



AUDITS

DCVMN – Hyderabad, India

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GENERAL OVERVIEW OF WORKSHOP OBJECTIVES



- ✓ To provide rationale, strategies, techniques and tips on how to plan and perform effective audits through practical examples, case studies and group discussions
- ✓ To explore the politics, psychology and technical aspects of auditing, including discussions of their tools and frequency
- ✓ To evaluate the talents and personnel characteristics required of those who consistently perform thorough audits which yield optimal compliance results
- ✓ Review and discuss cGMP requirements and their interpretation while developing criteria for categorization of audit findings
- ✓ To consider how to effect change and how to make audits a positive experience for the auditor, auditee and both companies / departments.

GENERAL OVERVIEW OF WORKSHOP METHODOLOGY



- ✓ Review and discuss among the group and class
 - ✓ Share knowledge
 - ✓ Role-play
 - ✓ Presentations

QUESTION



Are audits a low priority activity to show regulators some degree of compliance
or
an effective tool for continuous improvement?

PARADIGM



In which type of company do you feel you are in ?

Company type I: just to show regulators / customers that there is minimal effort to cover this GMP requirement ? (i.e. non-compliant, risky, immature)

or

Company type II: to implement a system / program as part of the continuous improvement goal, in synchronization with CAPA and the whole QMS ?
(i.e. compliant, risk-controlled, mature)

AUDITING, A VITAL FUNCTION WITHIN QMS



- Audits provide a mechanism to assess the **level of compliance** and provide an indication of the QMS status in terms of maturity level and effectiveness that might lead to product adulteration or patient harm
 - Audit process is mainly for the **process owner**

AUDITING, A VITAL FUNCTION WITHIN QMS



- Auditing should NOT be a police-punishing activity

Why ?

- Auditing is one of the PROACTIVE actions required by QMS

Which are other actions ?

DEFINITION



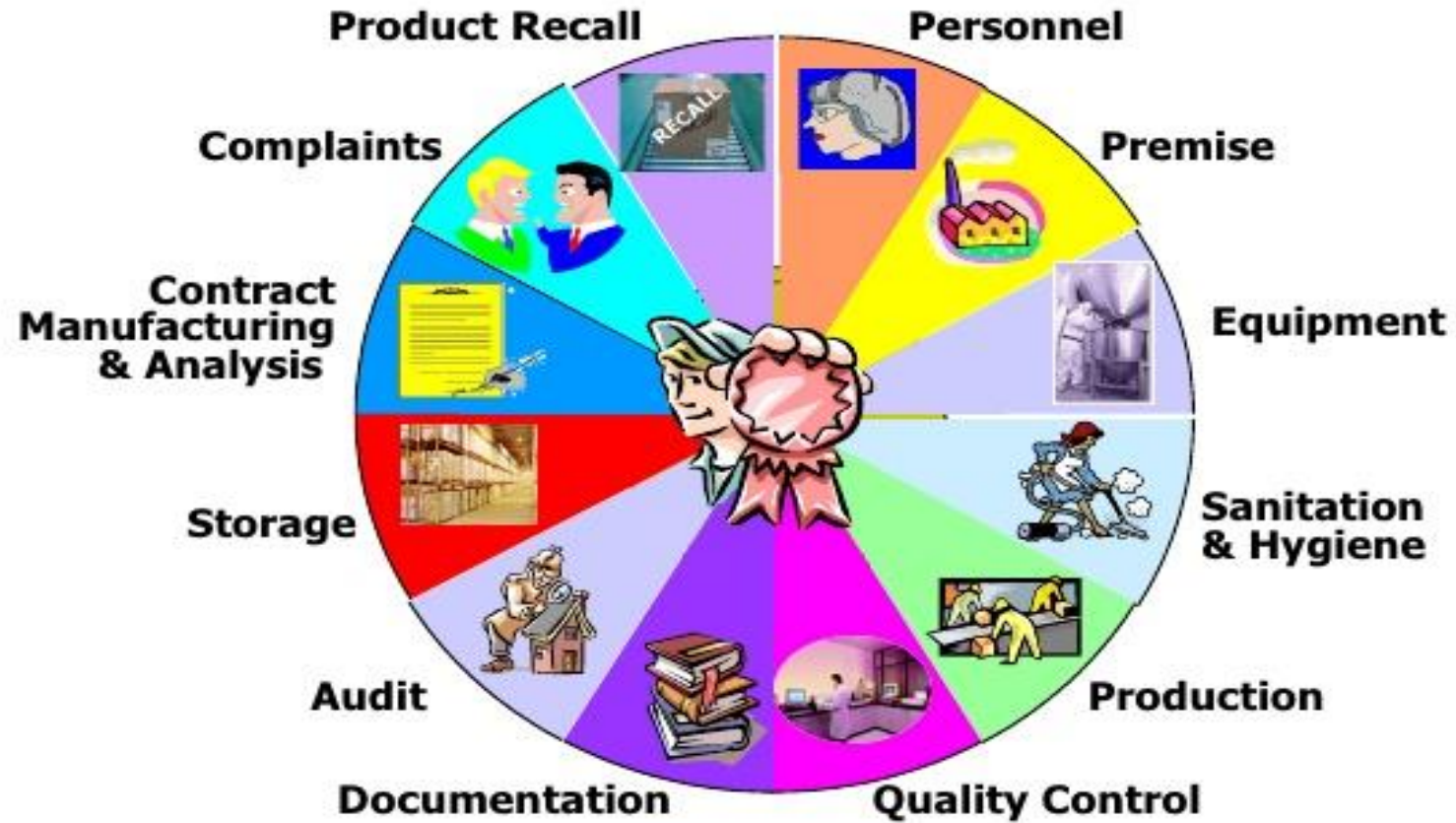
- An audit is a “systematic, independent and documented process for obtaining audit evidence [records, statements of fact or other information which are relevant and verifiable] and evaluating it objectively to determine the extent to which the audit criteria [set of policies, procedures or requirements] are fulfilled.” [ISO 19011:2011—Guidelines for auditing management systems](#)

