CAPA, RISK MGMT & CHANGE MGMT

LINKS TO MAINTAINING QUALITY

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AGENDA

WELCOME

- Q9 Quality Risk Management
- CAPA
- CAPA Trending
- CAPA Impacted Systems
- Change Management

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QUALITY SYSTEMS

Q10 PHARMACEUTICAL QUALITY SYSTEM

- **Quality System Elements include**
  - **CAPA System**
    - Resulting from Investigations whose depth will be based on the level of risk
  - **Change Management System**
    - Quality risk management will be used to evaluate proposed changes.

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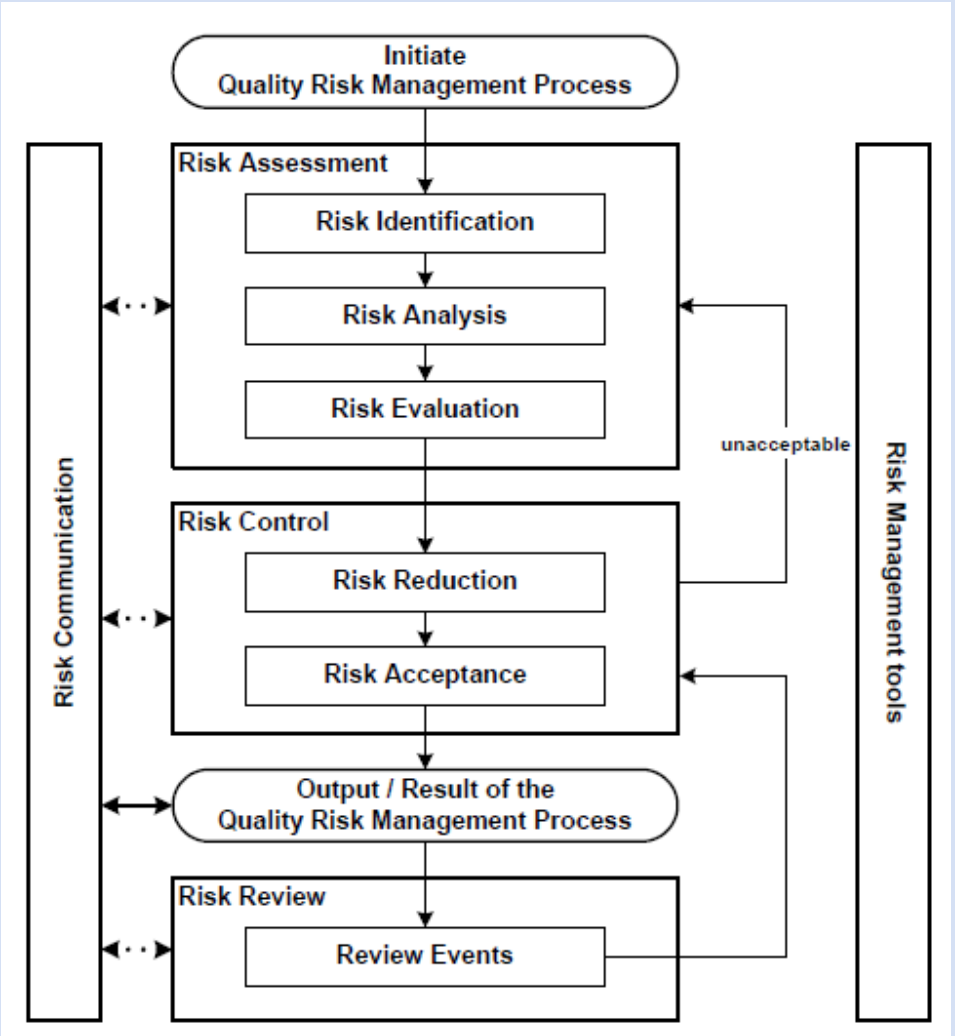
Q9 QUALITY RISK MANAGEMENT



Q9 QUALITY RISK MANAGEMENT

RISK: The combination of the probability of occurrence of harm and the severity of that harm.

Detectability: The ability to discover or determine the existence, presence, or fact of a hazard.

