

Self-Inspection

DCVMN WORKSHOP

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Benefits which are derived from Audits are given as:-

1. Assuring GMP compliance.

2. Detecting Potential Problems.

3. Effecting Programmed improvement.

4. Increasing management awareness.

Types of Quality Audits

Carried out by.....

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.

3. Regulatory Audits

Regulatory Bodies

- * MCA (UK).
- * USFDA(USA)

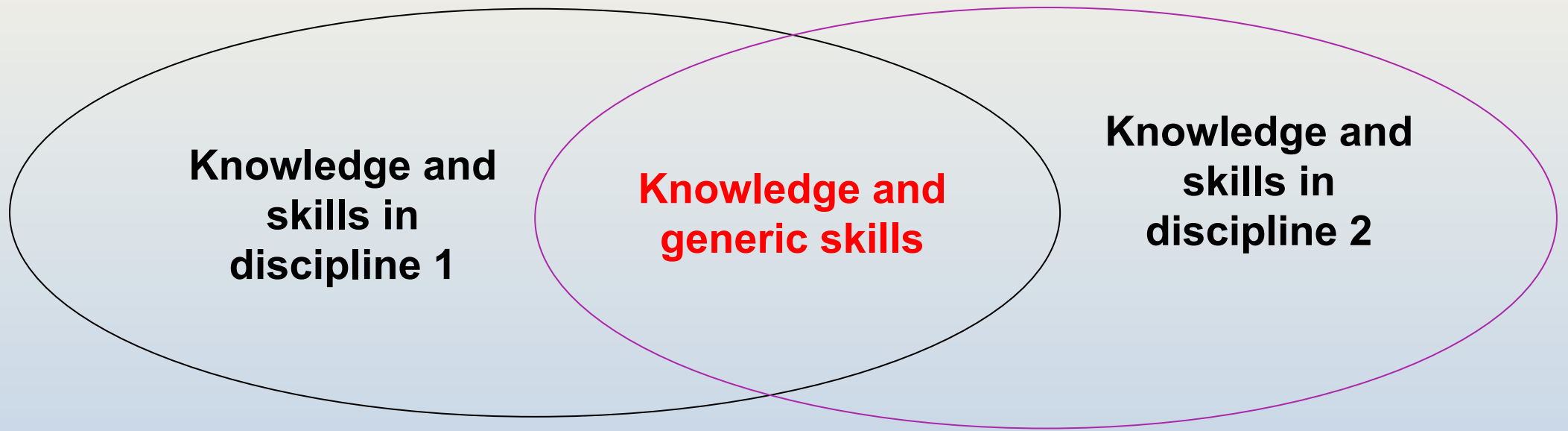
Or by an external contractor

Or First Party audit

Or Second Party audit.

Or Third Party audit (ISO audits included).

Competence and evaluation of auditors



Education

**Auditor
education**

Job Experience

Audit Experience

Personal Behavior (attitude; common sense)

