ejpmr, 2017,4(7), 358-364

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A REVIEW ARTICLE ON SELF INSPECTION AND QUALITY AUDIT

Yogesh Waghmare* and Sonali Mahaparale

Department of Quality Assurance Technique, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune-411044, Maharashtra, India.

***Corresponding Author: Yogesh Waghmare**

Department of Quality Assurance Technique, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune-411044, Maharashtra, India.

Article Received on 06/05/2017 **Article Revised on 27/05/2017** **Article Accepted on 17/06/2017**

ABSTRACT

The goal of an audit is to express an opinion on the person, system, procedure and organisation, inspection have become a standard assessment tool deployed by regulatory authorities and standard bodies when monitoring external organisations. Producing and using spatial data as well as web services has reached the level of mass market, leading to new research challenges. Self inspection should be conducted in order to monitor the implementation and compliance with good manufacturing practices to process necessary corrective measure. The pharmaceutical auditing expertise includes writing and review of validation policies, ICH guidelines and Standard Operating Procedure (SOP) from design qualification to performance qualification. The audits are an effective means of evaluating compliance with the objective of the quality system. The various concepts are community, certification, accreditation, inspection, audit, quality assessment, quality control, quality assurance facing increasing risks of misusing given products. Personnel matters, premises, equipments, documentation, quality control, distribution of the medicinal products for dealing with complaints and recalls and self inspection. These guidelines provided by European Union (EU) gives a general guidance on conducting inspections. All self inspections should be recorded and also statements on the actions subsequently taken should also be recorded.

KEYWORDS: The spatial data quality, auditing, certification, GMP components, regulatory aspect, accreditation and procedure of an audit.

INTRODUCTION

The quality, safety and efficacy of drugs have always been a matter of concern for public. Drugs being a very important component of health care system need special attention in regard to their quality, safety and efficacy. A brief review of over half a century of drug scenario in India will show us how we have come a long way in controlling the quality of drugs. The quality control systems were designed on the concept that if a formulation conformed to the prescribed standards, it should be taken as a product of quality, safety and efficacy. But this concept of good manufacturing practices (GMP's) emerged in nineteen hundred sixties in united state of America (USA). But not many people become aware of the concepts in the sixties. WHO played a significant role in making manufactures of drug formulation and national governments aware of GMPs through its certification scheme and India was no exception. But except for multinational companies in organised sector, GMPs did not find favour with a large number of small and medium scale pharmaceutical companies. The scenario known for regulation which would make GMPs obligatory for manufacturers of drug formulation. In view of the above and to fall in the line with other nations, the government of India amended the Drugs and Cosmetics rules, 1945 date 24 June 1988 and prescribed GMPs under schedule M to the rules. An audit should not to be seen as interrogation with the auditee as permanent loser. The APCI audit programme is designed to ensure that effective independent audit are performed by certified auditors and this guidance document is used as a key reference to provide advice. The goal for the inspector should be to determine whether the various elements within the quality assurance system are effective and suitable for achieving compliances with GMP principles. The personnel matters, equipment, documentation, production, quality control, distribution of the medicinal products arrangements for dealing with complaints. The self inspections should be conducted in an independent and detailed way by designated competent persons from the company.

PURPOSE OF SELF INSPECTION

1) The purpose of self inspection is mainly to monitor the implementation of and compliance with schedule M and to propose necessary corrective measures.
2) Audit is normally designed for one or more of the following purpose;
3) To determine whether the quality system being implemented needs the quality objectives of the company as stated in the quality policy.

4) To provide the audited functions with an opportunity to improve the quality system.
5) To meet requirements.

General Aspects

A quality audit is an independent review conducted to compares some aspects of quality performance with standards for that performance. The term independent is critical and is used in the sense that the reviewer called the auditor is neither the person responsible for the performance under review nor the immediate supervisor of that person. An independent audit provides an unbiased picture of performance. Quality audit are used mainly by companies to evaluate their own quality their own quality performance and the performance of their suppliers, agents and licenses other and by regulatory agencies to evaluate the performance of organizations which they are assigned to regulate. The usual purpose of quality audit is to provide independent assurance that plans for attaining quality are such that, the intended quality will be attained;

a) Products are fit for use and safe for the user.
b) Laws and regulations are being followed.
c) There is conformance to specification.
d) Procedure is adequate and is being followed.
e) The data system provides accurate and adequate information on quality to all concerned.
f) Deficiency is identified and corrective action is taken.
g) Opportunities for improvements are identified and the appropriate personnel alerted.