- Recognize sources of variability in the ability to discover: The more personnel involved in investigations and CAPA generation plus QA review, the greater opportunity for variability.
- Robust systems in place to enhance the probability of detection – appropriately managed

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Q9 QUALITY RISK MANAGEMENT

Detectability

- Mitigate sources of variability in DETECTABILITY
  - Train, qualify, supervise & manage
  - Enhance policies, SOPs and practices to ensure accurate reproducibility
  - Enforce SOP requirements – Supervisors & QA
  - Product/Process knowledge
  - Appropriate SMEs
  - Company Culture

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Q9 QUALITY RISK MANAGEMENT

Risk Assessment: A systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.

Risk Control: Actions implementing risk management decisions

- Is the risk above an acceptable level?
- What can be done to reduce or eliminate risks?
- What is the appropriate balance among benefits, risks and resources?
- Are new risks introduced as a result of the identified risks being controlled?

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Q9 QUALITY RISK MANAGEMENT

- **Risk Review**: Review or monitoring of output/results of the risk management process considering (if appropriate) new knowledge and experience about the risk. Once a quality risk management process has been initiated, that process should continue to be utilized for events that might impact the original quality risk management decision.

- Risk review might include reconsideration of risk acceptance decisions.

- ***Risk acceptance*** is a decision to accept risk. For some types of harms, quality risk management practices might not entirely eliminate risk. In these circumstances, it might be agreed that quality risk is reduced to a specified (acceptable) level. This acceptable level will depend on many parameters and should be decided on a case-by-case basis.

CAPA

SYSTEM FOR IMPLEMENTING CORRECTIVE ACTIONS AND PREVENTIVE ACTIONS RESULTING FROM INVESTIGATIONS

- Complaints
- Product rejections
- Nonconformances
- Recalls
- Deviations
- Audits
- Regulatory inspections and findings, and
- Trends from process performance and product quality monitoring
- Investigation effort, formality, & documentation should be commensurate with the level of risk. CAPA methodology should result in product and process improvements and enhanced product and process understanding.

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INVESTIGATION GENERATED CAPAs

- **Thoroughness of the investigations & documentation**
- **Commensurate with the level of risk**
  - Do factors point to other company/corporate sites, vendors, contractors? Were all the branches on the Ishikawa diagram pursued and evaluated? Were these pursued?
  - If vendors/contracts contributed to the deviation, do not fail to evaluate the Vendor Qualification System and its robustness
  - Key individuals appropriately interviewed & results documented
  - **Root Causes –** Identification continues to be challenge
- **Products & Systems impacted - for how long – Suspect product on the market?**
  - Risk – Past, Present & Future

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INVESTIGATION GENERATED CAPAs

- **Is this an isolated event? What is your lookback policy?**
  - Search for same, similar and related events for a minimum of 12 months
  - The robustness of the search data set will impact search outcomes.
- **What do repeat investigations for same, similar and related events say about the efficacy of the current CAPA system?**
  - Does the CAPA system need a CAPA?

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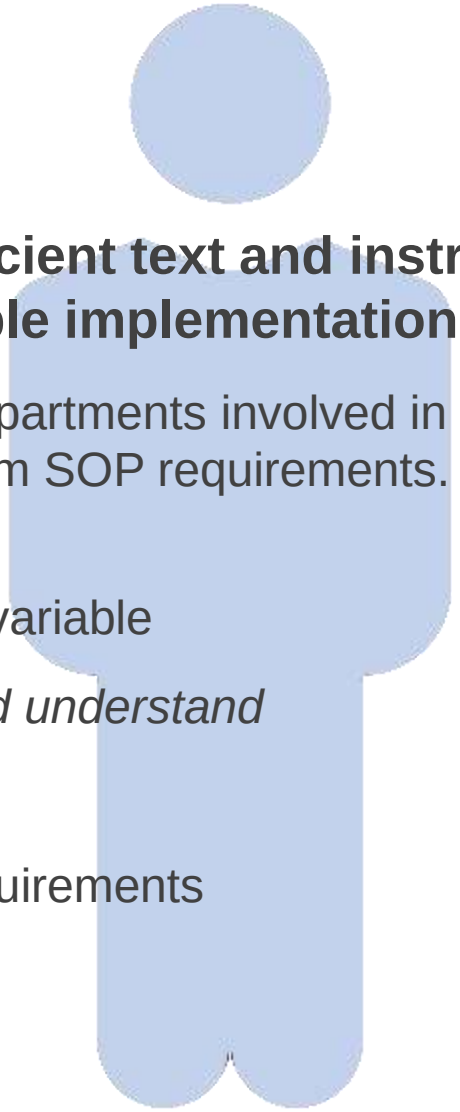
ELEMENTS OF A CAPA SOP