Self-Inspection

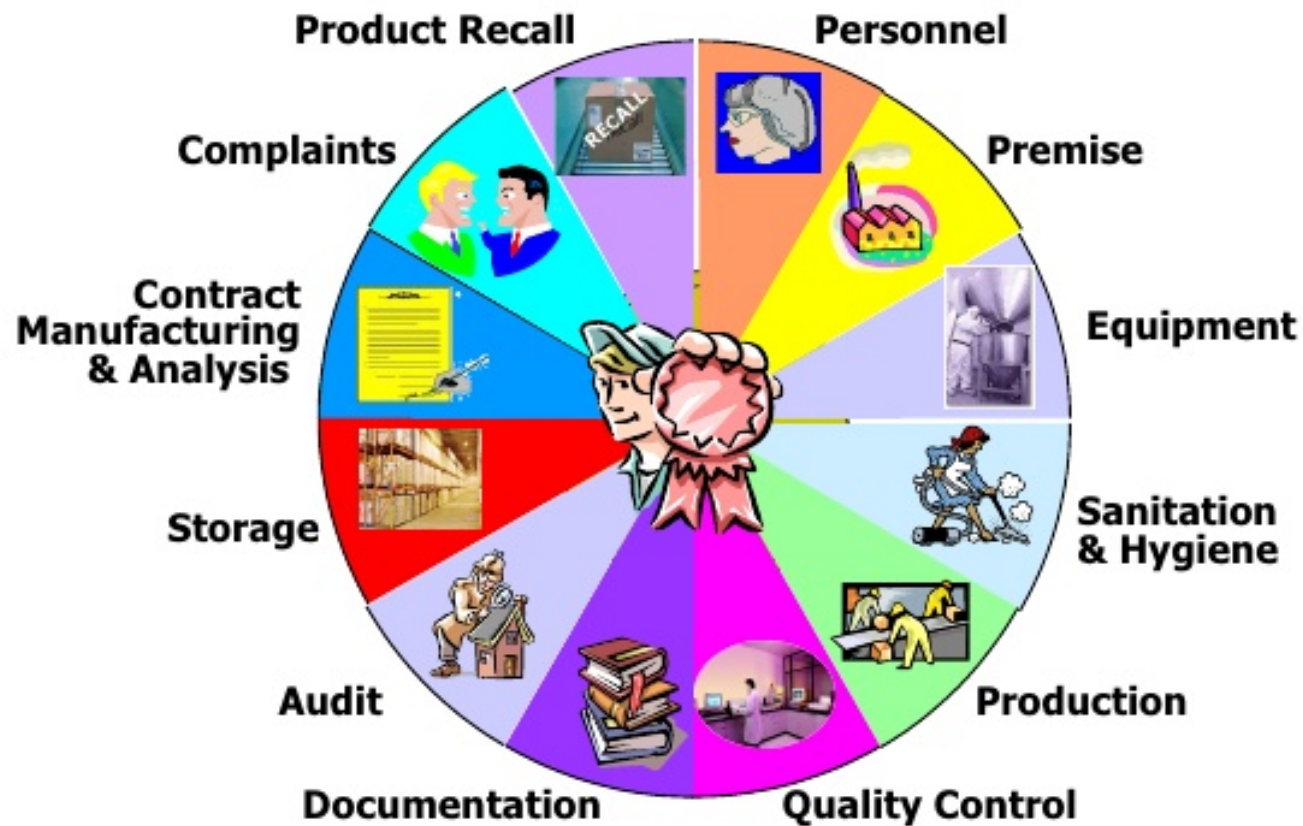
Principle (3)

- Self-inspection team should consist of personnel who:
 - can evaluate the situation objectively
 - have no conflict of interest
 - Have been trained and with previous experience as observers of a self-inspection
 - can be lead self-inspector after a qualification process
- Procedure should be documented
- Effective follow-up programme

