

QUALITY MANAGEMENT SYSTEM DOCUMENTS

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Abstract:QMS is defined as an organised system that helps in documenting the responsibilities, procedures and process to a degree that the quality policy and objectives can be accomplished. A QMS helps to synchronize and direct the company's activities to meet regulatory requirements, so that it could improve performance and productivity on a day to day basis. If it is not written down, then it did not happen! appropriate documentation and record upkeep is the primary step in any good manufacturing practice. Documentation gives us a detailed information of the past events and the present status of the work being carried out in an organisation. Thus it provides a means of what is going to be done in future or for the growth of the process which is being carried out in the organisation. Efficient documentation serves as the only way of conveying the required information to the regulatory authority. It gives all the necessary information for carrying out the manufacturing of the drug product and all the specifications for the regulation of the drug product. A brief overview of different documents used in the industry and also the significance of documentation and record maintenance in pharmaceutical industry is outlined here.

Keywords: Documentation and records, good manufacturing practices, good documentations practice, quality assurance.

I.INTRODUCTION

Document is a piece of manually written, typed or electronically stored information that provides proof or that serves as an authentic record. Quality management documents are conventionally written instructions intended to ensure the persistent manufacture of quality product. Quality of pharmaceuticals has always been a prime area of interest for regulatory agencies across the globe with the intention to facilitate production of drug product without batch to batch variations. So persistent maintenance of quality is very essential to prevent health hazard as many pharmaceutical drugs are lifesaving. So if the products are not of good quality then the resultant product may cause severe adverse effects or even death of the patient or recipient. Documentation serves as a proof or evidence that the action was performed to prove to the regulatory authority when they come over for audit. Different documents can depict the diverse activities which is carried out in a pharmaceutical company and its real image. So if any action or work that goes wrong will be documented and due to this documentation, the recipient will be saved from further harm as all the necessary measures will be taken before the release of the drug product and its consumption by the patient or recipient.

II.Importance of Documentation

It has been 46 years since the shocking Devonport incident¹. This incident took place in the hospital in Devon. Due to the failure to release all the air from the bottles, bottles of 5% dextrose infusion fluid in the lower part of the autoclave were not properly sterilized. The batch with this improperly sterilized bottles got released into the market, after 11 months these contaminated bottles were used in the hospital in Devon. Due to the presence of gram negative organisms in the bottle 4 patients died from massive endotoxic shock, fifth patient recovered successfully. Later, in the investigation it was found out that because the change in the autoclave operation was not documented, but communicated orally between the operators the incident took place and there were several violations of what we now consider good manufacturing practices GMP. The current necessity for documented evidence may be driven by this incident of the Devonport.

III. Good Manufacturing Practices

Good manufacturing practice (GMP) is a system for ensuring that the product are consistently manufactured and controlled in accordance with the quality standards. GMP necessitates documented proof so that there is consistent adherence to the established procedures at every stage in the production process. GMP is necessary because it is intended to minimise the risk involved in any pharmaceutical production which cannot be removed through testing the final product.

The most frequently and effectively referenced GMP guideline by pharmaceutical manufacturer are:

- The US Current Good Manufacturing Practices for Finished Pharmaceuticals regulations (the US cGMP).
- The Guide to Good Manufacturing Practice for Medicinal Products of the European Union (the EC GMP Guide).
- The ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients.
- The World Health Organization (WHO) good manufacturing practices.
- Schedule M 'Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for Pharmaceutical Products,' The Drugs and Cosmetics Act and Rules, India.
- PIC/S Guide to Good Manufacturing Practice for Medicinal Products.
- Centre for Drug Evaluation and Research (CDER): Manufacturing, Processing, or Holding Active Pharmaceutical Ingredients.

