

## Auditing Principles for a GMP Audit

<b>Title: Auditing Principles for GMP Audit</b>					
<b>Auditor Manual: 01</b>					
Prepared by:		Date:		Supersedes:	
Checked by:		Date:		Date Issued:	
Approved by:		Date:		Review Date:	

# Audit Training Manual: 01

## Auditing Principles for GMP Audit

## **Auditing Principles for a GMP Audit**

**Example:** How do you check in material coming into the plant site?

An open-ended question is usually followed by a probing question to clarify or amplify information.

**Interview:** Dialogue or conversation that occurs during the normal course of an audit.

**Opening meeting:** A meeting held between the auditee and auditors before the audit officially starts.

**Pre-PAI audits/Mock-PAI:** An audit performed by QA to determine if a site is prepared for a regulatory Pre Approval Inspection (PAI). This audit usually takes place prior to the submission of a regulatory filing.

**Probing Question:** A question used to clarify answers or discover more in-depth information. It is usually specific, focused and used after a general question has been asked.

**Example:** You mentioned that you documented the arrival of raw materials, what do you record on that documentation?

**Supplier:** An umbrella term that covers both Vendors and Contractors supplying API, intermediates, raw materials, packaging components, excipients, formulated products, packaged products and/or providing services, e.g. calibration, validation, laboratory testing etc. to the sponsoring firm.

**Vendor:** Provider of API, raw material, excipients and packaging components to sponsoring firm. A vendor supplies articles of commerce (i.e. available for purchase by other companies).

**Warning Letter:** A letter sent by the Food and Drug Administration (FDA) to management of a company indicating that GMP violations were found in a recent inspection and what the violations were. The expectation is that the company will respond within a designated time period with an acceptable corrective action plan.

## **Explanation of Topic**

### **Introduction**

This unit will outline the steps to follow and important factors involved in performing a quality assurance audit. This unit will not only focus on the actual audit process but also the techniques and skills the auditor should have to conduct a GMP audit and key elements of auditing an audit function.

Auditing essentials can be categorized into the following broad topics:

- The who, what, where, when and why of a compliance audit
- The Auditor's Role
- The Audit Process

The following sections will provide more detailed information on these categories.

## Auditing Principles for a GMP Audit

### Guidelines and Procedures.

A GMP audit is an evaluation tool that can:

- Verify if company policies and procedures are being followed.
- Assess sites' GMP practices.
- Verify that required systems and controls are in place and in compliance with GMP regulations.

Specific goals of GMP audits are to:

- Determine whether QA, production activities and systems comply with GMPs, regulatory agency requirements and site requirements.
- Facilitate early detection of problems.
- Help determine the depth of the identified problem in the area as well as across the company.
- Investigate and determine the root cause of the problem/deficiency.
- Assure compliance with regulatory agencies' requirements.
- Provide management with information regarding the level of compliance at the site and suppliers.
- Recommend approval and certification of a supplier.

Each audit that is conducted must be based on facts. Auditors are fact finders! All audit observations must be able to reference the GMPs and current industry standards. An audit should be balanced and include good practices **as well as** deviations. If deviations are found, they must be reported. An audit is a tool to improve site operations or supplier operations to assure that company products are of the acceptable quality, effectiveness and purity.

Long term and tangible benefits of an audit include:

- Identifying, eliminating and preventing problems early in the design and life of a process or system through pro-action.
- Decreasing the number of discarded, recalled and reworked lots.
- Decreasing the number of consumer complaints.
- Continually improving GMP systems and potentially transferring best practices across the corporation.
- Providing management with objective feedback based on facts that can help to identify critical liabilities that require capital and personnel resources (risk assessment).
- Ensuring company customers receive products of acceptable quality, efficacy, and safety.

Remember that the auditee is the primary beneficiary of the audit!

### The Auditor's Role

There are two necessary components for an audit to be successful. The first is an auditor with the right skills, education and experience. The second is the audit process itself.

The auditor is a key component of the audit. To increase the effectiveness of the audit, the auditor must have good auditing practices and techniques that will:

- Allow the auditor to easily access information about the process, facility or product being audited.
- Build a respectful relationship with the auditee.
- Quickly determine the necessary information to conduct an efficient audit.

## **Auditing Principles for a GMP Audit**

### *Interviewing/questioning*

Discussions with site personnel are excellent ways to determine potential problems. These may occur during the site's response to your questions, during the walk through or during documentation reviews. Your interviewing technique is very important. Be polite and do not use a tone that may be perceived as accusatory or confrontational. The following interview techniques can help make your audit more successful.