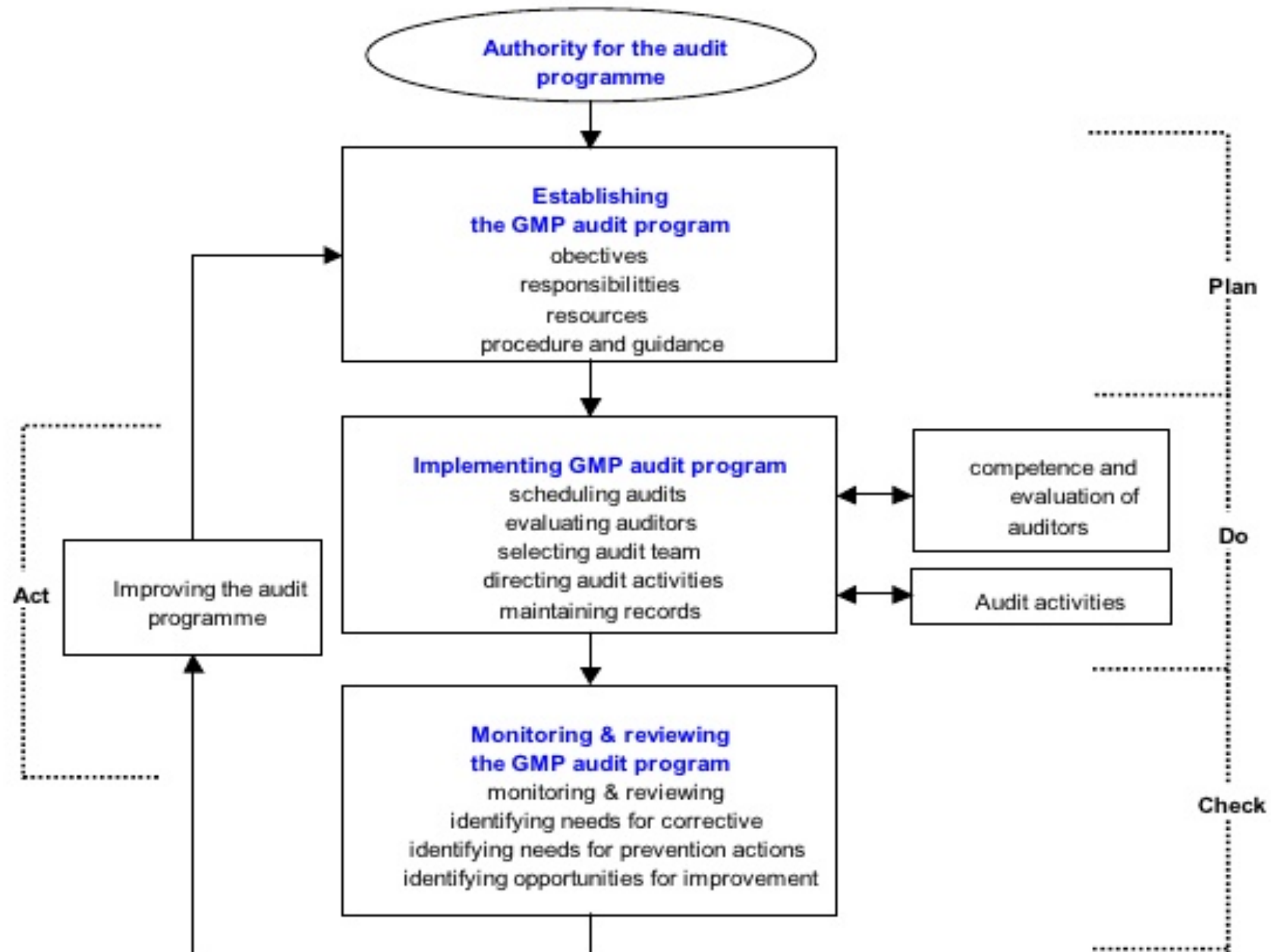
Scope of audits



SUMMARY GMP



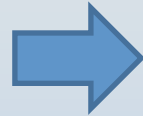
FLOW CHART OF AUDIT



Flow Chart – Overview of Typical Audit Process

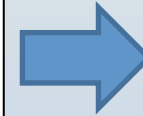
I. Initiate the audit

1. define audit objectives, scope and criteria
2. establish initial contact with manufacturer and/or auditee
3. appoint the lead auditor
4. determine feasibility of audit
5. select audit team



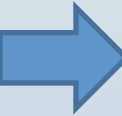
II. Document review

1. review relevant management system documentation and determine its adequacy with respect to audit criteria



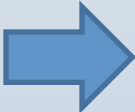
III. Prepare for the on-site audit activities

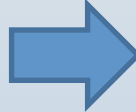
1. prepare audit plan
2. assign work to the audit team
3. prepare work documents



Flow Chart – Overview of Typical Audit Process

IV. Conduct on-site audit activities

- 
1. conduct opening meeting
 2. communication during the audit
 3. roles and responsibilities of guides and observers
 4. collect and verify information
 5. generate audit findings
 6. prepare audit conclusions
 7. conduct closing meeting



V. Prepare, approve and distribute the audit report

1. prepare audit report
2. approve and distribute audit report



VI. Conduct audit follow-up

	GLOBAL INTERNAL QUALITY AUDIT PLAN						
	YEAR: _____						1/1

Sector	Process	Applicable requisites	Date of Audit		NCF / Observations	Date Verified	Auditor/s
			Planned	Actual			

Audit Annual General Plan / Schedule

- ✓ Self-inspection / Supplier audit
- ✓ SOP
- ✓ Criteria:
 - ✓ Risk based
 - ✓ History
 - ✓ Quality Metrics
 - ✓ Changes
- ✓ Living document
- ✓ Status
- ✓ Upper management approval and support

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

Conductance of audit

- The audit should commence with an opening meeting to introduce auditor(s) to relevant auditee staff and Senior Management Representative. (especially relevant for an external audit or inspection).
- The opening meeting also provides an opportunity to
 - ➡ to explain the audit rationale
 - ➡ clarify the audit plan.
 - ➡ agree communication channels .
 - ➡ clarify ambiguous replies in the pre-audit questionnaire.
 - notes; photos
 - classification of findings
 - wrap-up meetings; closing meeting
 - Safety
 - and Thank the company / department

Conductance of Audit

- 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)
- Discuss with clarity the potential deviations (do not leave this for the closing meeting, or, what is worse, for the report.