WHICH IS THE MAIN PURPOSE OF AN AUDIT?



- A well designed and robust audit program is a key stone of an **effective** Quality System
- Many internal company quality audits and many external supplier/contractor quality audit programs are **ineffective**
- Goal: **effecting change** to bring about compliance to company
- Determining operational deficiencies is only one aspect of an audit

SCOPE OF AUDITS



TYPES OF QUALITY AUDITS



Carried out by.....

Or First
Party audit

1. Internal Audit
* Staff of section or
department of
company
OR
* Local Quality
assurance Group.

2. External Audit
•A company on its
vendors. Or
Sub contractors.

Or Second
Party audit

3. Regulatory Audits
Regulatory Bodies
*MCA (UK).
* USFDA(USA)

Or Third Party audit
(ISO audits included)

6 KEY STEPS OF THE AUDIT PROCESS



1. Audit preparation / planning
2. Audit performance
3. Assigning non-compliances
4. Audit reporting
5. Audit follow-up & closure - Audit responses – CAPA
6. Management oversight & commitment

1. PREPARATION OF AN AUDIT - PLANNING



- ✓ Audit team: number; lead auditor
- ✓ Contact auditee early (e.g. >1 month)
- ✓ Auditing company defines objective/scope
- ✓ 1st. communication with auditee
- ✓ Draft plan - need to see on-going operations of interest – no disruption
- ✓ Final plan – check for absence of key auditees !
- ✓ Safety issues

1. AUDIT PLANNING



Done in advance by auditors and auditees, to ensure that the audit complies with the objective. The preparation stage of an audit begins with the decision to conduct the audit, and ends when the audit itself begins.

Could include data gathering.

Key aspects:

- audit frequency,
- a risk-assessment approach to streamline audits
- vertical and horizontal audits
- trending and reviewing audit data
- audit team selection and qualification
- audit plan

1. AUDIT PLANNING



A risk-assessment approach for auditing

- Consider the complexity of operations and the need to use resources effectively
- Methodology that links internal auditing to an organization's overall risk management framework. Saves time
- Areas of risk (departmental operations or systems, e.g., transfer of samples, a manufacturing step, a specific test method)
- Manage costs (e.g. avoiding batch rejection, remediation costs associated with the audit process such as follow-up audits and corrective and preventative actions)

1. AUDIT PLANNING



A risk-assessment approach for auditing

- How to best select the audit subjects to examine and how often to audit
- Streamline audits so that they are more effectively targeted and non-compliances can be effectively addressed
- Changes

1. AUDIT PLANNING



Consider the degree of confidence in control measures

- If an inherent risk such as product contamination is very high, but there are good controls such as procedures, controlled environments and top of the line technology in place together with an appropriate testing regime, what would your approach be?

