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What You Need to Know About Promoting Quality with a Proactive CAPA System

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Agenda

1. Quality Oversight - Roles and Responsibilities
2. Challenges
3. Tools
4. Governance
5. CAPA Approver Skill Sets
6. Lessons Learned for CAPA Success

Quality Oversight
Roles and Responsibilities

Quality Oversight in Pharma Medical Safety

Good Pharmacovigilance Practice (GPVP):

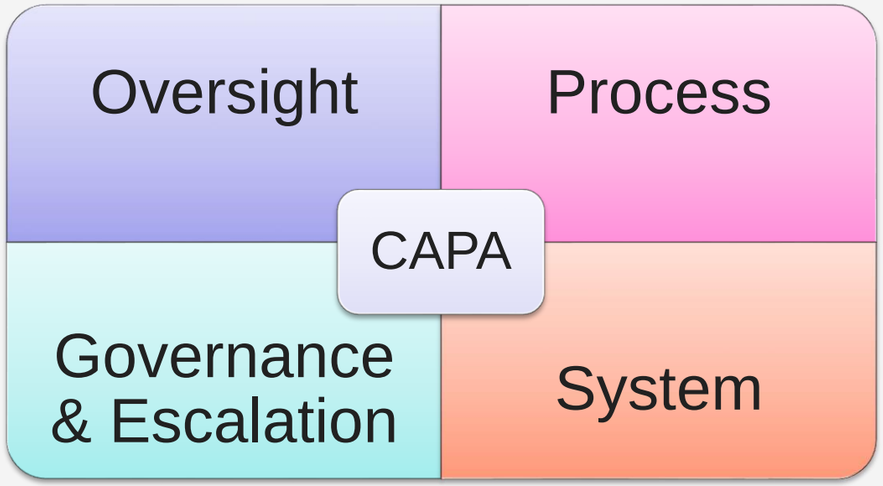
The science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine or **drug-related safety problems**.

CAPA (Corrective Action/Preventive Action):

“The purpose of the corrective and preventive action subsystem is to collect information, analyze information, identify and investigate product and quality problems, and take appropriate and effective corrective and/or preventive action **to prevent their recurrence**” – US FDA Inspection Guide

Quality Function – Key Roles and Responsibilities

- Independent review/approval
- Business Process Owner and Subject Matter Expert (SME) for nonconformance/CAPA
- Effectively and efficiently contribute to the NC/CAPA process in a manner that does not introduce unnecessary delays in timelines
- Governance & Oversight – Periodic reviews of status and progress
- Best Practice Sharing – Support a Continuous Learning Culture



Quality Function – Key Roles and Responsibilities

- Examples of Effective/Efficient Methods of Proactive NC/CAPA Support:
  - PV CAPA CoE Approver requests an invitation to Audit/Inspection Close Out meetings to get an idea of the observations before the audit/inspection report is issued.
  - PV CAPA CoE is copied on all audit/inspection reports. Once the report is issued, PV CAPA CoE opens records in the CAPA system immediately and schedules a Kickoff Meeting to develop the Audit/Inspection Response.

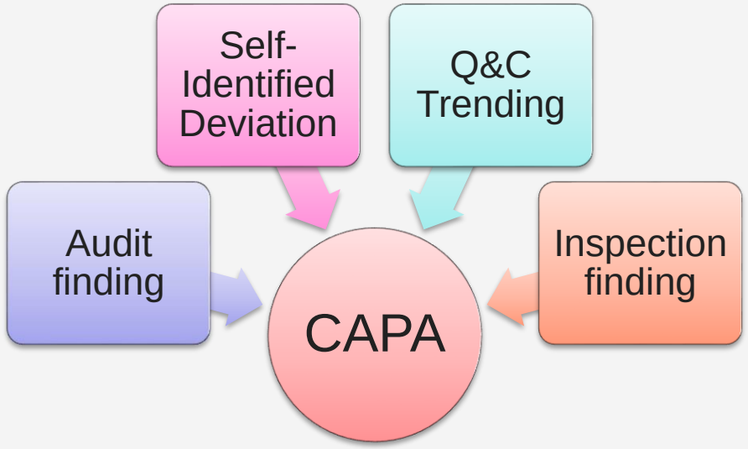
- Governance & Oversight – Periodic Reviews:
  - Quality can periodically review all open NC/CAPAs to identify at risk records in the business.
  - Monitor the overall health of the CAPA system & CAPA effectiveness across business units, functions & regions.
  - Centralized, end-to-end, global oversight of CAPAs.
  - CAPA Review Board Meetings.