Conductance of Audit

In closing meeting:

The **closing meeting** is particularly important since it allows the auditor (or audit team) **to communicate the audit findings and conclusions in a logical and co-ordinated manner to the auditee's management.**

- A simple agenda and a **short written summary of observations** should be provide.
- It is important **to emphasise the good news as well as highlight the areas for improvement** together with supporting evidence.
- Audit **deficiencies should also be classified** to highlight the priority for actions to the auditee and their Senior Management.

Conductance of Audit

Audit Analysis

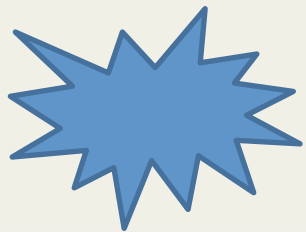
- Analysis should be done with the deficiencies.....

Deficiencies are classified as follows:-

1. Product Quality / Patient Safety Related deficiency (**Critical**)
 2. Significant cGMP Deficiency but with no **direct impact on Product Quality /Patient Safety (Major)**
 3. GMP deficiencies that are either considered to be minor isolated examples or there is insufficient information to classify them as Major (**Other**)
- The auditee should be given the opportunity to clarify and fully understand the evidence for the deficiencies.
 - It is the auditors role to identify what needs to be achieved when a problem is identified, in the case of Second or Third Party Audits he/she should not be prescriptive in „how“ to achieve it, although advice may be offered, if specifically requested.

3. Assigning non-compliances

- 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 ?
- Be careful with **recommendations** – Opportunities for improvement
- Goal is that **auditee understands and agrees** on the deficiency raised.



Possible criteria to categorize non conformances

NON CONFORMANCES DEFICIENCIES	Isolated or Systemic ? Major or 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

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.

Audit Report

It provides a record which identifies and may be useful for prioritizing (e.g. Critical, Major, Other) areas for improvement.

✓ Should highlight main concerns (executive summarized section and detailed section)

The audit report should be drafted, and the final version issued, as soon as possible after completion of the audit.

There are **two important reporting phases**:-

- i) Preliminary reports during the audit
- ii) Final report to the management.

✓ Convey the audit report to the process owner

✓ Serves as evidence of the performance audit

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

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; usually, E.M. is performed 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

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. Review of audit responses and any follow-up audit may lead to an alteration in the risk assigned to specific non-compliances.

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 deal

with 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:

Audit Follow Up

- Timely implementation of corrective actions, and verification of their effectiveness,
- It is a good reflection to the auditees management is that 1st to start the **major remedial action** as soon as possible. **Followed by minor** remedies.
- Major issues should be should be reported within a agreed timeframe.
- It may also be **necessary to re-audit** to ensure **that serious remedial action has been satisfactorily completed** for Critical or Major deficiencies.

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).

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.

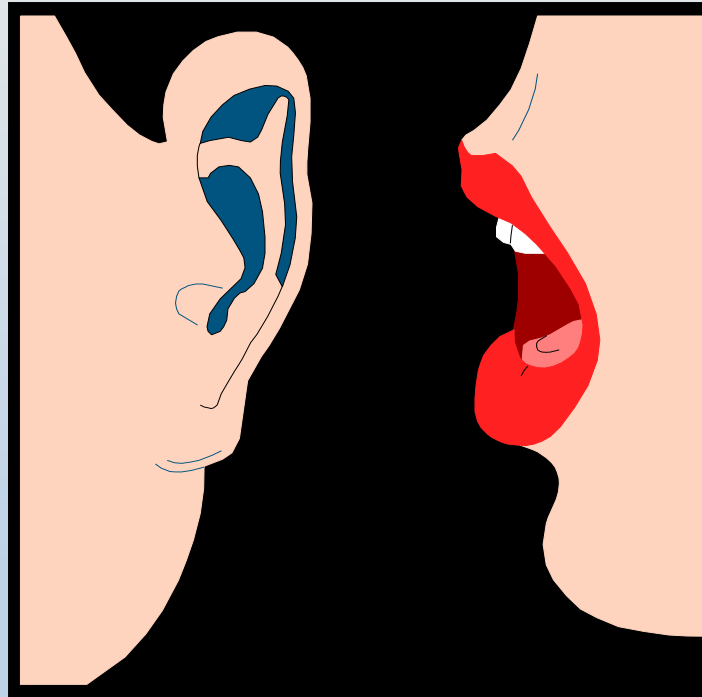
Auditing Skills & Techniques

GMP knowledge and coached communication techniques.

