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# Auditing as A Management Tool in Pharmaceutical Companies

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## Abstract
Quality audit is a key management tool for monitoring the suitability of a company's quality management system and in driving continuous improvement leading to Good manufacturing practice compliance and inspection readiness. Conducting internal audits and external audits of suppliers and outsourcing operations are key elements of a good quality system. Auditing in the pharmaceutical sector serves two different categories: regulatory compliance and business needs. By establishing a high-quality audit system throughout the industry, the level of compliance will increase. This article explores the establishment of an auditing program for both internal audits and external audits including key elements to address when implementing an auditing program.

**Keywords**
Quality audit, compliance, management tool, FDA, good manufacturing practice.

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## INTRODUCTION:

**Quality auditing** is regular process of examining a system for its quality which is conceded by either in-house auditor or external quality auditor or else by a team of people designated by the management for this purpose. These audits may also be extended to suppliers and contractors. A quality audit consists of an assessment and examination of all or component of a quality system with a main intention of reviewing and improving it. The quality related to pharmaceuticals has been the main concern of World Health Organization (WHO) since its inception.

Quality audits in general are worked on at different time period with a gap interval which assures clearly about the organization's system of internal monitoring principles which brings a correlation to the actions efficiently. These helps to establish an idea of whether there is a compliance of quality system that is been defined by the organization and if so whether that can be engaged to provide a criteria for evaluation based on results and that has consistency with regulatory requirements.

Being an ISO 9001 key element that is established as standard quality of systems, Quality audit is one of the important parts of an institution's quality management system.

Auditing is an essential part of any programme that needs an improvement in their quality. The FDA cGMP does particularly have a basic requirement for an internal auditing to be conducted by all the organizations that are involved in pharmaceutical products which is a determination of their effectiveness in system of quality. Quality Assurance (QA) or Regulatory Compliance as a function, have auditors as a distinctive component to assess and approve a company and provide a trail for examining the data to ensure procedures are followed by them appropriately at all times.

Pressure on the pharmaceutical industries to audit has always been higher and continues to increase.

Decisions on supply chain and batch release are solely based on audits and self- inspections. Hence, a high level of scrutiny is being placed on the development and training of the auditors and self-inspectors. The article hereby provides us with process of auditing briefly along with any other issues that may be witnessed programmatically with such procedural operation.

**STANDARDS & REGULATIONS:**

The world's topmost developer of standards is identified as ISO which boosts curiosity in quality audits among developers and business corporations by ISO 9000 protocol issued in 1987. At present, internal audits are required for accepted standards including ISO 9001: 2000, ISO 14001:2004, and ISO 13485 (or the environmental management system in the case of ISO 14001: 2004). Audit serves as an intercession for evaluating and improving quality under these standards. Reflection of similar principle is witnessed in various regulations imposed by the FDA. Regular appraisal of quality standard requirements for pharmaceuticals and blood and blood components is comprised under the cGMP21CFR parts 210-211 & 206.

Importance of audits is also emphasized by pharmaceutical industry and blood institutions. For instance, "Guidance for Industry Quality Systems Approach to Pharmaceutical cGMP Regulations" proposes in-house and supplier review.

The rationale for conduction of both internal and external audits requires the following elements of ICH Q10.

- Internal and external audit results are included as component of product quality monitoring system & process performance.
- Result of audit observations employs both corrective and preventive actions.
- Management review should include audit results as one of its part.
- Feedback Considered from external periodic internal audits show continuous improvement.

**AUDIT COMPONENTS:**

Auditing includes the subsequent 5major mechanism:

- Challenges faced by an organization include a significant risk factor that is identified, analyzed and whose significance is considered relatively by a mechanism termed "**Risk Assessment"**
- All the activities performed during an audit is covered and identified in the scope as statements. Everything from the description of project, deliverables justification including the success criteria is mentioned clearly.
- Audit Program involves the document containing both events and objective of audit.
- Collection, analysis and documentation during audit is done through a definite errand of procedures. The procedure should clearly define the audit's objective.
- Appraisal program comes to an end with the final touch of evaluation and interrogation which is evident through detailed work papers.