....then the residual risk defined as the risk remaining after controls have been taken into account may be low, and therefore not worthy of examination at high a frequency

- If an area or function has weak controls, poor detection methods, and laboratory analysis have led to past errors, what would your approach be?

... might require an elevated frequency of auditing

- This approach can also be adopted for external audits of third party suppliers

1. AUDIT PLANNING



Weaknesses can be determined from historical examination of past audits and other sources:

- **Trend analysis** helps define frequency and to identify weak points
- A Department with **poor history** in terms of compliance and the associated number of recorded non-conformances
- A department that has been **slow to respond** to audit action items
- A department that has **not responded effectively** to audit action items
- A **poorly performed** assay
- **Samples** incorrectly stored

1. AUDIT PLANNING



- The **annual plan** is an important document and should be reviewed & approved by senior management. The annual plan can feed into a strategic plan
- Prioritize potential audit topics and areas to be audited. An area can be a department or function (e.g., the chemistry department as a whole; or the function of analytical testing for a given control standard and associated documentation)
- Not every part of an audit universe needs to be examined during the course of the year. Focus on key parts within the quality system and rarely seek to cover all aspects during each audit
- Performed at defined intervals and for a specified duration

1. AUDIT PLANNING



- Without knowing the role and function of each area, an adequate risk assessment cannot be performed
- The auditor must be familiar with the area or quickly get up to speed with what the area does
- Once an area is understood, the likely events that impact upon these objectives and the inherent and residual risks involved can be identified
- Plan updates

1. AUDIT PLANNING



Vertical & Horizontal audits

- Vertical top-down processes audit -- where different elements of the organization are audited of an entire department
- Horizontal or cross-functional audits evaluate an entire process or allow a sample to be tracked (e.g., a sample which requires multiple laboratory tests, techniques, sampling containers, labels, delivery of samples to different laboratories; sample receipt; sample storage; and the testing for different attributes (e.g. chemical content; protein; bioburden))
- The audit approach will include a combination of top down (vertical) and cross-functional (horizontal) slices

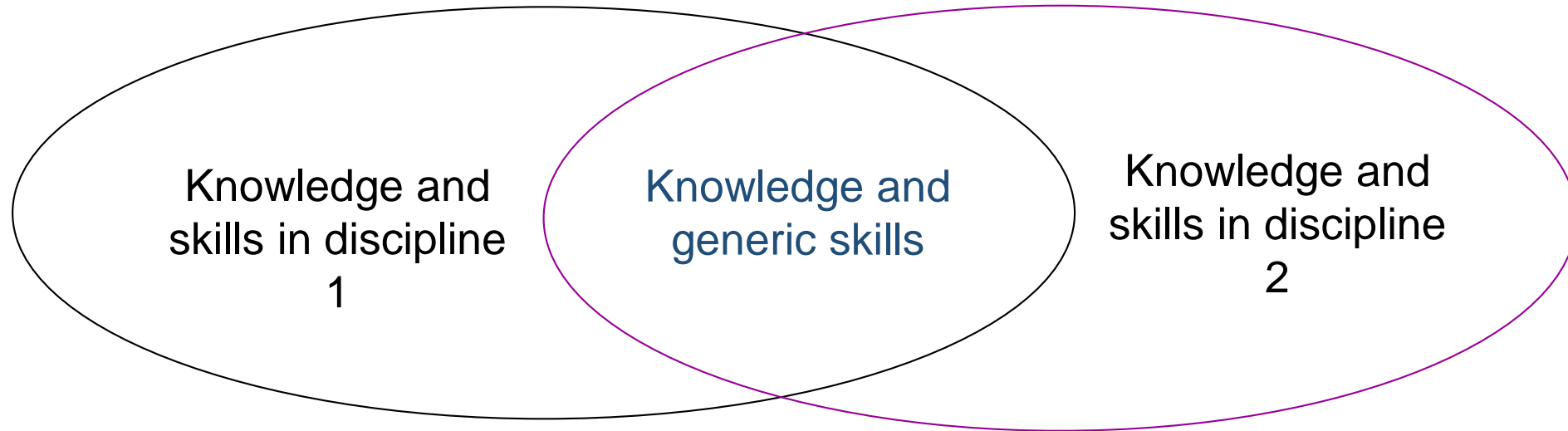
1. AUDIT PLANNING



Audit team selection and qualification

- Independence from the auditee / audited area
- Communicational & Interpersonal skills
- Organizational skills
- Audit function is typically overseen by a defined group within Quality Assurance