- Read the interview with the two instructors: L. Hartmann & P. Zimmermann.
 - Summarize and highlight the key concerns / recommendations around these 9 questions
- 1. What is more important in conducting audits - knowledge in GMP details or communication skills? Why?**
 - 2. Which job training elements are required for a good auditor?**
 - 3. What are the most common mistakes of auditees?**
 - 4. What is your advice to guarantee a successful audit?**
 - 5. What are the most relevant reasons leading into conflicts in an audit?**
 - 6. What can we learn from daily life to improve audits?**
 - 7. What is the most relevant skill to conduct an audit?**
 - 8. How can we detect early warnings of escalating conflicts during audits?**
 - 9. What is your advice to guarantee a successful audit?**

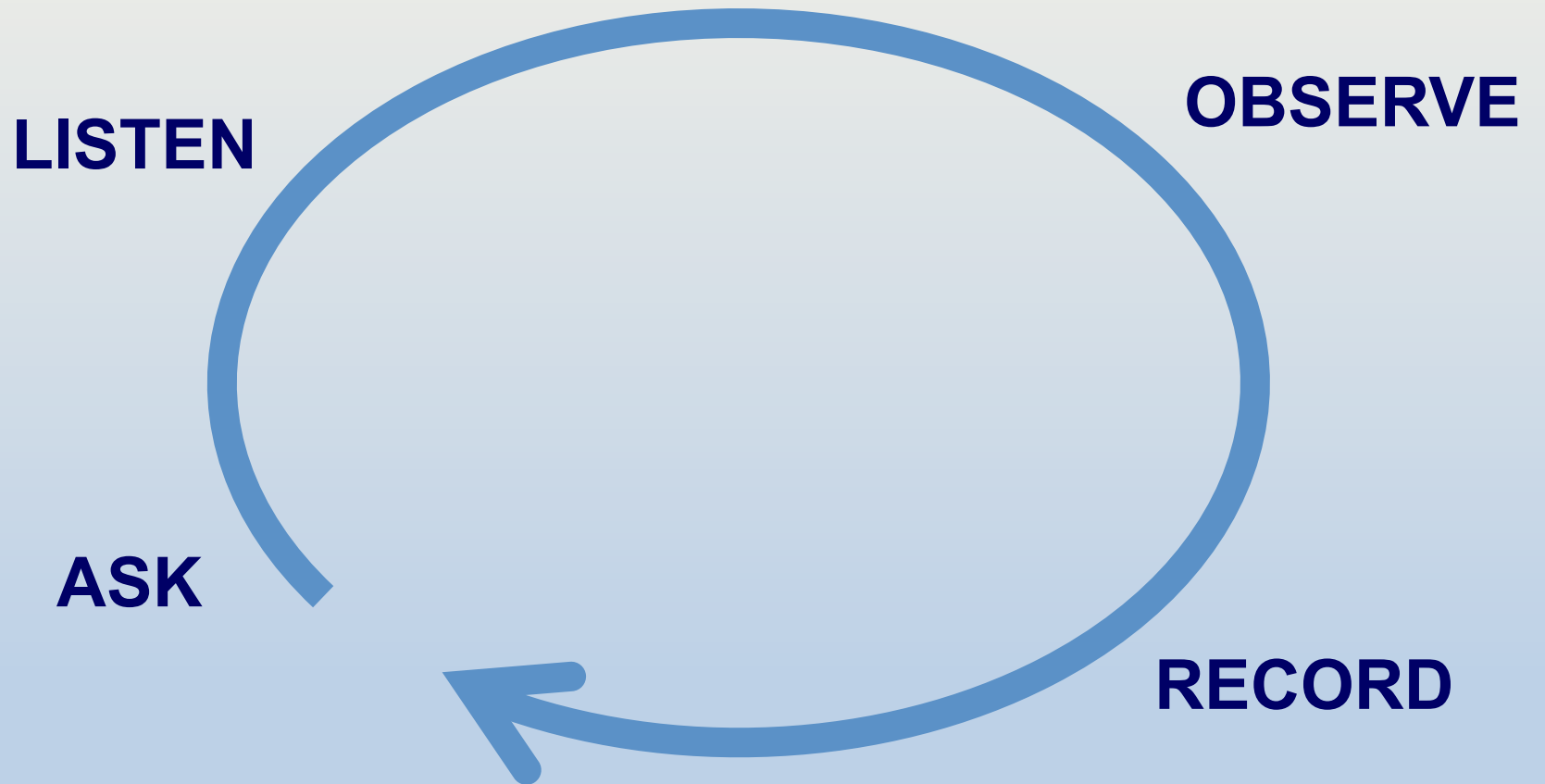
Interview handling

The value of listening



Auditors: Remember to invest most of your time listening

INTERVIEW PROCESS



Open questions

Seek specific information.

