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Documentation in Pharmaceutical Industry

Aishwarya Nale[1], Aishwarya Mali[2], Sandhya Kadam[3], Vivekkumar Redasani[4]

Students[1,2], Assistant Professor[3], Principal[4]

Department of B. Pharmacy

YSPM'S Yashoda Technical Campus, Faculty of Pharmacy, Wadhe, Satara – 415001

Corresponding Author's Email: *aishwaryanale01@gmail.com*

Abstract

The purpose of documents as a data source in qualitative research is examined in this article, which also explores document analysis procedures in the context of real-life research experiences. The paper, which is aimed at research beginners, presents a step-by-step method for document analysis. It discusses the nature and types of documents, as well as the Advantages and method of document analysis, and provides concrete instances of how documents might be used in the research process. A grounded theory study is used to demonstrate the use of document analysis. We may notice major trends in information systems that have an impact on their evolution, including documentation. As a result, the approaches to systems from the perspectives of IT project management, roles, and resource allocation, as well as the relevance of documentation for the success of a development project, have changed.

Keywords*: Documentation, Batch manufacturing record (BMR), Manufacturing formula record (MFR), Standard operating procedure (SOP), Good documentation practices (GDP), and Quality audit.*

INTRODUCTION

Documents or records are written, printed, magnetic, or electronic media that include information or data on the formulation and manufacturing process of a product. Paperwork needs to be produced or written in a clear and readable manner, be traceable, and include sufficient information on the event's history and activities. Records or documentation certify

that the goods are produced according to previously established procedures and requirements[2].

Documentation is an important component that should be used in all aspects of GMP in the quality assurance system. All manufacturing personnel should be aware of what to do and when, and all information needed to determine whether to produce a drug batch for sale should be available to authorized individuals. Documented evidence and traceability should also be ensured. Finally, all manufacturing and control materials and methods specifications and processes should be defined. This reduces the possibility of miscommunication and/or error in oral communication because the document's design and use are based on the manufacturer's information and control system. As a result, the quality and consistency of all goods and services are improved by providing clear, clear instructions for people participating in specific activities, including active pharmaceutical substances that are legally required[6].

Since documentation is a crucial component of the quality assurance system, it must be connected to every facet of GMP. It attempts to provide an audit trail that will allow the history of any suspected defective batch to be investigated, specify the requirements for all materials and the manufacturing and control process, and guarantee that all personnel involved in the manufacturing process have the information needed to determine whether or not to release a batch of a drug for sale. The conditions that must be met by the goods or materials utilized or obtained during manufacture should be covered in depth in the specifications. They provide a foundation for assessing quality. Documentation gives auditors a way to evaluate the general standard of operations within a company and the final product[7].

Documentation

Documentation is an essential component of all effective production processes. It establishes a structure for information and control to reduce the possibility of miscommunication during spoken communication. Because of this, the quality and consistency of all goods and services are improved by precise instructions that must be followed, including the use of legally required active pharmaceutical substances by those in charge of certain tasks[6].

Objectives

- The construction and the premises All the components of pharmaceutical production that need proper documentation need to be installed, validated, cleaned, and upkeep.
- Staff: training, sanitation, etc.
- Installed, calibrated, validated, maintained, and cleaned equipment[6].

The 'Documents' Model

The "DOCUMENTS" model lists out the areas required for GMP documents for implementation:

D- Design, development, deviation, dossiers, and Drug Master Files for regulated markets distribution records.

O- Operational procedures/ techniques/methods, out of Specifications (00S). Out of Trend (00T).

C- Cleaning, calibration, controls, complaints, container and closures, contamination, and change control.

U- User requirement specifications, utilities like water systems, HVAC, AHU, etc.

M- Man, materials, machines, methods, maintenance. Manufacturing operations and controls, monitoring, master formula, manuals (quality, safety, and environment), medical records

E- Engineering control and practices, Environmental Control, Equipment qualification documents.

N- Non-routine activities, new products, and substances.

T-Technology transfer, training, testing. Trend analysis, technical dossiers.

S- SOPs, safety practices, sanitation, storage, self-inspection, standardization, supplier qualification, specifications, standard test procedures, and site master file[7].