COMPETENCE AND EVALUATION OF AUDITORS



2. AUDIT PERFORMANCE



- – or *fieldwork*. It is the data-gathering portion of the audit and covers the time period from arrival at the audit location up to the exit meeting
- It consists of activities including:
 - on-site audit management
 - quick understanding the process and system controls
 - verifying that these controls work
 - communicating among team members
 - communicating with the auditee

2. AUDIT PERFORMANCE



Opening Meeting

- Thank the company / department
- Review audit plan
- Agree on communication channels
- Clarify doubts
- Notes; photos
- Criteria for classification of findings
- wrap-up meetings; closing meeting
- Safety

2. AUDIT PERFORMANCE



- Checklists: not ideal to facilitate communication; may not give value. Good for time management; covers a lot but superficially
- Track forward (chronological stepwise: good for understanding the process for non-expert auditors)
- Track backward (good for traceability verification)
- Random selection (used by experienced auditors)
- Walk through (data integrity issues, e.g. contemporary recording; facility conditions; interviews; calibration; behavior-training)

2. AUDIT PERFORMANCE



Final Wrap-up auditor's meeting

- Before closing meeting
- Discuss among auditors with clarity any identified deviations, especially the major or critical ones (do not leave this for the closing meeting, or, what is worse, for the report).
- Reconsider as needed or check again if doubts. Misinterpretations and misunderstandings may happen.
- Prepare a brief executive report if possible

2. AUDIT PERFORMANCE



Closing Meeting

- Allows the auditor to communicate the major findings / concerns, and possibly conclusions of the audit.
- All deficiencies must be clarified with the audited company's manager BEFORE the closing meeting. No surprises !!!
- Major or critical deficiencies should be supported by clear, complete objective evidence.
- An executive audit summary may be provided
- Highlight strengths as well, and thank the company.

2. AUDIT PERFORMANCE



- **Closing Meeting**
- Give auditee the opportunity to clarify and fully understand (ideally, agree on) the deficiency
- DO NOT be prescriptive on HOW to implement corrections and corrective actions, however, you may give a general guidance on how to approach the problem

3. ASSIGNING NON CONFORMANCES



- A non-compliance /non-conformance is the failure to adhere to an act or its regulations, to comply with a requirement, standard, or procedure
- Avoid **subjectivity / bias** - Non-compliances need to be referenced against an audit standard citing specific clauses or aspect of GMP
- **Categorize** deficiencies. Systemic or isolated problems?

3. ASSIGNING NON CONFORMANCES



- **Major non-compliance:** deficiency that seriously impairs the effectiveness of the Quality Management System (procedures not written, developed, or implemented, or failure to take an effective corrective or preventative action to the extent that a product is defective). **Systemic**
- **Minor non-compliance:** does not seriously impair the effectiveness of the QMS such as failure to complete a training record or a procedure that is unclear but needs amending; Errors with records that do not lead to the release of a defective product. **Isolated**
- **A series of minor non-compliances** can, due to their number, be rolled into a major non-compliance



3. POSSIBLE CRITERIA TO CATEGORIZE NON CONFORMANCES



NON CONFORMANCES DEFICIENCIES	Isolated / Systemic / Major / Minor
Accidental rip of glove in class A	
Aseptic gowning SOP does not instruct to check gloves	
Wrong expiration date on a reagent bottle label	
BR poorly written; instructions may be confusing	
Operator repeatedly spills samples	
Management does not reinforce requirement to record information properly (Data Integrity)	
A preventive maintenance task was delayed	
Preventive maintenance does not include filling machine	

4. AUDIT REPORTING



- The audit report communicates the results of the audit. The report should provide correct and clear data that will be effective as a management aid in addressing important organizational issues. The audit process may end when the report is issued by the lead auditor or after follow-up actions are completed

4. AUDIT REPORTING



- The audit results should be documented and communicated to management
- Reports should clearly describe the audit team's observations, including specific examples when possible, and the level of risk ascribed to each audit finding
- A recommendation should be made as to the future frequency of the next audit to be conducted for the department or system

4. AUDIT REPORTING



- ✓ Provides a record which identifies Critical, Major, Other deficiencies and areas of improvement
- ✓ Should highlight main concerns (e.g. executive summarized section and detailed section)
- ✓ The Audit report should be issued as soon as possible after completion of the audit.
- ✓ Convey the audit report to the process owner
- ✓ Serves as evidence of the performance audit

4. REPORT PREPARATION



DO NOT include in the report:

- Subjective opinions
- Confidential information
- Criticism to individuals
- Ambiguous statements which give possibility to different interpretations
- Too many unnecessary details
- Observations, findings and non conformities which were NOT discussed with the auditees

4. REPORT PREPARATION



Avoid writing:

“Some Equipment are not under preventive maintenance”

“Many....records do not have the results of ...”