- Give me an example of
- How does this work...?
- Any other comment ?

ADVANTAGES:

- Clarifies.
- Verifies the meaning of words and statements
- Avoids misunderstandings.

Closed questions

Short answers.

- Were you involved in this process ?

ADVANTAGES

- Allows the auditor to verify the information and avoid misinterpretations and misunderstandings.
- Good for timid and communicative auditees

Biassed Questions

Biased Questions influence the auditee.

- I suppose you already know this violates basic GMP norms?
- Shouldn't this be in under quarantine?

DISADVANTAGES

- These questions suggest the answer.
- The information gathered is strongly distorted or influenced

AGRESSIVE questions

- Were you the incapable person that did this ?
- Couldn't you have placed this in the right place?

DISADVANTAGES:

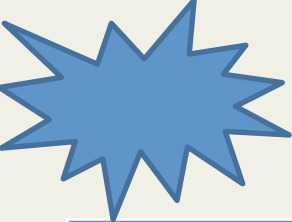
- Places the auditee on the defensive, stressed, out of control. Interferes with audit process.
- Information gathered may not be reliable.

MULTIPLE Questions

- - When did you start in the company?
- - How were you trained for the task you are performing?
- - Do you believe you are following the right procedure?

DISADVANTAGES

- - They bring confusion to the auditee
- Induces the auditee to deviate from important points



Identify the question as Open, Closed, Aggressive, Biassed

QUESTION	TYPE ?
- Of course, for you it is obvious this is the wrong seal, correct?	
- Would you please tell me more about the adding of Thiomersal to inactivate ?	
- After having been working all this time, why didn't you read the cleaning procedure ?	
- Did you record all the fermentation process?	
- What do you mean with inactivating the bulk ?	

Handling of Interviews

Recommended:

- Start with open questions (inviting the auditee to speak freely and give more information)

¿How ...?

¿In which manner?

¿With which criteria ...?



- Then, use closed questions to confirm data

- Use questions with alternatives only if time is running out

EXERCISE – COMMUNICATION SKILLS

“feel the power of communication”

Watch the video and summarize / highlight the key concerns, techniques and recommendations to consider during the performance of the audit.

AUDITORS, BE PREPARED !!

Auditees may be:

- Timid
- Aggressive
- Distracted
- Very busy
- Evasive
- Stressed
- May have pre-prepared samples of documentation
- Influenced by local culture
 - Limited answers
- Trying to hide by being instructed to do so or by their own decision.

TIPS FOR THE AUDITOR

Auditing Techniques

Do

- Stop talking
- Calm the Auditee
- Focus on listening
- Remove distractions
- Empathize
- Patience
- Hold your temper
- Question
- Be humble
- LISTEN

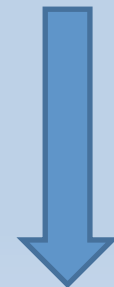
Don't

- Judge
- Embellish
- Inattentive
- Speak unclearly
- Talk excessively
- Phrase yes/no questions
- Display an attitude
- Argue
- Criticize
- Answer your question



“to improve or beautify by adding detail or ornament; adorn”

Empathize:
“identify with,
understand,
relate to, feel for,
sympathize with,
have a rapport”



Be understanding to get the necessary information & evidence

TIPS FOR THE AUDITEE

- Do not volunteer information or data you were not asked for, but NEVER lie
- Be honest, open and cooperative
- Ask the auditor if you're not sure
- Never leave the auditor alone, unless for their own closed door meetings.
 - Never argue in front of the auditor, or with the auditor.
 - Be ASCERTIVE, not confrontational.
 - Company's audit team leader coordinates the selection and participation of auditees and SME.

CONCLUSIONS

Nobody likes to be audited.....

It is a means to have continuous improvement