- Best Practice Sharing to Support Continuous Learning:
  - Quality reviewers can learn from each other. Regular Team meetings can be utilized for Quality Approvers to discuss/leverage Best Practices for unusual scenarios and to collaborate on new Tools.

Challenges

Challenges

- Global Working: Language & time zone differences, most communication via email and conference calls
- Complexity: Diverse sources & inputs to CAPA (internal and external)
- Resourcing: The occurrence of issues is not predictable or consistent - issues may arise simultaneously causing resource conflicts
- Expertise: Subject Matter Experts with varying levels of expertise & experience in conducting an investigation or developing a robust CAPA



How Does Quality Address These Challenges?

Tools

- Quality can support the business by providing users with tools to enable them to execute the CAPA process independently.

Governance

- Quality plays a key role to provide visibility to management for CAPAs at risk and to escalate when required.
- Management plays an important role to remove roadblocks and provide resources.

Expertise

- The Quality organization is the CAPA process experts that provide coaching and guidance to ensure documentation is robust, adequately resolves the identified nonconformance, and complies with the CAPA process requirements.

Challenges for Quality:

- As a Quality Approver, what would you do if you were working with an Investigation owner for an internal audit observation who:
  - Has no experience with CAPAs?
  - English is a second language and communication is challenging?
  - Has no experience using the CAPA system to create records?

Challenges for Quality

- As a Quality Approver, what would you do if you are working with an Investigation owner for an internal audit observation who:
  - Has no experience with CAPAs?
  - English is a second language and communication is challenging?
  - Has no experience using the CAPA system to create records?

- Options:
  - Help the Investigation Owner/Investigation Team develop an Investigation Plan.
  - Begin working on smaller manageable pieces of the CAPA process:
    - Focus only on the Investigation first.
    - Root Cause Analysis, CAPA, and the Effectiveness Check comes later, after the Investigation is final.
  - Schedule regular check in meetings (daily, bi-weekly) with milestones to check progress and provide support and coaching.
  - Enlist help from someone else familiar with the issue under investigation.
  - Find a translator.
  - Identify a buddy in the owner's functional area they can work with.
  - Schedule time to help create records in the CAPA system, field by field or, designate another person to create records for them.

Challenges for Quality

- As a Quality Approver, what can you do when a CAPA Investigation has an unexpected challenge or roadblock for timely completion and the due date is approaching?

PV CAPA Challenges for Quality

- As a Quality Approver, what can you do when a CAPA Investigation has an unexpected challenge or roadblock the due date is approaching?

- Options:
  - Escalate – enlist the help of leadership to remove roadblocks, address resource constraints, reprioritize.
    - Next level management will have a better understanding of the big picture.
  - Facilitate – schedule regular check in meetings to resolve outstanding comments quickly.
    - Focus the discussion by communicating expectations and goals before each meeting.
    - Publish meeting minutes with action items, owners, and due dates for next steps.
  - Find out who the decision makers are to resolve the blockage and meet with them.
  - Request input/suggestions from subject matter experts on the Investigation Team for resolution.
  - Ensure everyone has the same understanding of the issue to be addressed. Perceived differences or roadblocks could be due to a misunderstanding of the issue or semantics.

Tools

Tools

- Procedures & Instructions
- Training
- Role-Defined User Aids & References
  - Quality Approver Checklist.
  - One Pagers, Field Guides, One Minute Videos.
- Templates and Structured Approaches
  - Project Management Approach (plan first, then execute).
  - Kickoff Meeting.
  - Word Templates to enable Subject Matter Experts to contribute (in writing) to the investigation, root cause analysis and CAPA plan development.

Procedures, Instructions, & Training

- SOPs, Work Instructions, and Training available for:
  - CAPA Process for PV Audits and Inspections
  - CAPA Process for Self-identified Nonconformances
  - Governance (high level)
  - CAPA Review Board meetings
  - CAPA System

Aids: Quality Approver Checklist

1
- Problem Statement
- Immediate Actions

2
- Investigation
- Root Cause Analysis

3
- CAPA Plan
- Effectiveness Checks

4
- Good Documentation Practices followed
- Technically Correct, Evidence/Supporting Data Attached

Aids: Quality Approver Checklist

- Problem Statement – A problem well-defined is a problem half-solved!
  - Is the Problem Statement clear, complete, and concise?
    - What happened?
    - When was it discovered?
    - Who discovered it?
    - How was it discovered?
    - What was deviated from?
    - What is the scope of the issue?
    - What are the known or imminent risks?