“Few ... internal auditors do not have independence..”

“Most of the quality agreements are expired”

“Many ... operators do not know where the SOPs are stored”

“Long non conformities with irrelevant information”

“Reference to names”

“Expressing personal opinions”

EXERCISE – AUDIT REPORT QUALITY



Read carefully these deficiencies. Please make comments based on the aspects/what constitute good inspection report, such as:

- Format
- Code (PIC/S GMP GL)
- Clarity
- Reference
- Evidence
- etc.

EXERCISE – AUDIT REPORT QUALITY



“What appeared to be an uncontrolled copy of an SOP, had been placed by the company inside the raw materials dispense booth. As these SOPs were constantly handled, they provided a critical contamination source for raw materials being handled in the booths.

There seemed to be no environmental monitoring ever performed; the company should perform E.M. daily using settling and surface plates.

The operator being interviewed showed disrespect when asked for details because he did not agree with the observation, and his English was very poor. He also was very busy and did not stop his activity to answer the auditor’s questions. (Major) “

EXERCISE – AUDIT REPORT QUALITY



The suitability of product contact equipment including effectiveness of cleaning was not demonstrated. Further, there was a lack of traceability of cleaning through records.

For example:

- The cleaning of the sampling tools was not documented in the procedure. [4.26]
- The cleaning procedures were not always consistent with regards to the time specified before the re sanitation of equipment. [4.26]

5. AUDIT FOLLOW UP AND CLOSURE



- According to ISO 19011, clause 6.6, “The audit is completed when all the planned audit activities have been carried out, or otherwise agreed with the audit client.” Clause 6.7 of ISO 19011 continues by stating that verification of follow-up actions may be part of a subsequent audit.

5. AUDIT FOLLOW UP AND CLOSURE



- Each non-compliance requires addressing and resolving. Responses to non-compliances are in the form of corrective and preventative actions
- While corrective actions put right what was detected at the time of the audit; preventive actions are focused on improving the quality system so that the same unfavorable observations are not made again
- Depending on the observations made and the commitments to corrective actions, a follow-up audit may be necessary.

5. AUDIT FOLLOW UP AND CLOSURE



- Risk assessment can also be used to frame audit responses. Although auditors are not responsible for determining the risk response, they may have views on its effectiveness
- Auditors are not responsible for putting in place mitigation actions and must assess the effectiveness of control activities in terms of its impact on residual risk

5. AUDIT FOLLOW UP AND CLOSURE



Types of actions as part of the audit responses.

- **Corrective action** is action taken to eliminate the **causes** of an **existing** nonconformity, defect, or other undesirable situation in order to prevent recurrence (**reactive**). Root cause investigation needed at least when dealing with major deviations
- **Preventive action** is action taken to eliminate the **causes** of a **potential** nonconformity, defect, or other undesirable situation in order to prevent occurrence (**proactive**). Quality Risk Management is one of the best tools to identify preventive actions
- **Correction:** Action to eliminate a detected nonconformity (**reactive**). It does not treat the causes. A correction can be made in conjunction with corrective action

5. AUDIT FOLLOW UP AND CLOSURE



Types of actions as part of the audit responses.

- Example of correction:
- Example of corrective action:
- Example of preventive action:
- Other means / tools for identifying preventive actions:

6. MANAGEMENT OVERSIGHT & REVIEW



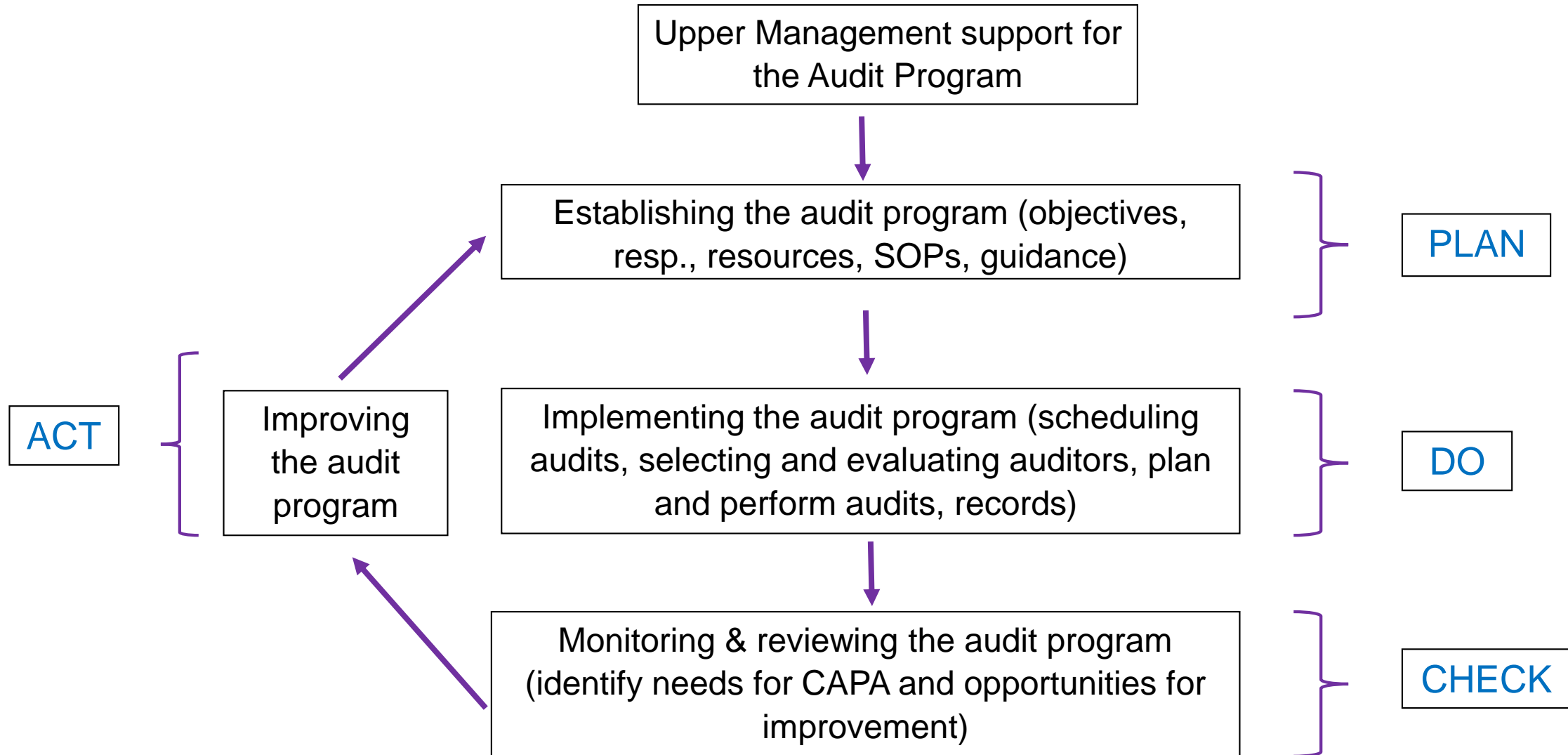
- Audit findings should be reviewed by senior management for decision-making
- Audit findings should be trended and risk-rated so that the organization can direct resources appropriately
- Findings from such quality reviews should be used by the auditors to help plan the next series of audits and to alter, as necessary, risk ratings for departments, functions and systems.
- In a sense, auditing is a perpetual cycle

6. MANAGEMENT OVERSIGHT & REVIEW



- Post-audit review feedback across the organization. If something similar to one audit finding could be found in another department, develop common preventative actions (Proactive), rather than waiting for the next audit of the area (Reactive)
- When external audits occur, the robustness of the internal audit process should be reviewed. If the external audit or inspection has found several items that should have been detected by the internal audit team, then the internal audit process should improve.
- In turn, these can inform about future audits and which areas need to receive a higher risk rating going forward (especially if findings reveal long standing problems)

6. MANAGEMENT OVERSIGHT & REVIEW



SUMMARY



- Importance of quality auditing within the pharmaceutical sector
- Approaches that can be used to assess audit outcomes
- How a risk assessment approach can help to streamline audits so that audits are more effectively targeted within the organization and so that non-compliances can be effectively addressed.
- Trending and reviewing audit data. Past audits
- Frequency
- Pinpoint weak points within the Quality Management System of the organization