General Requirements

- Good documentation constitutes an essential part of the quality assurance system. Written procedures prevent errors resulting from spoken communication, and documentation permits the tracing of activities performed.
- Documents must be designed, prepared, reviewed, and distributed with care.
- Documents must be approved, signed, and dated by the appropriate competent and authorized persons.

- Documents must have unambiguous contents. The title, nature, and purpose should be clearly stated. They must be laid out in an orderly fashion and be easy to check. 'Reproduced documents must be clear and legible.
- Documents must be regularly reviewed and kept up-to-date. When a document has been revised, systems must be operated to prevent inadvertent use of superseded documents: (e.g., only current documentation should be available for use).
- Documents must not be handwritten; however, where documents require the entry of date, these entries may be made in clear legible handwriting using a suitable indelible medium (i.e., not a pencil). Sufficient space must be provided for such entries.
- Any correction made to a document or record must be signed or initialed, and dated, the correction must permit the reading of the original information. Where appropriate, the reason for the correction must be recorded[8].

Purpose

- To define the specifications and procedures for all materials and methods of manufacture and control,
- To ensure that all personnel know what to do and when to do it,
- To ensure that authorized persons have all the information necessary for the release of a product,
- To ensure the existence of documented evidence, and traceability and to provide records and an audit trail for investigation. To ensure the availability of data for validation, review, and statistical analysis[2].

Advantages

Availability: Many documents are in the public domain, especially since the advent of the Internet, and are obtainable without the authors' permission. This makes document analysis an attractive option for qualitative researchers. As argued, locating public records is limited only by one's imagination and industriousness. An important maxim to keep in mind is that if a public event happened, some official record of it most likely exists.

Cost-effectiveness: Document analysis is less costly than other research methods and is often the method of choice when the collection of new data is not feasible. The data (contained in

documents) have already been gathered; what remains is for the content and quality of the documents to be evaluated.

Lack of obtrusiveness and reactivity: Documents are ‘unobtrusive’ and‘ non-reactive’—that is, they are unaffected by the research process. Therefore, document analysis counters the concerns related to reflexivity (or the lack of it) inherent in other qualitative research methods. About observation, for instance, an event may proceed differently because it is being observed.

Reflexivity: which requires an awareness of the researcher’s contribution to the construction of meanings attached to social interactions and acknowledgment of the possibility of the investigator’s influence on the research is usually not an issue in using documents for research purposes.

Stability: As a corollary to being non-reactive, documents are stable. The investigator’s presence does not alter what is being studied. Documents then are suitable for repeated reviews.

Exactness: The inclusion of exact names, references, and details of events makes documents advantageous in the research process.

Coverage: Documents provide broad coverage they cover a long period, many events, and many settings.

Insufficient detail: Documents are produced for some purpose other than research they are created independent of a research agenda. (Again, previous studies located in documents Glenn A. Bowen, 'Document Analysis as a Qualitative Research Method' consequently, they usually do not provide sufficient detail to answer a research question.

Low irretrievability: Documentation is sometimes not retrievable, or irretrievability is difficult. Has noted, access to documents may be deliberately blocked.

Biased selectivity: An incomplete collection of documents suggests 'biased selectivity'. In an organizational context, the available documents are likely to be aligned with corporate policies and procedures and with the agenda of the organization's principals. However, they may also reflect the emphasis of the particular organizational unit that handles record-keeping (e.g., Human Resources) [1].

Types of Documents

- **Quality manual:** A global company document that describes, in paragraph form, the regulations and/or parts of the regulations that the company is required to follow.
- **Policies:** Documents that describe in general terms, and not with step-by-step instructions, how specific GMP aspects (such as security, documentation, health, and responsibilities) will be implemented
- **Standard operating procedures (SOPs):** Step-by-step instructions for performing operational tasks or activities.
- **Batch records:** These documents are typically used and completed by the manufacturing department. Batch records provide step-by-step instructions for production-related tasks and activities, besides including areas on the batch record itself for documenting such tasks.
- **Test methods:** These documents are typically used and completed by the quality control (QC) department. Test methods provide step-by-step instructions for testing supplies, materials, products, and other production-related tasks and activities, e.g., environmental monitoring of the GMP facility. Test methods typically contain forms that have to be filled in at the end of the procedure; this is for documenting the testing and the results of the testing.
- **Specifications:** These list the requirements that a supply, material, or product must meet before being released for use or sale. The QC department will compare their test results to specifications to determine if they pass the test.
- **Logbooks:** Bound collection of forms used to document activities. Typically, logbooks are used for documenting the operation, maintenance, and calibration of a piece of equipment. Logbooks are also used to record critical activities, e.g., monitoring of clean rooms, solution preparation, recording of deviation, change controls, and corrective action assignments released for use or sale[1, 10].