The Farrow 1987 explains how audits also assist in managements decisions making, allocation of resources, and improving moral. The subject matter of quality audits extends across the entire spectrum of the quality function, but the bulk of auditing is performed under several well established categories;

1) Audits of policies and objectives- this review is conducted at the highest level of company operations and hence is normally done by upper management.
2) Audit of performance against company objectives- because company objectives are quit broad, this review is also conducted by upper management and is based largely on the data presented by the executive report on quality.
3) Audits of plans, procedure and systems- These measures are reviewed to judge their adequacy for enabling the company to meet its quality policies and objectives- This includes audits of computerised system to detect errors in computer programs, Willborn 1987.
4) Audits of execution- This audit are conducted to determine whether execution follows the plan, system and procedures. The term quality system audit is often used in contrast to product audit.
5) Product audit- this audit is conducted to determine whether the product meets specifications and the needs of fitness for use.

ADVANTAGES OF SELF INSPECTION AND INTERNAL AUDIT

1) To check quality system in the company.
2) Helps to comply with the regulatory authorities.
3) Way of constant improvement in quality related to each and every aspect of company.
4) Helps for routine check up and follow up.

LEGAL ASPECT

a) As per schedule M, Inspection should be performed routinely and may in addition, be done on special occasions. Example in case of repeated rejections, frequent reprocessing or incidence of excessive product residues.
b) They should be conducted in a independent and detailed way by competent personnel with inn the company from different functions but who are familiar with GMP.

AUDIT OF QUALITY PLANS

The term audit of quality plans refers to review of entire family of elements of quality planning to judge their adequacy for meeting the quality mission of the company. The more complex the product, the greater the need to review the quality plans, systems, procedures and other measures to judge their adequacy.

SUBJECT MATTER

The scope of audits cover wide range all functions affecting quality, a single function Example handling of complaints, or a single activity Example calibration of measuring equipments. Since quality related activities are numerous. Priorities must be determined. Priorities should emphasize activities impacting on fitness for use and contractual requirements and then activities which affect the cost of poor quality. In setting priorities attention should be focus on the opportunities for improvement versus the cost of performing the audit. Thus, as audit identify and help to correct a problem. Audit resources should be switched to other areas or the frequency of audit for the improved areas should be reduced.

Identifying the Broad Areas of Quality

The Kane 1984 discuss an example which identifies various elements for auditing at a manufacture of refrigeration equipment.

Establishing For Each Chosen Subject

A detailed checklist of the feature to be studied and the questions to be raised, the checklists benefit both the auditor and auditee.

TABLE:

Sr. No.	The Quality Program Requirements
1	The Quality policy
2	The Organisation
3	The Quality programme documentation
4	The Personnel selection and identification
5	The Document control
6	The Measuring and test equipment
7	The Records
8	The Performance feedback
9	The Quality costs
10	The Corrective action
11	The Marketing activities
12	The Design Assurance
13	The purchases and contracts
14	The Manufacturing activities
15	The Material identification and control
16	The Examination, Inspection and Test
17	The Non-conformance
18	The Special processes
19	The Handling, storage and shipping
20	The Deliverable software
21	The Installation and service
22	The Audits
23	The Performance improvement

The reference standards for Auditing

Audit of quality plans requires reference standards against which to judge the adequacy of the plans. The reference standards available include;

a) The written policies of the company as they apply to quality.
b) The stated objectives in the budgets, programs, contracts.
c) The customer and company quality specifications.
d) The pertinent government specifications and handbooks.
e) The company, industry and other pertinent quality standards on product, processes and computer software.
f) The published guides for conduct of quality audits.
g) The pertinent quality department instructions.
h) The general literature on auditing.

PLANNING AND PERFORMING AUDITS

According to ANSI/ASQC 1986 the main steps in performing audits are as follow:

AUDIT INITIATION

The auditor or inspecting team must be mentally conditioned to evaluating only systems, procedures and functions and not the performance of individuals. A helpful attitude helps to overcome any resistance that may be in the areas audited. What exactly is to be audited and against what criteria the audit is to be done should be clearly specified to the audit team, As suggested earlier a questionnaire based on schedule M covering the various aspects may be kept for reference in order to ask the right questions. Prior notice of inspection may or may not be given.

AUDIT PLANNING

An audit plan should be prepared to inform the manager of the activity being audited and the participating auditors regarding the details of the impending audit. Vital element of plan includes a definition of scope and objectives of audit, identification of area to be audited. Identification of auditors, a schedule including the expected start and completion time for the audit, reference to any relevant standards or procedures and audit documentation.