- **CAPA SOP**
- **Well-designed with sufficient text and instruction to ensure accurate and reproducible implementation**
- NOTE: The more staffing/departments involved in this process can provide opportunities for variance from SOP requirements. Same applies to investigations SOP.
- Recognize and mitigate this variable
  - Training – *Not self-read and understand*
  - Supervision
  - Enforce proceduralized requirements
  - QA oversight

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ELEMENTS OF A CAPA SOP

CAPA Action Plans address all the root causes

- On site
- Off site, e.g., other company/corporate sites, vendors, contractors, etc.
- Management of the various work streams onsite and offsite clearly defined
- Risks to Impacted Products & Systems, Past, Present & Future, are addressed
- Mitigation Action Plan/Interim Controls to address risks pending CAPA completion

ELEMENTS OF A CAPA SOP

TARGET DUE DATES & JUSTIFICATION - FIXED vs RISK/PRIORITY BASED

- Risk/Priority
  - High/Medium/Low
    - Impacting product safety/quality – patient safety
    - Impacting key systems
    - Response to regulatory inspections
    - Product shortages
    - Business targets
    - Response to client requests
- Impacted/Responsible Area(s)
- Responsible Person(s) for managing each work stream

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ELEMENTS OF A CAPA SOP

Due Date Extension Requests

- CAPA Work Stream Owner
  - How to request an extension
  - When to request an extension to receive approval prior to due date
  - Who can request it
  - Justification for the extension
  - Risk Assessment for the extending completion date
  - Mitigation Plan for any risk of extending completion
- QA
  - Justification for granting extension, e.g., risk reduced/controlled to an acceptable level
  - Justification for rejecting an extension request – Completion action plan
  - How many times can an extension be granted – Once/Twice/?

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ELEMENTS OF A CAPA SOP

TRACKING CAPA PROGRESS – WHO & HOW

- Due date
- Extended due date
- Owner notification of pending due dates
- Owner interim reporting per SOP requirements
- Failure to meet due dates
  - Risk of delayed completion
  - Root causes for the failure(s)
  - Follow up action plans

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ELEMENTS OF A CAPA SOP

Effectiveness Checks

PLAN FOR MEASURING EFFECTIVENESS

Plan for measuring effectiveness

- What will be monitored, at what frequency, for how long, to what standard
- Sampling/ testing to be performed
- Observations of operations for x time for x criteria
- Data to be analyzed and trended
- Validations, Etc.

Completion date for effectiveness checks

EFFECTIVENESS CHECKS FAILED

- Investigation
- Root Causes
- Risk Assessment
- CAPA

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CAPA TRENDING

Trending

- Open CAPAs by priority/risk
  - Are they on target for completion by due date
- Overdue CAPAs
  - How many days, weeks, months, years past due for the following:
    - Past Original Due Date by priority/risk
    - Past Extension Dates (1st, 2nd, ?) by priority/risk
  - Open Effectiveness Checks by priority/risk
  - Past Due Effectiveness Checks by priority/risk
- Comparison with past trend data
  - Quarterly
  - Yearly, Etc.