Master Formula Record

Definition: A document or collection of documents that lists the starting materials and their quantities, the packaging materials, and the processing instructions, including the in-process controls, along with a description of the steps and safety measures needed to produce a given amount of a final product.

Master Production Record, or MFR, is another name for the Master Formula Record. Manufacturing units prepare batch manufacturing records (BMR) using MFR as a reference standard. The company's research and development staff prepares it. It includes every detail regarding the product's manufacturing process. Any pharmaceutical product has a master record called a Master Formula Record (MFN). MFR has a significant role. For every product and batch size to be made there must be Master Formula records relating to all production processes. The head of production and quality control, as well as other qualified technical staff, will create and approve these. A master formula record is created using the knowledge of ineffectively qualified personnel, such as manufacturing or analytical chemists, or prepared based upon batch manufacturing record of a batch size[1].

MFR includes

- **Product Details: -** Name, logo, and address of the manufacturing company
- Dosage form name. Brand name, Generic name
- Product code and Label claim of all ingredients
- **Product description:** Batch size, Pack size, and packing style
- Shelf life and Storage conditions
- **MFR number and date:** Supersede MFR number and date
- Effective batch number
- Authorization by the production and quality assurance head
- **Equipment:** A list of all required equipment and machines required in the Manufacturing process with their capacity[1].

Steps in preparation for MFR

It is divided into two sections: a) Manufacturing and b) Packaging[1]

Form Number MF-001-V1 Date Original Issue: JULY 2021 Date Revised: Page 1 of 1	MASTER FORMULA

PRODUCT NAME:			
FORMULA REFERENCE:			
FORM PREPARED BY:			
		LOT NUMBER:	
		THEORETICAL YIELD:	
START DATE:		FINISHED PRODUCT SIZE:	
MIX TANK:		BATCH SIZE IN LBS:	

PRODUCT DESCRIPTION:
Example: Anhydrous emollient skin balm, white in color. Bulk product is manufactured by xxx and packaged in white stick with orange cap. Then sent to third party for label and tag application and shipped to client from there.

RESPONSIBILITY:
The person in charge of making products is responsible for making this product. This formula is confidential, and should not be shared with others outside the company.

MATERIALS/EQUIPMENT/SUPPLIES:
1. Mix tank 3
2. Scale X
3. Bowls
4. Blender
5. Measuring cups/beakers
6. Thermometer

INGREDIENTS:		
Phase A		%
Phase B		%
Ingred #		
Ingred #		
Ingred #		
Ingred #		
Ingred #		
Ingred #		
TOTAL		100.00

Fig no.1- Master Formula Record

Batch manufacturing record

Definition: A batch manufacturing record is a written document created during the pharmaceutical manufacturing process. It includes real data as well as a detailed manufacturing procedure for every batch. A batch manufacturing record provides proof that the batches were manufactured correctly and inspected by quality control staff.

Batch production records should be generated for each intermediate and API/formulation, and they should include all relevant information about batch production and control. Before being

distributed, the batch production record needs to be verified as the right version and a clear, accurate replica of the relevant master production instruction. A reference to the most recent master production instruction in use should be included in the master document if the batch production record is generated from a different section of it. Before starting any processing, it is important to make sure that the workstation and equipment are free of materials, records, or old goods that aren't needed for the intended operation, and that everything is clean and in working order.

BMR should include

- Dates and, when appropriate, times.
- Identity of major equipment used (e.g., reactors, driers, mills, etc.)
- Specific identification of each batch, including weights, measures, and batch numbers of raw materials, intermediates, or reprocessed materials used during manufacturing.
- Actual results recorded for critical process parameters.
- Any sampling performed.
- Signatures of the persons performing and directly supervising or checking each critical step in the operation.
- In-process and laboratory test results.
- Actual yield at appropriate phases or times.
- Description Of packaging and label.
- Representative label (commercial supply).
- Any deviation noted, its evaluation, and investigation conducted (if appropriate) or reference to that investigation (if stored separately).
- Results of release testing.
- All analytical records relating to the batch, or a reference that will permit their retrieval.
- A decision for the release or rejection of the batch, with the date and signature of the person responsible for the decision. The production record review[7].