IV. The 10 basic principles of GMP²

1. Get the facility design right from the start
2. Validate processes
3. Write good procedures and follow them
4. Identify who does what
5. Keep good records
6. Train and develop staff
7. Practice good hygiene
8. Maintain facilities and equipment
9. Build quality into the whole product lifecycle
10. Perform regular audits

V. Documentation

Documentation is an essential part of GMP. It specifies a system of information and control of it, so that it could reduce the risk of misinterpretation and mistakes that could occur in verbally or casually written communication. So that there can be unambiguous procedures which can be followed, there can be confirmation of performance, there can be calculations which can be checked and this can be treating of back history. Documents are mirror that shows the actual image of the pharmaceutical company. This is the reason why regulatory bodies are interested to see the documents. By checking the documents they could assess the overall quality of operation which are carried out in the company and also the quality of the final product.

Given below is a list of most common types of documents along with description of each and importance of them

a) Facility Related Documents:

1. Site master file³

The manufacturer must prepare a document call 'Site Master File', which should contain specific and actual GMP about the production and control of pharmaceutical manufacturing procedures performed at the premises. It should contain the description of the following general information about the organisation, premises equipment, production, personnel, sanitation, quality control, documentation, licence manufacture and licences, self inspection and export of drug.

Importance of site master file: It gives entire information of the pharmaceutical plant.

2. Quality policy

It is a document that defines in general terms how all the GMP aspects like responsibilities, documentation, health and security will be implemented.

3. Quality manual

Quality manual is a document that describes the company’s objective for carrying out the processes within the quality management system.

4. Validation master plan (VMP)³

The validation master plan will explain the process of preparing, examining and approving protocols. The main content of protocol must be explained to accomplish uniformity in documentation in various protocols. The VMP must explain the process of implementation, review and approval of the validation. The essential people and the responsibilities of them, team responsibilities for carrying out validation should be stated. The VMP is prepared by a team, reviewed by senior team and later it is approved by GM QA and QC .It is reviewed once a year.

Importance of validation master plan: A VMP helps in management, it helps all the members of the validation team, there is will be no organized way of performing activities, if VMP is not written.

b) Documents to Be Maintained By Analytical Research and Development and Quality Control Department:

1. Preventive maintenance⁴

Preventive maintenance is a schedule of planned maintenance activities aimed at the prevention of mechanical breakdown and failure of plant equipment .In simple words it can be described as “Prevention is better than cure”. The main objective of preventive maintenance is to prevent the failure of equipment ahead of its actual failure, ensuring that the plant equipment are safe to run and it increases the equipment life. Preventive maintenance is carried out by maintenance department, production department and a separate group of seniors and Inspectors.

Importance of preventive maintenance: It reduces unexpected production interruptions due to this we can achieve maximum production at minimum repair cost and it also ensures safety of the workmen.

2. Standard operating procedures⁴

It is a step by step instructions for performing operational task or activities.

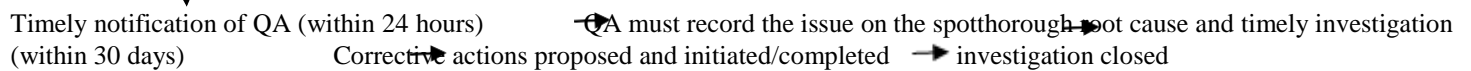
3. Deviation

Deviation is an unanticipated events that occurs during the ongoing operation or activity or at any stage of manufacturing, analysis and distribution of raw material or intermediate or drug product or packaging material or during documentation.

Table 1: A table showing types of deviations

<i>Types of deviation</i>	
Planned	Pre-approved deviation from current operational document/system, covering a specified period of time
Unplanned	An uncontrolled event in the form of non-compliance from the designed systems or procedures

When deviation occurs



4. Lab incident report

Any event that is against cGMP guidelines but it may or may not affect the product quality is called an incident.

5. Corrective action and preventive action (CAPA)⁴

Corrective action and preventive action is a process which investigates and solve issues, identifies the causes and takes corrective actions and prevents reoccurrence of the problem. The main purpose of corrective action and preventive action is to ensure that the problem will never occur in future. Corrective action and preventive action is raised when deviation or incident takes place. Its form should be maintained by quality assurance person for easy traceability

Importance of corrective action and preventive action: The quality issues are resolved, there is continuous improvement and regulatory requirements are met.