SCHEDULING

Most auditing is done on a scheduled basis. This enables all concerned to organised workloads, assign personnel and conduct other necessary activities in an orderly manner. It also minimizes the irritations that are inevitable when auditors are unannounced. Example blank audits, where the need to avoid cover –up may require surprise audits.

AREAS TO BE AUDITED

The amount of execution of plans is simply enormous and priorities must be determined. Consequently the audit of execution must be based on sampling, even the choice of sampling methods turns to be an intricate problem. The sampling for audit of plans is fairly simple. Plans change slowly, so that periodic audit even every two or three years are adequate. In one large electronic company the audit of divisional practice conducted by corporate staff auditors employs a plan of sampling

based on selected combinations of the product lines made by the company. The functional activities engaged in, example design production. And the subject matter within these product and activities, example instrument accuracy, record keeping. This sampling approach replaced the former approach of auditing a specific product line within a specific division and reporting the result with recommendations for action. Another form of audit sampling is by product control centres. This approach a group of related product control stations is regarded as a centre for sampling purpose. Each month so sample of about various decisions is allowed to proceed, the sample is extended or a product audit is instituted. As per WHO and schedule M questionnaires on GMP requirements must cover at least following;

1) The personnel.
2) The premises including personnel facilities.
3) Maintenance of buildings and equipments.
4) Storage of starting materials and finished products.
5) The Equipments.
6) Production and in process controls.
7) Quality control.
8) The Documentations.
9) The sanitation and hygiene.
10) Validation and revalidation programs.
11) Calibration of instruments or measurements systems.
12) The recall procedures.
13) Complaints management.
14) The labels control.
15) Results of previous self inspection and any corrective steps taken.

DOCUMENTATION

The necessary working paper for audit should be identified and created. These are the entire document required for an effective audit, including flowcharts, checklists, and the auditing approach, forms for reporting observations and results of previous audits.

OBJECTIVITY

The auditor is expected to be objective. Where objective standards are available, there is less need for the auditor to make the subjective judgement and there by less opportunity for wide differences of opinion.

DISCOVERY OF CAUSES

In many companies the auditors is expected to investigate major deficiencies in an effort to determine the cause. These investigations then become basis for the auditor's recommendation. In other companies the auditor is expected to leave such investigations to the lie people, the auditors recommendations will include proposals that such investigation be made.

COMPETENCE OF AUDITORS

The basic education and experience of auditors should be to enable them to learn in short order the technological aspects of the operations they are to audit. Lacking this background they will be unable to earn the respect of operational personnel. In addition they should receive special training in the human relations aspects of auditing. In 1987 the American society for Quality Control embarked on a program for the certification of quality auditors.

AUDIT IMPLEMENTATION

The heart of this phase is the collection, analysis and evaluation of factual information and the drawing of conclusions from these facts. The four elements be covered in auditing an activity i.e. a) Person, b) Item, c) Equipment and d) Documentation. In making observation, it is important to include a representative sample, if several shifts are involved, all operative shifts should be at least partially audited. The information collected is consists of a combination of both documented evidence and information obtained through interviews of various personnel. As a guide the audit information collected is considered sufficient when it can be seen that the analysis of the evidence by some other qualified person who had not collected the information would reach essentially the same conclusions.

POST AUDIT MEETING

The important part of the implementation phase is the post audit meeting that is held with the manager of the audited activity. At this meeting the audit observation are presented so that the manager can plan for corrective action. In addition the manager can point out to the auditor any mistakes with respect to the fact that have been collected.

AUDIT REPORTING

The audit result should be documented in a report and a draft should be reviewed at the post audit meeting with the management of the activity that was audited. The report may be jointly issued by the auditor and auditee, for a report to be viewed as erodible it should be balanced in perspective and be depersonalized.

BALANCE IN REPORTING

An audit which reports only deficiencies may be factual as far as it goes. Yet it will be resented, because nothing is said about the far greater number of elements of performing which are well done. Some companies require the auditors to begin their reports with commendable observations others have evolved overall summaries or ratings which consider not only deficiencies. One serious and common criticism of audit reports is the tendency for the reports to emphasize deficiencies that are minor in nature at least in the opinions of those who were audited, for audits to be viewed as useful and constructive, the importance of the deficiencies reported should be analysed. Such an analysis must be based on determining what the impact of the deficiency is on other activities.