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CAPA TRENDING

Trend Analysis

- Interpret the Findings: ↑↓↖↗↘↙↔
- Any new issues identified
- Risks?
- What is impacted –*Product, Process, System*
- Conclusion
- Root Causes for incomplete/ineffective CAPAs
  - Is it the CAPA process, the Investigation process, Both, Other?
- Action Plans to address trends
- Due Dates

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CAPA IMPACTED SYSTEMS

Change Management

- Change Control Committee - Standing diverse group with supplemental expertize as necessary
- Change Control Elements
  - Types of Changes
    - Facility
    - Equipment
    - Like for Like (Who is authorized and has the expertise to make this call)
    - Specifications
    - Documents
    - Emergency
- **CC Committee must evaluate the Risk/Impact the change will directly or indirectly have on related systems, both in-house and other company/corporate sites, vendors, CMOs, Regulatory**

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CAPA IMPACTED SYSTEMS

Change Management - continued

- Mitigation plan to address identified risks pending completion
- Due Date based on risk/priority
- Due date extension provisions with corresponding risk assessment
- Interim reports, as appropriate
- Tracking – All work streams at all applicable sites/vendors
  - Due date
  - Extension due date
  - Interim reporting
- Post implementation evaluation to confirm the change objectives were achieved
  - No deleterious impact on system/product quality
  - No other risks created

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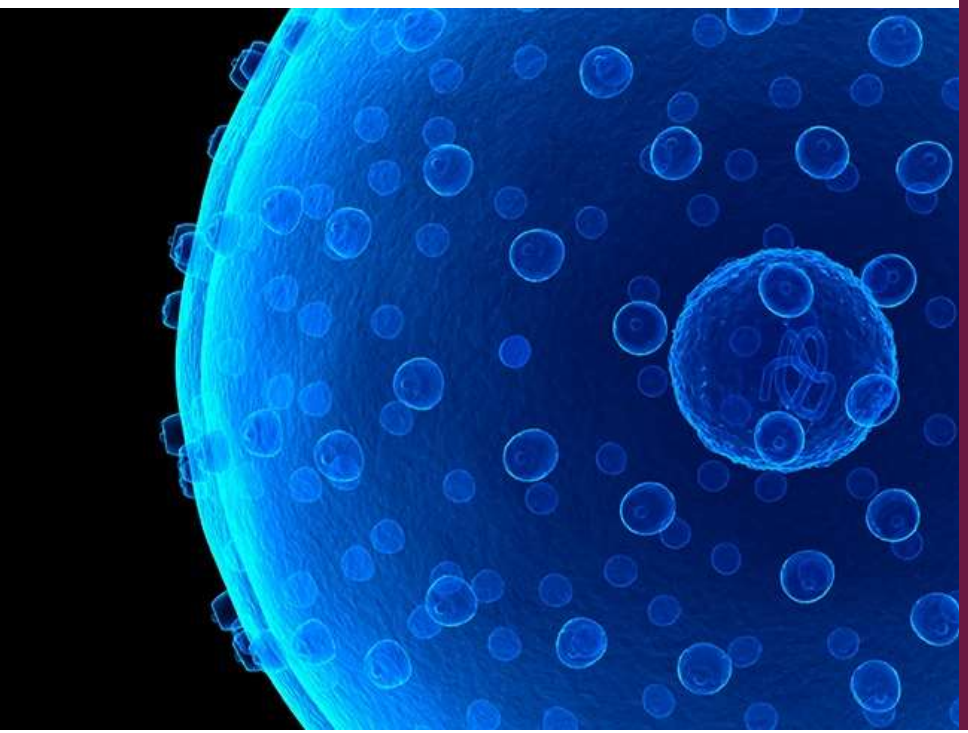
CAPA IMPACTED SYSTEMS

- **Calibration**
- **Validation**
- **Further investigations**
- **New staffing/Transfer existing staffing**
- **Training**
  - New Training
  - Repeat Training – *Old Time Favorite*
    - Justification
    - If the initial training was ineffective, how will repeating it be effective

CAPA IMPACTED SYSTEMS



Training (continued)

- Justify Training Method
  - Self-read and understand
  - Classroom
  - OJT
  - Off site
  - Combination
- Means of establishing effectiveness of training
  - Testing – when, how, frequency
  - Performance evaluation – when, how, frequency

CAPA IMPACTED SYSTEMS

SOPs

- Create new one(s)
- Revise existing one(s)
  - Root Causes for approving incomplete/ineffective SOPs
  - How did the SOP creation/review system fail?
- Are the appropriate SMEs/operators involved in creation/revision/review/approval of SOPs to minimize repetitive revision of QA approved SOPs when their use results in deviations

THANK YOU

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