**AUDIT OBJECTIVES**

1. To ascertain a quality system's conformance or non-conformance by evaluation of specific requirements.
2. Success verification of implemented quality system to check whether they convene to specific quality objective.
3. Provision of an opportunity to the team members for improving quality in their system.
4. Another main objective includes meeting the regulations required.
5. To register the quality system of audited institutions [1].

Rationale behind audit initiation involves the following:

1. Evaluation of supplier with whom a contractual bond has to be established.
2. Continuous verification of quality system of the supplier is also a part of contract framework to inspect whether they are implemented and within the specifications.
3. The organization's implemented quality system should also have undergone verification to confirm its compliance with specifications.
4. Assessment of one's own system to view its alignment with standard system of quality [2].

**SIGNIFICANCE OF AUDIT IN PHARMACEUTICAL ORGANISATION-AN OVERVIEW: -**

The key for success of any pharmaceutical development lies in auditing. Crucial part of regulatory agencies in the pharmaceutical companies is seen in assuring that products of good quality are being delivered to the public in effective and safe way. Regulatory agencies expectation of a quality product is similar worldwide [3]. The two basic elements that determine the quality is basically the firm complying with requirements of GMP and decision making that is justified in a scientific way. With the new GMP Systems approach Pharmaceutical companies are taking a proactive stance with additional efficient internal auditing and

amplified regulatory consciousness all over the corporation. Excellence as a challenge is accomplished only when each person collectively plant effort [4].

1. People lives depend on medicinal products and thus its high quality. Testing of end products from each batch though being important is just not enough for ensuring the quality. It should also be erected from the start of manufacturing course.
2. An effective pharmaceutical QA system has to be established and implemented by all pharmaceutical manufacturers to ensure quality.
3. GMP compliance is verified through an efficient system of auditing which is preferred commonly by the pharmaceutical producers [5].
4. Assurance of GMP and QA systems effectiveness is performed through the process of regulatory audits and sometimes by even self-inspection.
5. Audits are intended to verify the controlled operation of manufacturing systems that is required for potential problem detection which may help in timely corrections.
6. High degree of self-assurance can be established through audits which help management to have satisfactory plane of control [6].

**REGULATORY PERSPECTIVE—INTERNAL AUDIT**

Even though the USA drugs current good manufacturing practices do not necessitate for internal auditing, self-assessment programs are required for drug production by other global GMPs. Conduction of internal audit are normally measured as an expectation of US regulatory agency. ICH Q7, "Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients", calls for internal audits to be conducted. US medicinal devices Quality System Requirements (QSR), found on ISO principles, also call for in-house auditing. US GLP policies conduct analysis. QA units (Q. A. U) assure reliability studies non-clinically. Though various regulations require conduction of internal audits, they are generally implemented internally to improve operations. Under the Food, Drug, and Cosmetic (FD&C) Act, FDA has the authority to review internal audit findings; however, FDA has chosen not to exercise such authority except in the case of litigation.

**REGULATION PERSPECTIVES—EXTERNALLY AUDITING:**

Generally international drug products (CGMP) require supplier assessment, although in some cases like vendor certification or validation programs auditing is required. Materials are purchased only from approved suppliers as required by all CGMPs. Recent actions, such as the recalls due to contaminated heparin, attention have focused upon assuring control in place for the entire supply chain. Drug product manufacturers are required to use active pharmaceutical ingredient that are only produced according to GMPs as required by amended European Union Directives 20011/8333/EC. API supply audit is a major part of auditing ensuring that the API's are produced according to GMPs and only these materials are used to meet the necessary quality features. US drug CGMPs do not address auditing of outsourced operations, although they do assign responsibility to the quality control unit for "approving or rejecting drug products manufactured, processed, packed, or held under contract by another company."

Chapter 7 of the EU GMPs [7] defines a number of requirements for addressing contracted operations or services (i.e., outsourced operations) including the requirement that the outsourced operation be assessed to determine that the Contract Acceptor is competent to carry out the work required and to ensure that GMPs are followed. The EU GMPs further state that the contract between the Contract Acceptor and the Contract Giver should permit the Contract Giver to visit the Contract Acceptor's facilities. The methods for evaluating or assessing outsourced operations are left up to each pharmaceutical company to determine. EU GMP Annex 8 provides the following useful items to include when evaluating a supplier, which can also be used for evaluating, outsourced, or contracted operations:

- Supplier quality management system and operation of outsources.
- Material production and controlled materials and its conditions.
- They also provide the materials category and products nature that is going to be useful for their production.