6. Change control⁴

According to WHO change control is a “formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect the validated status. Change refers to any modification in equipment, manufacturing, material, utilities, formulation, process, packaging and labelling, computer system and all the associated documents like SOP, quality manual.

Importance of change control: It reduces the risk that a change can have on the quality or process characteristics. Quality assurance representatives and quality assurance head carries out change control activity.

7. Out of specification (OOS)

Test results that fall outside the set acceptance limit which have been established in official compendia is said to be out of specification.

8. Out of trend (OOT)

The data that represents abnormal pattern from the normal pattern is called out of trend.

9. Test methods⁵

These are documents which are used by quality control department. They provide step by step instructions for testing supplies, material and products.

10. Specifications⁵

It is documents that list the requirements that a material or a product must meet before it is released into the market. The quality control department will compare the obtained test results to the specifications to check if results meet the requirements.

11. Log books⁵

These are forms which is used to document performed activities. These are used to document the operation, maintenance and calibration of equipment. They are used to record the vital activities performed.

C) Record Keeping In Formulation Department

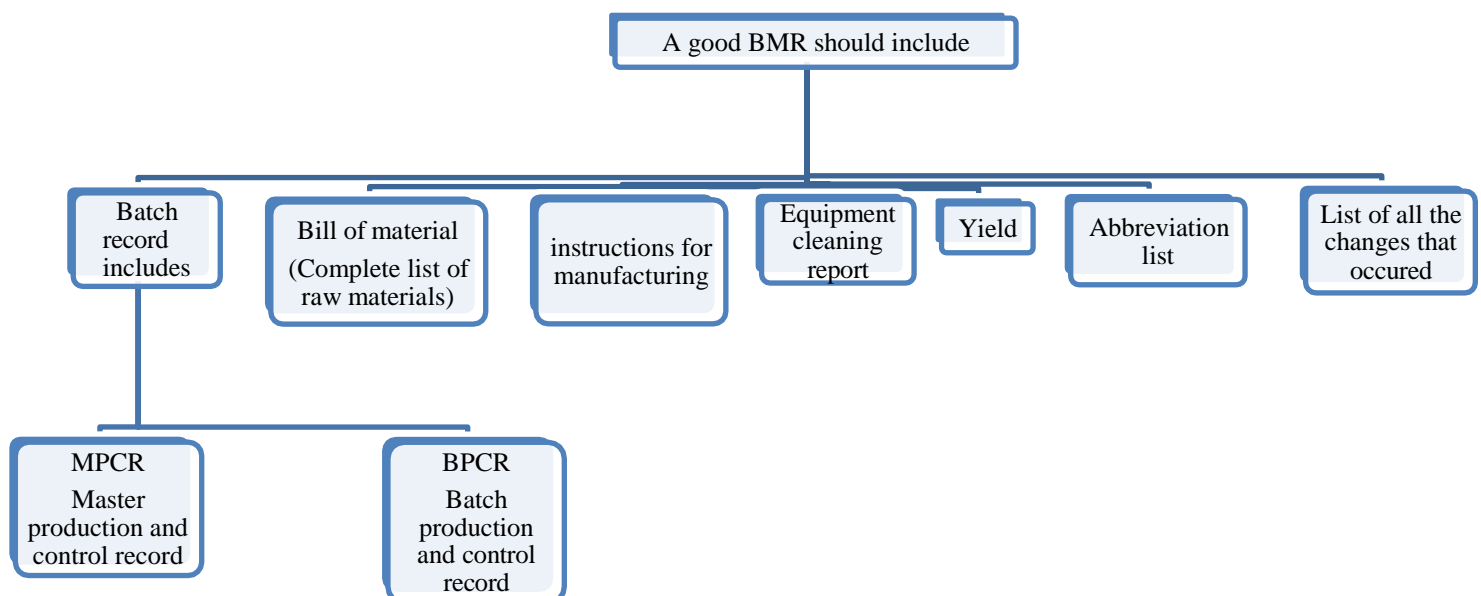
1. Batch record⁵

These documents are used by the manufacturing department which provides step by step instructions for production.