### **Interviewing/Questioning**

- Introduce yourself to the interviewee.
- Be polite, patient, professional, ALWAYS.
- Do not exhibit a confrontational attitude.
- Don't become emotional and remain objective.
- When asking for information, phrase your question to assure that you are NOT providing the answer.
- Don't ask yes/no questions.
- Start with overview questions and open-ended questions.
- If you receive answers that fully explain or provide the information you need, stop there.
- If you do not receive the information needed, start using probing questions. If probing questions are used, be attentive and encourage further explanation by interjecting response phrases like "I see" from time to time. When appropriate ask to see examples of information provided.
- Use your body language to encourage further discussion.
- Ask direct questions and if a general answer is given, then request an example or documentation to support the response.
- Determine the employee's function; ask for the pertinent procedures, forms, and data relevant to the task. Confirm your understanding of the task by asking questions.
- If you do not believe that you are receiving accurate information, ask confirmatory questions by asking the same question to a different interviewee or ask a different or re-phased question on the same subject to the same interviewee.
- Do not criticize an individual's performance even if you believe that it is not satisfactory. Determine if their performance is a result of their training and/ or procedures they use, or lack of management involvement.
- At the completion of the interview always thank the person for their time.

### **Listening technique**

Another key skill that you need is a good listening technique. Unfortunately most people plan what they are going to say instead of listen to what the other person is saying. You can miss many pieces of information during an audit if you are not prepared to listen and give the auditee their time to talk.

In the following section of the text are some techniques to help increase your listening skills.

Since you will be receiving information verbally, it is important that you confirm the information collected during your interviews with documentation or field verification (observations).

- Listen—often people will be happy to provide more information than you originally requested—you just have to give them a chance!
- Give the interviewee time to respond. Keep silent. Many times people will attempt to fill awkward silence with more details.
- Practice "active listening". Ask questions at appropriate times or indicate that you are listening by interjecting, at appropriate times, small comments like "I see".
- Do not let your opinions or expectations influence what you hear!

## Auditing Principles for a GMP Audit

These are some suggestions but you may have others that may also contribute to a successful audit.

### Analyzing information and data

Within a short period of time, (e.g. a day or a few days) you will be reviewing many kinds of information, from verbal responses to written documents. You will need to analyze the information and determine what should be communicated verbally in the exit meeting and what should be included in the report that will be given to the auditee and management after the audit is finished.

- Use your judgment on what to report. Report deviations from GMPs and local procedures. Identify systematic problems, providing examples.
- Identify trends of non-compliance.
- Remain objective.
- Evaluate the seriousness of each observation.
- Determine whether the evidence points to a deficiency that will cause a regulatory action, jeopardize the quality of the product, or whether the observation should be classified as a “recommendation,” not representing a deviation from GMP.
- If you have questions about some information and have questions about its classification, contact your QA management.
- Remember to use standards. Using standards as reference produces effective, efficient, and objective audits.

Auditors must be knowledgeable about requirements, technical processes, and trained in auditing techniques to be effective.

In summary the auditor should demonstrate the 5 “Ps.”

- Polite
- Prepared
- Professional
- Patient
- Persistent

### The Audit Process

The audit process may begin many months before the actual audit is conducted. The framework for the audit process is shown below:

- Audit preparation
  - Determine who will conduct the audit - an individual/team.
  - Develop the audit agenda.
  - Confirm audit and agree on a date with supplier/area to be audited.
  - Gather information, which could include a supplier questionnaire.
  - Review documents received from the firm.
  - Prepare audit notes.
- Potential On-site Audit Activities
  - Conduct opening meeting.
  - Walk through warehouses, manufacturing facilities and laboratories as appropriate.

## Auditing Principles for a GMP Audit

- 6) What technical information should be reviewed to understand the process.
- 7) documents to be reviewed during the audit.

The purpose of the audit should be clear to both you and the auditee. By defining the purpose, it will help to keep the process focused on a common goal and to increase audit effectiveness. You should always ask yourself “Why is this audit to occur?” By answering the **why**, it helps to focus all parties involved on the purpose of the audit.

Since you will be performing a GMP audit, you should consider the GMP areas below:

- Quality System
- Material Handling System
- Laboratory Control System
- Production System
- Facilities and Equipment System
- Packaging and Labelling Systems

During the audit, you should plan to pay particular attention to the Quality System. The manner in which a firm handles deviations, complaints and out of specification test results will provide insight to the company’s Quality Culture and adherence to GMPs.

### *Notify supplier/area to be audited about upcoming audit*

Work with the auditee to determine a time that will fit within your time frame and will be convenient to the auditee. Once a date is agreed upon, notify the auditee in writing with your requirements for the audit and request appropriate documents. Include the purpose summary in the notification to the auditee as well as in the final report.

### *Review documents*

The following documents and information should be reviewed prior to performing the audit.