**TYPES OF AUDITORS:**

Auditors are generally of three categories:

1. **First-Party Audit:** Self-audit or internal audit are types that come under such audits. Here single organization is responsible for auditing as well as those getting audited. Various

procedures are performed by internal auditors. These chiefly focuses on internal control and effectiveness of company on its reports over finance. Internal auditors being dependent on organization in which audit procedures are executed are requested to directly contact director of board or committee formed for such purpose and report their findings rather than to the management. Hence, in order to reduce the risk, internal auditors will be pressurized for an assessment that is favorable for their administration [8].

2. **Audit by second party:** This is an audit conducted by a customer on a contractor or supplier person. An example can be quoted with a medical company producing devices which carried out an audit on its contract laboratory to establish evidence that they comply with quality system regulations. Supplier survey is different from that of an audit in which same company can audit for any raw material or device parts supplier for assurance of ISO 9001 compliance and standards [9].
3. **Audit through third party:** This type of audit is conducted neither by a customer nor by a supplier. Such audits are conducted either for compliance purpose or certification/registration by agency. An independent body can also get involved in such works. Current GMP inspection conducted by FDA in a pharmaceutical production unit falls under this category. Accreditation of colleges and universities through evaluation and inspection is also quoted as third party audit.

ISO themselves doesn't carry out assessment for conformity but rather have ISO standard incorporated private sector bodies or regulatory agencies in country to evaluate on behalf of them. Due to such action's audits performed by both second and third parties are entitled as external audits. [10]

Categorization of audit is also done on the basis of rationale point. The below mentioned types are predominantly related to ISO- certified and industries regulated by FDA.

- **Compliance Audit:** Such auditing is performed for checking conformance with rules and regulations. Meeting the concerned regulatory requirements is the main objective of such audit which involves checking the systems, processes, actions. The result is generally white or black, ie, a process or product or any system undergoing audit check will be evaluated for pass or fail. Compliance audit is conducted by the FDA in a pharmaceutical industry for CGMP inspection. ISO certification obtained through conformance assessment can also be quoted as example. Compliance or certification is the final part to which both cases outcomes are coupled. The primary concern of the companies being audited is to pass the audit check with flying colours.
- **Performance Audit:** In Improved Performance audit (Third edition), Arter Dennis quotes three about how an audit projection will be like: acceptance with principles, exercising those regulations for efficiency, appropriate employment of rules for achievement of organization's goals. A performance audit is performed not only to check whether ISO estimation of system quality is met by the organization, but also to boost production and profitability by improving the system's efficiency. This type of audit is usually considered as an internal audit that looks into the business results of a company. It also helps a company in deciding about a new contract with the supplier.

**AUDITING PROCEDURE:**

The 10 steps of audit process are as follows:

1. **Notification:** Notification is the first step with which an audit begins. This process alerts about the date and time of conduct of audit to the party about to be audited. It lists the documents to be reviewed for understanding the organization of an institution.
2. **Planning:** Before an audit, the auditor takes few steps to identify areas of concern and also key areas of risk. This is termed as planning.
3. **Opening assembly:** Gathering of the recipient organization's superior responsibility persons along with their directorial people with auditing staff. Procedure that is to be undertaken will be described by the auditors. The schedules of the consulting employees and areas of concern will be described to them by the management [11].
4. **Field job:** Fieldwork begins as soon as the regulation of terminal audit plans is done with the help of meeting reports. Employees will be notified regarding the audit. Schedules will be planned for audit staff reaction. Initial investigation begins after procedures of business are acknowledged. Other procedures include interviewing of key staff, testing of existing business practices with the method of sampling, testing and reviewing of law practices and internal rules for reasonable [12].
5. **Communication:** In order to clarify procedures and processes there should be a constant communication between the team of people

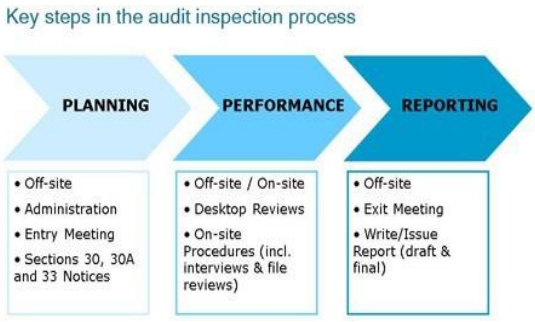
auditing and the auditors. They also have access to documents.

