system
  - Part 11-compliant solution
- Testing performed, User Manual developed, Training slides created
- Tool development challenges included figuring out access control/ view so that Owners would not see other's CAPA in the system

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