- Immediate Actions
  - If Immediate Actions were taken, are they logical and clear?
  - If no Immediate Actions were taken, is that appropriate based on risk?
  - Is evidence attached to demonstrate the Immediate Actions taken?
  - Has risk been assessed and mitigated until the CAPA can be implemented?

Aids: Quality Approver Checklist

- Investigation:
  - Is the investigation completely documented, understandable, and clear as written?
  - Typical elements of an Investigation Plan include but are not limited to:
    - Issue Background
    - Procedures to be reviewed
    - Data or Processes to be reviewed
    - Interviews to be conducted
    - Training records to review
    - Risk Assessment
    - Impact Analysis – patient safety, product, processes, and or regulatory compliance, as appropriate
  - Is a summary of the Investigation Results included with conclusions and any gaps identified?
  - Are there any gaps identified in the Investigation that are not addressed with a CAPA, Correction, or Preventive Action?
  - Are all supporting documents referenced in the investigation attached as evidence?

Aids: Quality Approver Checklist

- Root Cause Analysis:
  - Was the appropriate tool or methodology used? Is it attached?
  - Human error can NOT be used as a root cause.
  - Is the root cause clearly stated, well documented, and easily understood?
  - Is the root cause logically supported by the Investigation results?
  - If multiple root causes were identified, is there at least one CAPA for each root cause?

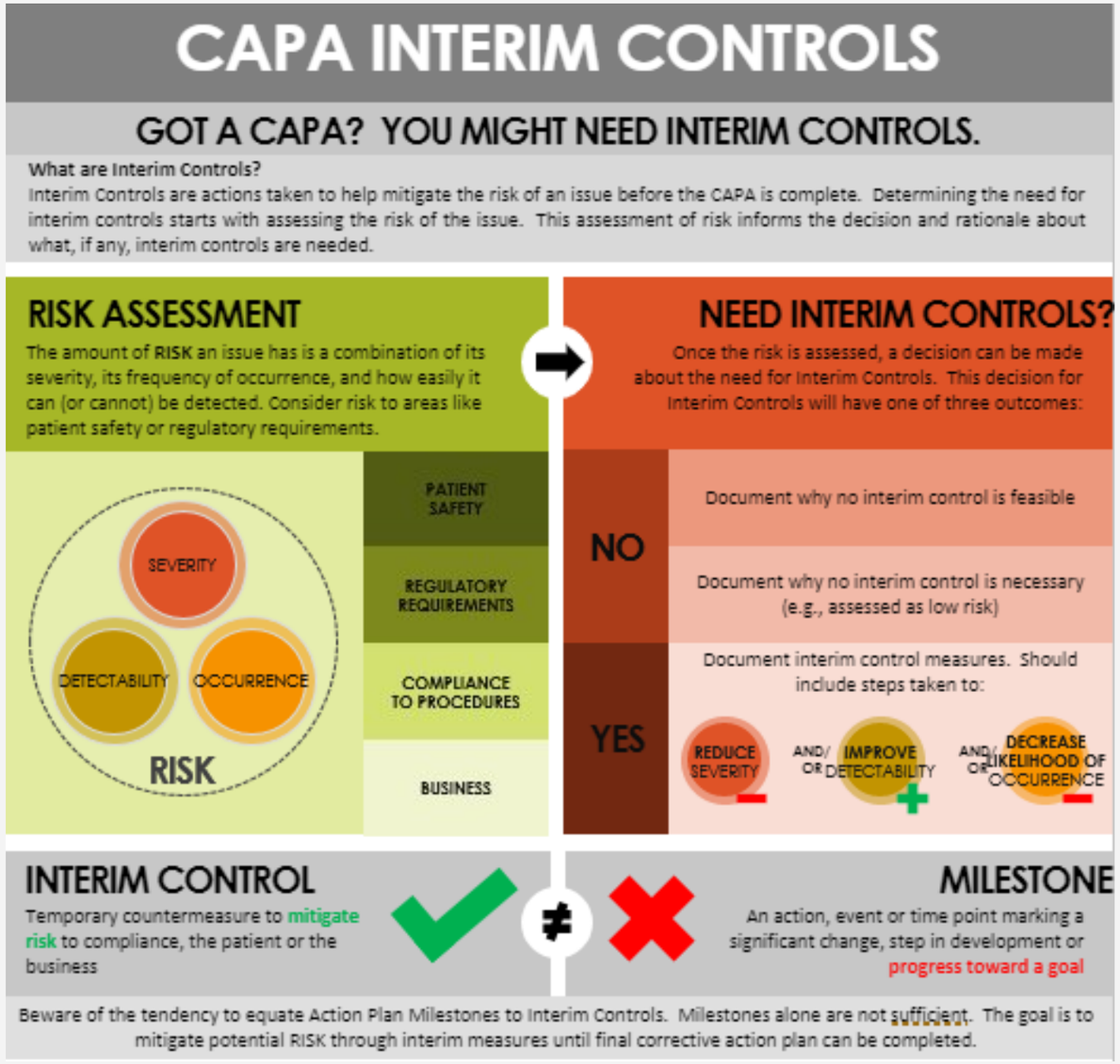
- CAPA Plan:
  - Does the CAPA address the root cause?
  - If no CAPA is required, is an appropriate, plausible, rationale clearly documented?
    - This should be very rare and MUST be challenged by the CAPA Approver.
  - Can you clearly see a connection between the Investigations results, root cause, CAPA, and EC?
    - **INV-RC-CAPA-EC**
  - If the CAPA Plan takes an extended period to complete, were appropriate interim controls implemented to mitigate risk until the CAPA is implemented?
  - Are CAPA due dates realistic, achievable, timely, and based on complexity? Were the due dates determined with input from all relevant stakeholders?