Standard Operating Procedures (SOP)

Definition: A Standard Operating Procedure (SOP) is a series of written instructions that document a routine or repetitive operation performed by personnel in a company. SOP creation and application are essential components of an effective quality system. It offers

guidance on how to carry out tasks correctly and consistently to meet predetermined requirements and produce high-quality outcomes. SOs must support ongoing enhancements to service standards and demonstrate a dedication to patient safety.

SOP Requirements

- Prepare apex documents like Quality Policy, Quality Manual, Site Master File, Validation Master Plan, etc. to describe the quality commitments of the management
- Define the roles and responsibilities of all personnel working in the organization
- Prepare policy for periodic review of documents. Ensure that the current industrial practices and Pharmacopeial requirements are fulfilled by the current versions of documents
- SOP for document (SOPS, MPCR, BPCR, validation/qualification protocols, formats preparation, review, approval, training, distribution, control, and retention
- Procedure for maintaining revision history
- Management, control, and retention of superseded or obsolete documents
- Document archival and retrieval procedure
- Handling, archival, retrieval, and retention of electronic records/documents
- Procedure for control of electronic signatures
- Equipment cleaning and sanitation procedure
- Issuance and control of equipment logs
- Document describing measures taken for avoidance of cross-contamination and its training records
- Cleaning validation master plan
- Procedure for batch-to-batch and product-to-product cleaning and its verification to ensure removal of residue of previous batch/product
- Records for incoming raw materials and packaging materials
- SOP for preparation of process validation protocol and reports
- SOP for preparation of master production control records
- SOP for preparation of batch manufacturing and control records
- SOP for allocation of batch number
- Calibration master plan and calibration reports
- Batch release procedures

- SOP for preparation and control of QC datasheet
- SOP for allocation of analytical control number
- Procedure for review of analytical data
- SOP for investigation of OOS results
- SOP for change control, revision of any process or documents, or upgradation of facility or equipment should be routed through impact assessment and change control procedure.

Format of SOP

In general, technical SOPS will consist of five elements:

- Title page
- Table of Contents
- Procedures
- Quality Assurance/Quality Control
- References[7].

Quality audit

A systematic and independent review to establish whether quality activities and related results are consistent with the planned arrangements, as well as whether these arrangements are effectively implemented and appropriate for achieving objectives.

Usually, quality audits are carried out at predetermined intervals. If they are not implemented correctly, the results could be made public and the quality certification could be revoked.
Principles:

- **Ethical conduct:** the foundation of professionalism, trust, integrity, confidentiality, and discretion are essential to auditing
- **Fair presentation:** the obligation to report truthfully and accurately
- **Due professional care:** the application of diligence and judgment in auditing
- **Independence:** the basis for the impartiality of the audit and objectives of the audit conclusions. Evidence-based approach: the rational method for reaching reliable and reproducible audit.

Types

- A first is an audit performed by an organization on itself i.e. an internal audit.
- A party audit performed by one organization on its behalf on another usually on a supplier by a customer.
- A third-party audit is an audit by an independent organization other than the customer or a supplier.