#### *Regulatory Documents*

- Regulatory Agency Regulations, guidance documents and guidelines
- Recent regulatory information which may include: FOI documents, regulatory issues about the process to be audited, recent 483’s either concerning the auditee or auditee’s process, and Warning Letter citations
- Appropriate regulatory agency compliance programs related to the pharmaceutical technology/area to be audited

#### *Company Documents*

- Contracts, including Quality Agreements
- Relevant supplier and product changes
- Previous QA audit reports, investigations, etc.
- Quality standards/specifications for components/products including regulatory filings
- Company guidelines and procedures
- Relevant QA Auditor training modules
- Examples of Certificate of Analysis, complaints/atypical reports associated with supplier and a list of lots, including those rejected provided by end user manufacturing site(s) if auditing suppliers
- A copy of the draft filing and quality standard, if applicable, before conducting a PAI audit internally

## Auditing Principles for a GMP Audit

- auditee representatives.
- A review of the complete audit agenda and schedule and a review of the supplier questionnaire if applicable.
- A review of the audit purpose and scope.
- A list of audit activities and auditors assigned to each activity.
- Projected times for the beginning and end of daily activities.
- Projected times for daily meetings with the auditee, as appropriate.
- Auditee information about plant logistics and safety rules as well as other critical administrative issues.
- An explanation of how the audit will be conducted.
- An explanation of how observations will be communicated during and after the audit.
- Projected times for the closing meeting and requested attendees.
- Projected times for auditor daily briefing meetings.

During the opening meeting, ensure that the auditee understands their role in the audit. The auditee management should:

- Cooperate and assist the audit team.
- Provide support to ensure a successful audit.
- Review findings.

The opening meeting is an opportunity to gather data and impressions about the supplier or area being audited.

### *Walk-through*

Audits may begin with a “walk through” of the facility and laboratory. This is generally done at the beginning of the audit and should include a review of available records in the processing/laboratory areas. Walk throughs/tours should be conducted throughout the audit as appropriate.

During the walk through, it is recommended that you “follow a product” beginning with the receipt of raw materials and ending with the release of the finished product. It is expected that the audit program should reflect the process followed by regulatory agency investigators.

Before beginning the walk through, you should obtain a flowchart showing the manufacturing process to be audited. You should observe the:

- Appropriateness of the facility design for the ongoing operation.
- The level of cleanliness of the facility/laboratory.
- The state of repair and maintenance of the facility and equipment (physical appearance).
- The demeanor and appearance of personnel.
- Personnel and material flow throughout the facility and laboratory.
- Documentation practices within a process.
- Facility controls, such as calibration, maintenance, validation, temperature/RH control and measurement, as applicable.

During the walk through, verify that procedures are being followed.

You should determine if the documentation is compliant. This would include observing a manufacturing process and completion of concurrent batch record, equipment use and cleaning logs, identification and calibration status of equipment and environmental monitoring, as appropriate. During the walk through, you should verify that SOPs are accessible to operators. You should also ask to see process or operating documents (i.e. in-process batch records/laboratory notebooks) to see what their normal documentation

## Auditing Principles for a GMP Audit

- Be prepared to discuss and clarify all findings/observations with the auditee.
- Be objective.
- Do not argue.
- Verbally explain each observation.
- Prioritize the observations in order of significance.
- Thank the auditee for their time and coordination function.
- Mention positive observations regarding auditee's operations.
- Determine which auditee staff member should receive the audit report and confirm timelines for issue of the report and response by the auditee.

Recommendations for corrective actions can be discussed at site audits. Please note the audit program should be based on not only identifying problems but also being able to assist with recommendations and provide solutions based on the regulatory compliance experience.

### Follow-up Audit Activities

#### *Document observations in a formal report*

Observations are deviations from recognized standards supported by objective evidence. When writing observations cite the deviation from GMPs and include specific examples found during the audit. List the examples using objective, clear and concise language. The audit observation reports are issued to the Senior Plant Manager or Quality management.

It is recommended that auditors draft audit reports as soon as possible after the audit.

Audit Observations must be classified into Critical, Major or Minor. Critical observations must be identified to site management and their corrective actions discussed.

Audit reports summarize the results of the audit activities. Information often included in the report is:

- Audit team members.
- The purpose of the audit.
- The areas of the auditee's operation that were reviewed.
- Audit observations and rating, if applicable.
- Supplier certification status, if applicable.
- A list of systems audited and systems not audited.
- Systems that do not comply with GMPs.
- Specific areas/systems that were reviewed and were compliant with GMPs.
- Good practices observed at the site.
- Expected response date for corrective and preventive actions from auditee.

The audit report is sent to the auditee, soliciting a response. Usually the report is issued to the Senior Quality Management.

#### *Evaluation of Responses from auditee*

Once you have issued the summary audit report citing the observations made at the audit, the auditee has a responsibility to respond to the audit within a defined time period, commonly 15 days. After those responses are received, it is necessary to analyze them and determine if the proposed timelines and corrective actions are acceptable. When the responses are deemed acceptable, a close out letter may be sent to the auditee.