Aids: Quality Approver Checklist

- Effectiveness Checks (EC):
  - Is the EC Plan measurable and quantifiable?
  - Does the EC measure the ELIMINATION OF THE ROOT CAUSE, not merely the elimination of a symptom?
  - Does the Effectiveness Check Plan contain:
    - High level description of the EC Plan.
    - Deliverables/Evidence.
    - Owner.
    - Actions: details of actions to be performed during the EC and by whom.
    - Metrics: Data that will be evaluated to determine effectiveness.
    - Duration/Quantity: must include the rationale for the length of EC monitoring and how many datapoints to measure.
    - Criteria for Success: must be a quantifiable value. Are the criteria appropriate?

Aids: ‘One Pagers’

- ‘One Pagers’ are concise, colorful, and visually appealing, and easy to understand.
- The goal is to help individuals understand what is needed so they can easily develop content and or create records themselves that are robust and compliant.
- ‘One Pagers” are useful as a reference for experienced individuals too!



References: CAPA System Field Guides

- To help owners create records quickly and easily populate fields correctly in the CAPA system, a Field Guide is useful to describe in more detail what to enter in each field in the CAPA system, supplemental to the procedural instruction.
- Field Guides are not how to use the CAPA system (a Work Instruction is available with that information). Field guides are what to enter, field-by-field in the system.
- Populating fields correctly:
  - Helps expedite approval of the record.
  - Ensures accurate information for Governance and CAPA metrics.
  - Enables accurate CAPA reporting to Health Authorities.