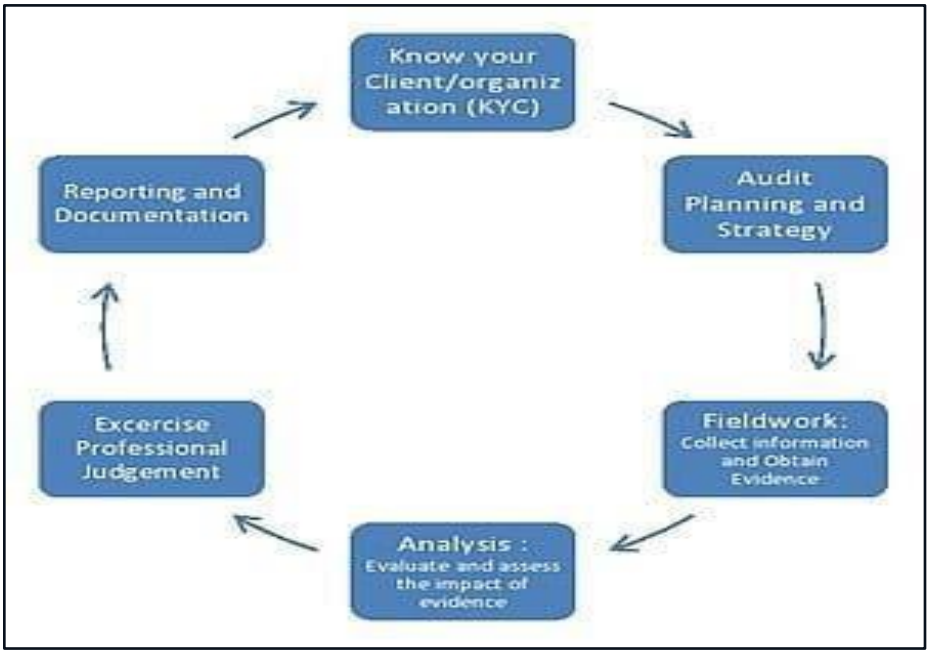

Fig no. 2- Flow chart of Quality audit

Phases

- **Phase-01 Preparation:** This phase precedes the actual review meeting it is the responsibility of the chairman and presenter to organize the quality review and notify all that are invited.
- **Phase-02 The review meeting:** the central phase of the quality review process is the review meeting itself during the review meeting the emphasis should be on error detection, in line with the criteria, and only limited discussion of corrective action should occur.
- **Phase-03 The follow-up:** following the quality review meeting there should be a follow-up period during which the error identification at the review that was committed to the follow-up action list is rectified and signed.

Objectives

- To determine conformity or non-conformity of the quality system elements with specified requirements
- To determine the effectiveness of the implemented system in meeting specific quality objectives
- To allow improving the quality system
- To provide managers with information

Audit methods and techniques

Audit methods and techniques are categorized based on the purpose of the audit.

Horizontal auditing

It includes an evaluation of each functional area of a company to ensure that quality is adequate and implemented properly. When it's important to determine whether a basic QMS has been installed, is being applied, and is being maintained, they are utilized for internal system auditing as well as second and third-party assessments. Every functional area is examined to ensure that it complies with all applicable quality system criteria.

Vertical auditing

It involves examining functional areas of an organization that are actively contributing to a specific work package or contractual requirement.

Random auditing

It examines the various aspects of an organization's operation as determined by the auditor and due to the need to closely examine a particular actively or generally randomly probe the system[7].

Fig no. 3- Quality Documentation Hierarchy

Quality manual

The Quality Manual is at the top of the hierarchy. This is the guiding document that describes the company's objectives, mission, and vision and was written and approved by high management. It needs to describe the goals and principles of the business. It provides a detailed explanation of the QMS's scope, which is what the quality system ought to contain. It goes into great detail explaining every ISO 9001 standard requirement. It includes all the information needed, including an explanation of the exclusions that should be removed from the Quality system. All of the QMS processes are described, along with references to the quality procedures that support them. The manual may also include the objectives and the quality policy[1].

The quality manual should include most of the following elements:

- Title and table of contents.
- Scope of the QMS.
- Exclusions from ISO 9001.
- Versioning info and approval.
- Quality Polity and Objectives.
- QMS description.
- The business process model of the organization.
- Definition of responsibilities of all personnel.
- Reference to relevant documents and relevant appendices[1].

Purposes

- To communicate management’s expectations for quality to the organization.
- To reveal the organization's conformity with ISO 9001 requirements.
- To serve as a measure of compliance with management's expectations for internal audits; ISO registrar audits; and Customer audits[7].

Quality policy

A policy is an organization's declarative declaration regarding quality and continual improvement. A clear and excellent policy is convenient and standard procedure because it is typically utilized for promotional purposes and should be posted on websites and displayed on the organization's property. The organization's quality goals are outlined in the quality

policy. Quantifying the Quality objectives helps firms identify their Quality goals. It ought to offer a framework for formulating, outlining, and evaluating how well you accomplish the Quality objectives. Arrangement For instance: We promise to continuously deliver goods and services that either match or surpass our clients' needs and expectations. We'll actively work to continuously improve quality by implementing initiatives that let every worker do their job correctly the first time and every time.