2. Batch manufacturing record^{6,7}

Batch manufacturing record is a written document of the batch prepared during manufacturing process. It contains actual data and step by step process for manufacturing each batch. It is like a proof that batches were appropriately manufactured and checked by quality control person. This ensures that appropriate ingredients are added and each processing step is completed according to the standard operating procedure and also ensures uniformity in finished product of a batch.

Fig 1: Flow chart indicating requirements of a good BM



3. Batch packaging record^{6,7}

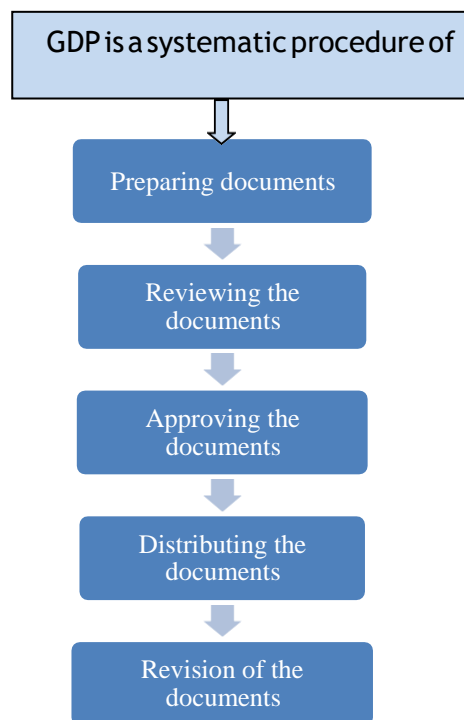
Batch packaging record is a document which is based on packaging operation . A good batch packaging record should include the name of the product, the date and time of the packaging operation, the name of the responsible person carrying out the operation, the initial of the operators in significant steps, records for identity and conformity with the packaging instructions including the results of in process controls ,the quantity and the reference number or identification of all packaging material and bulk product issued, used destroyed or return to the stock .

importance of batch packaging record: It is based on the relevant parts of packaging instructions and the method of preparation of such records are designed to avoid transcription errors .

VI. GOOD DOCUMENTATION PRACTICE (GDP)

Due to the importance of documentation in pharmaceutical industry “GDP” is necessary .

Fig 2: Flow chart showing systematic flow of documents



Control of documents is a vital part of GDP to minimise the errors and it also prevents the misuse of the documents.

Data integrity^{8,9}

The data integrity concepts like ALCOA and ALCOA+ has been adopted by different industries. These concepts make sure that data integrity is observed and maintained in each and every industry. ALCOA+ has been implemented and is in use by various Big regulatory authorities such as FDA, WHO and GAMP.

ALCOA¹⁰

The acronym ALCOA has been used since 1990's. It is used by regulated industries for ensuring data integrity and it is a key to good documentation practices (GDP). ALCOA relates to data whether paper or electronic and is defined by US FDA guidance as Attributable ,Legible, Contemporaneous, Original and Accurate .

ALCOA +¹⁰

The term ALCOA is an acronym, which stands for Attributable, Legible, Contemporaneous, Original And Accurate .ALCOA was then expanded to ALCOA+ by addition of few more concepts which are Complete, Consistent ,Enduring And Available .

VII. Conclusion

During the inspection of manufacturing sites, the regulatory authorities spends huge amount of time in analysing the documents and record of the company . A good documentation helps in understanding the kind of work carried out by quality department of that company . Proper record maintenance and documentation will help in GMP compliance . The main goal of documentation is to define procedures in written to the pharmaceutical manufacturers to reduce the errors, misinterpretation due to orally or casually written communication and helps in tracing the batches made and released , which eventually leads to production of quality products and such quality product is beneficial to company reputation and at the other end patient health is assured.

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