References: One Minute Videos

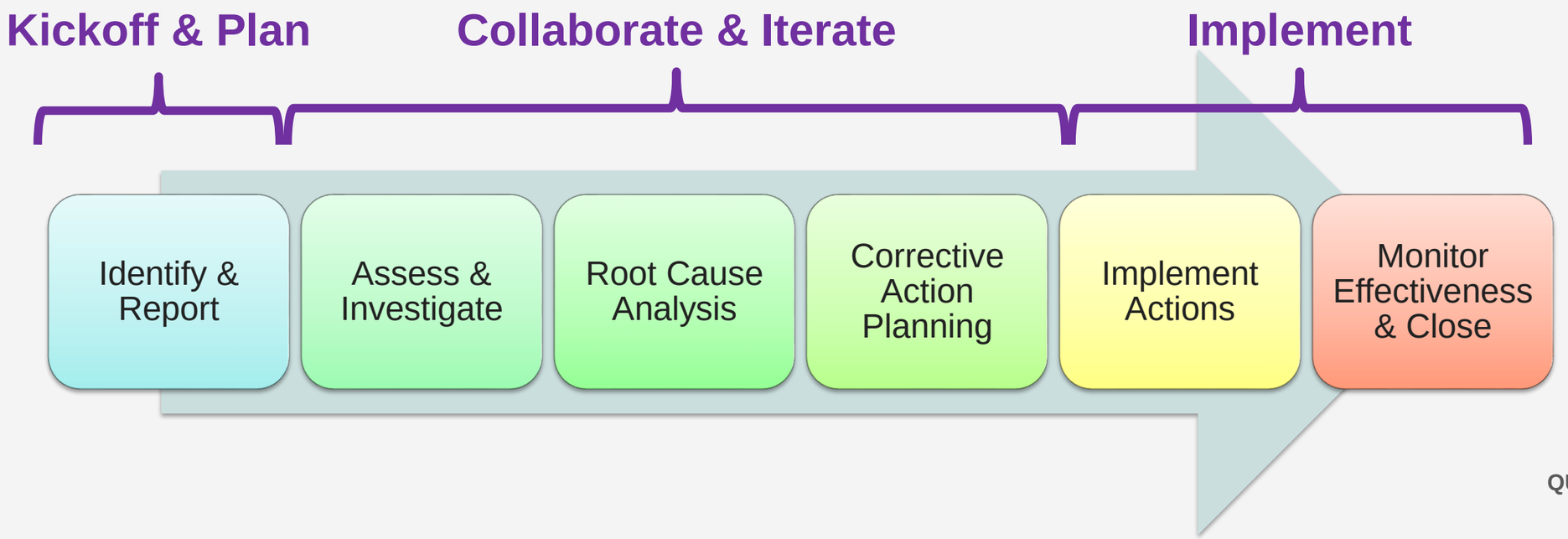
- Individuals learn differently, some prefer documents, some prefer videos.
- PV CAPA Center of Excellence recently began creating One Minute Videos on specific topics related to the CAPA process, developing content, or use of the CAPA System.
- The format is concise, visually appealing, and easy to understand.
- Videos are narrated with emphasis on the key takeaway messages.
- Examples of Topics:
  - Problem Statements.
  - Why Human Error is NOT a Root Cause.
  - How to send records for approval in the CAPA System.

Templates & Structured Approaches

Project Management is CRITICAL to success – coordinate SMEs and stakeholders, plan, then execute.

CAPA is a **process** - to be done in sequence every time AND

CAPA is a **project** - plan for the steps to be done and **schedule the time**



Templates & Structured Approaches

A Kickoff Meeting is scheduled with the Investigation Owner, Approver, and Subject Matter Experts to:

- Establish and agree on the timeline and key milestones for the CAPA and the Audit/Inspection response.
- Confirm the owner of the Investigation, Investigation Team members, and Approver(s).
- For audits and inspections, confirm the Investigation owner understands the observation.
- Clarify what is being deviated from.
- Review an overview of the CAPA process.
- Begin discussing the Investigation Plan and impact.
- Provide an opportunity for the Investigation owner, CAPA Approver(s), and Subject Matter Experts to meet.
  - Guidance is given to check with Stakeholders and Quality Approver “Early and Often”.

Templates & Structured Approaches

- Investigation owners may have limited CAPA experience or do not have access to the CAPA system but need to contribute content to an investigation.
- Word Templates can be useful tools with guidance provided in each section on the information needed. This allows SMEs to contribute, in writing, to the investigation to be included in the CAPA IT system
  - Templates can have sections for key content:
    - Problem Statement
    - Immediate Actions
    - Investigation and Risk Assessment
    - Root Cause Analysis
    - CAPA and Effectiveness Check
    - Corrections
    - Preventive Actions

Templates & Structured Approaches

H **EFFECTIVENESS CHECK PLANS (for Corrective Actions only)**

The Effectiveness Check (EC) verifies the solutions worked and should confirm the elimination of the ROOT CAUSE, not the symptoms. Define owner and due date for each EC measure required, if more than one. All elements of the Effectiveness Monitoring Plan should be appropriate and justified.

Instructions for Table below:

Please enumerate all EC plans below. Add a row for each individual EC.

- **Add rows of ECs**: Right-click the table and select **Insert Item After or "+"**.
- **Delete rows of ECs**: Right-click the table and select **Delete Item**.