DEPERSONALIZING THE REPORTS

In many companies auditors derive much influence from the fact that their reports are reviewed by upper management. Auditing department should be careful to

avoid misusing this influence. The idea is to depersonalize the reports and recommendation. The real basis of the recommendation should be the facts rather than the opinion of the auditors. A practice commonly followed to help to depersonalize is to omit the names of any individuals involved and instead to report the facts on the situation.

SELF INSPECTION TEAM

1) Management should appoint a self inspection team from local staff who are expert in their own fields and familiar with the GMP.
2) The members of the team may be appointed from inside or outside the company.

FREQUENCY OF SELF INSPECTION

The frequency at which self inspections are conducted may depend on company requirements.

SERIOUSNEES CLASSIFICATION

The audit programs make use of seriousness classification of discrepancies, this is quite common in the case of product audits when defects found are classified in terms such as critical, major and minor each with some weight in the form of demerits. These systems of seriousness classification are highly standardized. Some audit programs also apply seriousness classification to discrepancies found in planning, in procedure, in decision making data recording and so on, demerits values are assigned and total demerits are computed.

REPORT PUBLICATION

The agreement is reached on report format responsibility for editing lists of which managers are to receive what reports, in some organisation the report is given only to the manager of the activity that was audited. A follow-up audit can be distributed to upper management. The design of the audit reports is often modular to permit selective distribution; the report should be issued as soon as possible but no later than one month after the post audit meeting.

AUDIT COMPLETION

The audit is completed when the report is submitted to the client, except in those circumstances when the verification of corrective action is to be part of audit assignment and plan.

RESPONSIBILITY FOR CORRECTIVE ACTION

Auditors are commonly told to avoid becoming involved in designing remedies and making them effective. The operation managers are required to respond in writing as to what they plan to do with respect to discrepancies found or recommendations, they may conclude not to follow them, in which case they must state why not, this formality helps to assure that quality audits have a high priority of managerial attention. Auditors are expected to follow-up recommendations to assure that some action is taken, thus the recommendation is accepted or is considered and then rejected. A special situation exists when an auditor documents the symptoms of a problem but is unable, during the audit to identify the cause. The audit report should be directed to the manager of the auditing activity even though the underlying cause may rest within that activity or be elsewhere. The report should state steps required to determine the underlying causes. When discrepancies reported in an audit are serious, the auditor may recommend that a subsequent audit be held to assure that the necessary corrective action has been taken. Then finally a wrap-up of the audit involves deciding which records from the audit should be retained for period of time, and how access should be provided to authorize personnel who need to review such audit documents.

FOLLOW UP

The operating department should be responding and not react to the audit report and recommendation made.

They may not necessary agree with the suggestions made but they must follow and track any corrective actions resulting from the audit.

The audit team must be informed about these actions so that they too can monitor the corrective step taken.

After all audits are merely tools in the management of quality. How well the tool being used will be evident in the quality of the company products and in the company own reputation for quality.

A properly conducted audit can be a great help a badly performed one can be a disaster.

CONCLUSION

As spatial data are entering the consumer world a obligations has begun, it is many users the facto perceive spatial data as reliable for their uses. From the above review, it can be concluded that the ICH guidelines for audit and inspection according to the various regulatory agencies gives information about almost the similar requirements and instruct to follow same procedure. The increasing number of incidents and accidents involving spatial data is driving society to protect these users and against the risk of data misuses. The audit program should address both internal and external audits and such audits should be defined in written and approved procedures. The companies should be examining their auditing programs to ensure that the key objectives in product realization, process performance and quality management system described in ICH Q10 are being met. The use of risk management practices as defined in ICH Q9. The ICH guidelines specifically discuss about inspection of tablet manufacturing facility but still the information provided by the ICH guidelines are useful for inspection of the tablet and capsule manufacturing facility. Their perception of quality is different than that of experts. The increasing use of suppliers from less developed countries and outsourcing operations is

focusing more regulatory attention on API and excipients suppliers. We must expand our R&D horizons towards those concept involved in QA and QC. Although auditing may not always be required by regulation a good audit program can play an integral role. If someone complains about damages and wants to know who is liable for the quality of the data involved. Except for the ICH guidelines provided by USFDA, none of the other, we must develop the knowledge and services to stand in court as experts in front of judges and provide professional answers when needed.

ACKNOWLEDGEMENT

The authors grateful to express their gratitude to Glenmark Pharmaceuticals Ltd. Mumbai. The authors also thankful to my friends and Brothers. The authors are also thankful to Principal Dr. D. Y. Patil College of Pharmacy, Pune. For the providing all the facilities to carry out the research work successfully.