6. **Draft audit:** The next step after completion of audit is the preparation of a draft audit. This draft audit provides in detail with what was performed and what was established. It may also include a distribution catalogue of parties for obtaining initial results and a list of concerns [13].
7. **Response from the management:** The management will be handed over with the draft for the purpose of re-examining, amendment if recommend for any improvements; explore all concern premises with the effect of error correcting. After producing corrections that are terminal, management is produced with all reports for their replies. After this they are asked for their opinion as to whether they have an agreement to the problems cited, the correction made for such problems and the date expected by which all of these issues will have been acknowledged [14].
8. **Finishing and follow up:** A complete finish meeting is required to talk about the observation and interpretations at the end of an audit. Commitments for corrective actions can be possibly obtained from the management representatives present.

All parties present should clearly every perception for all the commitments that is observed for actions to be corrected. Auditing reports need timeframe which is available within which period observation responses should be forwarded.

Development of correct schedules for any corrective actions that has to be completed will be undertaken. Necessary of an audit in the form of follow up will be periodically made which is based on all the observations and commitments given during that period.

Review of corrective actions will be made with future audits in case follow up audit cannot be conducted. Rationale documentation for any following up audit is essential for reference. Unfavourable situations are prevented with help of preventive actions for future help [15].




**DOCUMENTATION:**

The audit results should be documented and communicated to management. The method of documentation and communication including the security and confidentiality of the audit reports should be defined in the procedure.

It is important to remember that those responsible for the audited operation should always receive a copy of the report, including outsourcing management and supplier management. Such reports should clearly describe the audit team observations including specific examples when possible. If commitments have been made to implement corrective actions, such commitments should be included in the report.

Security of audit reports should be strictly enforced, and distribution of the report should be limited. When providing audit reports to external sources such as outsourcing companies or suppliers, a subset of the internal report may be provided as long as the observations are included.

**REVIEW AND EVALUATION:**

If the objective of the audit is to evaluate the effectiveness of the quality management system, then it is imperative that management should view the results of audits as part of their periodic review of the quality system.

Management should review internal and external audit results and act upon the findings as part of the continuous improvement process. Management is responsible for ensuring the effectiveness of the quality system and should be made aware of any observations that impact the quality system.

ICH Q10 lists the following as potential outcomes of management reviews:

- "Improvements to the pharmaceutical quality system and related processes
- Allocation or reallocation of resources and/or personnel training

- Revisions to quality policy and quality objectives.
- Documentation and timely and effective communication of the results of the management review and actions, including escalation of appropriate issues to senior management."

**CONCLUSION:**

An audit is viewed as a valuable tool of any management system. Being an essential business process auditing provides recommendations for the improvement of an organization. Although, regulations do not always ask for an audit, a good audit program can play an integral role in product realization, process performance and quality monitoring, and continuous improvement within a quality management system as outlined in ICH Q10. Use of risk management practices as defined in ICH Q9 provides a useful tool for prioritizing audits.

The main objective of auditing is to make sure that the companies meet the requirements as described in ICH Q10 by various auditing programs. An effective program will help provide key components that help maintain quality of the products in a system of quality that is effectively managed. Any type of auditing, whether internal or external should be addressed and its definition is prescribed in a manner of writing. These objectives and procedural must be approved well in advance.

Audit evaluate efficiency of an organization's quality system. The final reports to the management of organization are provided to make them continuously improve in standards.

**A list of abbreviations**

| | |
|---|---|
| WHO | World Health Organization |
| FDA | Food and Drug Administration |
| cGMP | Current Good Manufacturing Practice |
| ICH | The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use |
| QSR | Quality System Requirements |
| FD&C | Food, Drug, and Cosmetic Act |

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