H1	**Link to CAPA # above**	*[Enter CAPA Number]*
	Effectiveness Check Rationale/Plan	***Action:*** *[Describe the EC plan/rationale]* ***Deliverable:*** *[identify the objective evidence to verify action completion]* ***Action Due Date:*** *Click or tap to enter a date.* ***Owner:*** *[Enter name of individual who will complete the action plan]*
	Action	*[Define what actions will be performed and who will perform these actions.]*
	Metric	*[Specify what will be measured to evaluate effectiveness and who will be responsible to measure, if different from Record Owner]*
	Duration / Quantity	*[How often will measurements be taken? Enter duration/interval that will be measured for effectiveness]*
	Criteria for Success	*[Specify a quantifiable (pass/fail) outcome that is expected to indicate that the CAPA actions were effective to eliminate the root cause. Pass/Fail criteria should be quantifiable (e.g. a specific number or percentage) of the intended sample size.]*
	EC Interim Updates Required?	*Y/N? [Specify milestone dates for interim status checks on EC progress]* *If Yes, complete grid below:*

Governance

Governance

- CAPA Review Board (CRB) Meetings ensure Governance and Oversight of PV CAPAs.
- CRBs are typically Led by Quality with Accountable Leaders attending & participating.
- Transparency and Awareness of how the business is performing in addressing its Quality and Compliance risks and commitments.
- Ensures management can intervene as needed to remove roadblocks and support resource needs.

Governance

- Depending on the Organization, single tier or multi-tier CRBs may be used:
  - Local or Functional Level CRB can be used for direct management accountability
  - Regional or Global Level CRB can be used for senior leader accountability
- Typical CRB Attendees are CRB Leads and Cross-Functional Leaders
- It is helpful to send CRB data to attendees before the CRB meeting so they can follow up on at-risk or overdue records before the meeting. Early follow up can:
  - Ensure records are closed before CRB.
  - For records unable to be closed before the CRB, individuals can bring information on roadblocks to the CRB for discussion and obtain support from CRB attendees for resolution.

Governance

- Data Presented at CRB can include:
  - CAPA Lifecycle/Timeliness Metrics (Age, Rate of Completion on Time & Extensions etc.).
  - Records At Risk for Late Closure/Overdue Records.
  - Owners Present an Overview of New Investigations to obtain Input from CRB Attendees.
  - Review status of significant CAPAs.
  - Ineffective CAPAs (if any).
  - Issues for Escalation (if any).
  - Action Items.

Quality Approver Skill Sets

CAPA Approver Skill Sets

- People – Our Secret Sauce!
  - The PV CAPA CoE is Comprised of a Diverse Team of Individuals with Extensive Quality and Compliance Experience
    - Diverse Backgrounds in Regulated GXP Industries
    - Training & experience in root cause investigation & CAPA
    - Excellent problem-solving and organizational skills
    - Highly developed communication and interpersonal skills
    - Strong negotiation skills
    - Good compliance judgement
    - Courageous
    - Able to Work Independently in fast-paced, ambiguous situations
    - Decisive
    - Willing and able to work flexible schedules
    - Adept at multi-tasking
    - Patient
    - Creative

Lessons Learned for CAPA Success

Tips for CAPA Success

- Lessons Learned
  - Get to know the Investigation owners and adapt your approach to work best with them.
    - What time of day do they like to work?
    - What level of support do they need and are they comfortable with?
    - Are they threatened by the perceived failure (nonconformance)?
    - If your initial approach for support does not work, change direction and try again.
  - Communicate, communicate, and communicate again. Do not assume everyone understood what is required and when it is required the first time they heard/read it.
  - Try to find investigation owners an experienced buddy in their area to work with.
  - Rapid resolution of issues requires verbal discussion.
    - Emails take too long for resolution. Pick up the phone or if possible, visit the individual in person.

Tips for CAPA Success

- Lessons Learned
  - Provide very detailed feedback to authors regarding what revisions are needed.
    - Assist in resolution of comments
    - If the revisions required are complex or a large number of changes are needed, they can be resolved more efficiently in a meeting.
    - Clear communication between the author and approver is key!
  - No matter how many gaps there are in the draft is you receive, find something good about it, you must keep people motivated and keep them moving forward. Be their cheerleader!
  - Be mindful that individuals who indicate they are experienced with CAPA may not have experience developing robust, well documented Investigations, root cause(s), and CAPAs.

Tips for CAPA Success - continued

- Lessons Learned:
  - Escalate roadblocks quickly.
  - It is OK to acknowledge that this can be stressful for the individuals you are working with. Be empathetic, and try to find opportunities to keep it light.
  - If you are having difficulty reaching someone, try reaching them in off hours – early morning or late evening.
    - Another option is to contact someone you know who works in the same office as the person you need to reach and ask them to visit the person and communicate the urgency of the issue requiring resolution.
  - Pace yourself. Keep your energy upbeat and positive so you can motivate others.
  - Expect the unexpected and plan time for it. Build in buffer time before “final” due dates

Questions?

Thank you.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