Quality procedures

It can have different formats and structures. They can be a narrative that is described through text; they can be more structured using tables; they can be more illustrative in those flow charts; or they can be any combination of the above.

1. Quality procedures should include the following elements:
2. **Title -** for identification of the procedure.
3. **Purpose -** describing the rationale behind the procedure;
4. **Scope -** to explain what aspects will be covered in the procedure and which aspects will not be covered.
5. Responsibilities and authorities of all people/functions included in any part of the procedures.
6. Records of the results from the activities described in the procedure should be defined and listed.
7. **Document control -** identification of changes, date of review, approval, and version of the document should be included following the established practice for document control.
8. **Description of activities -** this is the main section of the procedure, it relates all the other elements of the procedure and describes what should be done, by whom and how, when, and where. In some cases, “why” should be clarified as well. Additionally, the input and the outputs of the activities should be explained, including the needed resources[1].

Work instructions

It could be a component of a procedure. Alternatively, a procedure may call for them. Work instructions and procedures typically share a similar form and cover the same topics. The main difference between the two is that work instructions provide specifics on the tasks that must be completed, with an emphasis on correctness and the order in which tools and methods must be used. The requirement for extremely comprehensive job instructions is

reduced when staff are trained and used by competent individuals.

Work Instructions may cover many of the following details:

- The manner in which the work will be done.
- The equipment and tools that will be used.
- The environment or location associated with the work
- Material handling requirements.
- Safety alerts for the employees.
- Across-reference to any other required processes or work instructions.
- The critical process parameters to be monitored and the instructions on how to monitor.
- Equipment maintenance procedures.
- Methods for verifying that the product meets specifications.
- Other non-product related criteria for the final product[1].

Records

This last level of the system for quality documentation. Every piece of information, documentation, form, and so on is archived. The objective proof that the Quality System is being operated by protocol is found in quality records. Additionally, quality records detail the process by which the final product's quality was confirmed to have fulfilled both the requirements and the expectations of the client.

Records include the following sources:

- Non-Conformance Investigations.
- CAPA's
- Audit Results
- Supplier Documentation
- Calibration Results
- Maintenance records[7]

Good Documentation Practice

"Good documentation practice is an essential part of the quality assurance and such, related to all aspects of GMP" is the definition of GDP. WHO is the source of this definition. Good Documentation Practices (GDP) are procedures for logging, editing, and maintaining

documents, records, and data to guarantee the accuracy and consistency of information and data at every stage of a product's lifespan[3,4].

Objectives

- Establish, control, monitor, and record all activities, which directly or indirectly impact all aspects of the quality of medicinal products.
- Appropriate good documentation practice should be applied for the type of document
- Ensure that the document should maintain accuracy, integrity, availability, and legibility during the document life cycle.
- The document should be free from error and at any point, if the error is identified then rectify it with the proper reason for correcting including sign and date.
- The Term "Written" in any document means recorded/document on media from which data may be rendered in a human-readable form.
- Site Master File: A document describing the GMP-related activities of themanufacturer[9].

Purposes

- To provide the basic guide for good document practices about creation, approval, review, maintenance, correction or errors, verification, archiving, etc.
- To define the specifications and procedures for all materials and methods of manufacture and control.
- To ensure the existence of documented evidence, and traceability and to provide records and an audit trail that will permit investigation.
- Ensures availability of data for validation, review, and statistical analysis.
- To ensure that all personnel concerned with manufacturing know what to do and when to do it.
- To improve performance.
- Regulatory requirements[5].

Key Quality and Regulated Documents

Concise- Present information clearly so it can be easily understood with no room for misinterpretation. For example, the date format "05/06/12" can confuse. Use one that is unambiguous, such as "05 Jun 2012."

Legible

Information should be readable and leave no room for error (for example, hand-written data that are not legible may cloud data analysis or result in "Missing Data").

Accurate

Documentation should be error-free—properly reviewed, verified, and approved. Information should be recorded as an event happens and not after the fact, to avoid recording "What You Remember" rather than "What Happened."

Traceable

Documentation should be traceable. Make it clear who logged the information, what it was, and when and why it was documented[5].

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