REFERENCES

1. Quality assurance for pharmaceuticals-A compendium of guidelines and related materials, 2007; 2(2): 285-347.
2. Malik A, Kumar V, Dhiman SK, Sunil, Kumar T, J Chem Pharm Res, 2010; 2(5): 286-290.
3. Compilation of community procedures in inspection and exchange of information, European commission, Health and consumer protection directorate-general, EMA/INS/GMP/313513/2006 Rev 1, Compliance and Inspection; 17 March 2010.
4. Malik A, Kumar V, Renu, Sunil, Kumar T, J Chem Pharm Res, 2011; 3(2): 892-898.
5. Murugesh S, Mani D, Mandal BD, J Chem Pharm Res, 2011; 3(2): 762-764.
6. International Conference on Harmonization, Guidance for Industry Q10, "Pharmaceutical Quality System," June 2008.
7. ISO 9001-2000(E), Quality Management Systems — Requirements; 3rd edition, Dec. 2000.
8. Code of Federal Regulations, Title 21, "Food and Drugs, Part 211, Current Good Manufacturing Practice for Finished Pharmaceuticals," 1 April 2007.
9. International Conference on Harmonization, Guidance for Industry Q7, "Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients," August 2001.
10. Code of Federal Regulations, Title 21, Food and Drugs, Part 820, "Quality System Regulation," 1 April 2007.
11. Merrill, Richard A, "Food Safety Regulation: Reforming the Delaney Clause" in Annual Review of Public Health, This source includes a useful historical survey of prior food safety regulation, 1997; 18(3): 13-40.
12. Official (ISC) Guide to CISSP CBK. Risk Management: Auerbach Publications. 2007; 1065.
13. US FDA Compliance Program Guidance Manual http: //www.fda.gov/ downloads/ ICECI/Compliance Manuals/Regulatory Procedures Manual/UCM, http://www.fda. gov/ICECI/ComplianceManuals/RevisionstoComplianceManuals/ucm198975.htm.
14. Code of Federal Regulations, Title 21, Food and Drugs, Part 58, "Good Laboratory Practice for Nonclinical Laboratory Studies," 1 April 2007.
15. European Commission, "Commission Directive 2003/94/EC, Laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use," Official Journal of the European Union L262, 8 October 2003; 22-26.
16. MHLW Ministerial Ordinances on GQP and GMP 2005, Standards for Quality Assurance of Drugs, Quasi-drugs, Cosmetics and Medical Devices, (MHLW Ministerial Ordinance No. 136 Established as of September 22, 2004), published by Yakuji Nippo, Ltd, April 2005.
17. Health Products and Food Branch Inspectorate, Canadian Good Manufacturing Practices Guidelines, December 31, 2002; (2).
18. The European Parliament and the Council of the European Union, "Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on use," Official Journal of the European Union L136, 30 March 2004; 34-56.
19. The European Parliament and the Council of the European Union, "Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use," Official Journal of the European Union L 311, 6 November 2004; 67 – 128.
20. European Commission, of "The rules governing medicinal products in the European Union", Feb, 2008; 4, (http:// ec.europa.eu/enterprise/pharmaceuticals/ eudralex/homev4.htm).
21. Cutting, Thomas "How to Survive an Audit". PM Hut. http://www.pmhut.com/how-to-survive-anaudit. Retrieved December 13, 2009.
22. http://en.wikipedia.org/wiki/Audit".
23. http://en.wikipedia.org/wiki/Management_representation.
24. Nyholm J, "Persistency, bioaccumulation and toxicity assessment of selected brominated flame retardants", 2009.
25. Anderson K, "Intelligence-Based Threat Assessments for Information Networks and Infrastructures: A White Paper", 2005.
26. Iannone AP, Barry C, "Comparing apples to oranges: Risk of cost/benefit analysis" from Contemporary moral controversies in technology, pp. 64-65.
27. Flyvbjerg, Bent, "From Nobel Prize to Project Management: Getting Risks Right." Project Management Journal, August 2006; 37(3): 5-15.

28. Hollenbeck, William H, Quantitative risk assessment for environmental and occupational health. Chelsea, Mich.: Lewis Publishers, 1986.
29. Lerche, I. (Ian) Environmental risk assessment: quantitative measures, anthropogenic influences, human impact. Berlin: Springer, 2006.
30. A Review of risk assessment methodologies by the Congressional Research Service, Library of Congress for the Subcommittee on Science, Research and Technology. Washington: U.S. GPO, 1983.