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DOCUMENTATION IN PHARMACEUTICAL INDUSTRY : A BRIEF REVIEW

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Abstract: In the pharmaceutical industry, documentation is a fundamental aspect of both Quality Assurance and Quality Control systems and is crucial for adhering to GMP standards.

This work aims to outline the GMP documentation requirements within the pharmaceutical sector. Initially, it discusses the processing of documents, including preparation, issuance, usage, storage, retrieval, retention, and disposal, along with a brief overview of PMD.
Next, it details the specifications for key documents such as the Batch Manufacturing Record, Manufacturing Formula Record, and other elements like SOPs.
It outlines the specifications for all materials, manufacturing methods, and controls. This enables personnel to determine whether to release a batch for sale and facilitates the investigation of a product batch's history through audit trails.
This work focuses on creating effective documents for various processes within the industry. Additionally, the article provides insights into different types of documents and their contents. It emphasizes the significance and necessity of document preparation in the industry. The primary goal of this work is to assist pharmaceutical companies in maintaining documentation for good manufacturing practices, ensuring product quality and enhancingsafety.
Keywords: (GMP) Goodmanufacturing practices, (PMD) Pharmaceutical manufacturing documentation, (SOP) Standard operating procedure

1. INTRODUCTION:

The precise recording of information is a crucial aspect of pharmaceutical manufacturing. Effective management and control of documentation form a fundamental component of the Good Manufacturing Practice (GMP) program within an organization.(1) Good documentation represents a vital part of the quality assurance system, serving as a cornerstone for compliance with GMP requirements.

Documentation can exist in various formats, including paper-based records, electronic systems, or photographic media. It involves a structured process encompassing the preparation, review, verification, approval, storage, and periodic review of documents. Core GMP regulations mandate that pharmaceutical manufacturers maintain accurate and comprehensive documentation and records as part of their operational framework.

Maintaining thorough documentation helps to construct a detailed historical perspective of past activities while providing insights into current processes and laying the groundwork for future planning. Furthermore, effective documentation strengthens the transparency and reliability of the quality assurance system.[2]

Key functions of documentation include offering clear instructions on when, where, who, why, and how tasks should be executed while providing verifiable evidence that these tasks have been completed as required.

Additionally, documentation is pivotal in defining specifications for materials, manufacturing methods, and control procedures. To ensure credibility and compliance, these documents must be reviewed, approved, signed, and dated by authorized personnel.[3]

2 .PHARMACEUTICAL MANUFACTURING DOCUMENTATION (PMD):

"Pharmaceutical Manufacturing Documentation" (PMD) is an intricate topic. Compiling a comprehensive list of documents that satisfies the requirements of all companies can be quite challenging. To achieve this, one must assess the specific needs of each organization. Therefore, a one-size-fits-all solution for PMD is not feasible; it must be customized.

It is essential to thoroughly examine the organizational environment before developing the PMD for a particular entity. The following environmental factors should be taken into account:

- The manufacturing activities undertaken or planned by the organization, such as which formulations are currently being produced or are expected to be produced, including Injections, Tablets, Capsules, Liquids, Ointments, etc.
- The documentation requirements that the company must comply with, depending on the country, such as India, WHO, UK, USA, South Africa, Australia, Canada, or others.
- The level of computerization available within the organization for documentation purposes.
- Any additional considerations.

If approached systematically, the overall PMD program can transform this complex task into a more straightforward and manageable one. The author suggests the following steps to address the complete PMD program within the organization:

a) Steps in Total PMD Programme:

Step-1: Identify at least two knowledgeable individuals, one from production and one from QC/QA, who are well-versed in the organization's product profiles and QC/QA requirements.

Step-2: Compile a list of the manufacturing formulation departments, whether existing or planned.

Step-3: Enumerate the QC/QA activities, organized by section.

Step-4: Identify the countries to which the products are likely to be sold or distributed and gather any specific PMD requirements from each of those countries.

Step-5: Categorize the sets of documents necessary to fulfill the requirements outlined in Step 04, for example, the categorization should include:

First:

- Documents required for personnel training.
- Documents for QC.
- Documents for Building/Factory.
- Documents related to Equipment.
- Documents regarding Materials/Stores.
- Documents pertaining to Engineering.
- Documents for Distribution.
- Documents addressing Market complaints, etc.

Second:

Documents within each category can be categorized into the following types:

- SOPs.
- Lists.
- Charts/formats.
- Specifications.
- Test Methods.
- Reports.
- Both one-time and recurring documents such as MPCR and BPCR.

Step 06: Design the Documents by considering the following aspects:

- Contents.
- Formatting.
- Size and quality of paper, etc.

Step 07: Explain the document to the relevant individuals. Provide training on its usage.

Step 08: Conduct a trial run of the documents, analyze any challenges, and modify or redesign as necessary.

Step 09: Implement the document.

Step 10: Review by gathering feedback from users at regular intervals.

Taking all these points into account, here are some guidelines for those involved in PMD design and implementation within any organization.

b) Guidelines for designing and implementing PMD Programme:

i) Definition of Document:

- A document or record is defined as any written, printed, magnetic, or electronic medium that contains information or data related to a formulation and manufacturing process for a product.
- Documents must be clearly and legibly created, must be traceable, and should provide sufficient details of the activity along with an accurate history of the event.
- Documents or records serve as evidence that products are manufactured in accordance with pre-established processes and predefined specifications[23].

ii) Objectives of Documentation:

a) The primary objectives of comprehensive documentation can be summarized as follows:
b) Define the manufacturer's system of information and control.
c) Minimize the risk of misinterpretation and errors that are common in oral or informal written communication.
d) Provide clear procedures to be followed.
e) Confirm the performance of a task.
f) Allow for verification of calculations.
g) And ultimately, enable tracing of the batch history of any product.

iii) Significance of Documentation:

a) Good documentation is a crucial component of the quality assurance system and should be connected to all facets of cGMP.
b) It outlines the specifications for all materials and manufacturing and control methods.
c) It guarantees that all personnel involved in manufacturing understand what to do, how to do it, when to do it, and why it is necessary.
d) It ensures that authorized individuals possess all the information required to determine whether to release a batch of a drug for sale or distribution.
e) It offers an audit trail that allows for investigations into the history of any potentially defective batch[4].

3. GOOD DOCUMENTATION PRACTICES (GDP):

Definition:

Good Documentation Practice (GDP) refers to the standards by which documentation is created and maintained within the pharmaceutical industry. While the U.S. Food and Drug Administration (FDA) have established certain GDP standards, others are governed by the Current Good Manufacturing Practice (CGMP).

All pharmaceutical, bioscience, and healthcare companies, along with their vendor partners, must adhere to GDP or risk facing penalties imposed by the FDA.

- Effective documentation is a crucial component of the quality assurance system [5].
- Documentation is vital to a quality management and assurance system for several reasons:

- Written procedures offer clarity and help prevent errors that may occur during verbal communication.
- Records, documents, and reports provide a clear overview of completed tasks and ongoing work, aiding in better future planning.
- A thorough examination of the documents maintained in a pharmaceutical facility is often the key used by regulatory agencies to evaluate the facility's quality function.
- Precise and clear records facilitate critical process reviews, which can enhance quality and lead to cost-saving initiatives.
- Robust documentation is essential for achieving ISO certification and other industry-specific certifications.
- It supplies necessary operational details.
- It minimizes the risk of errors.
- It assists in tracking deviations from expected yields.
- It helps reduce batch-to-batch variations, ensuring that product quality remains within acceptable limits.
- It is regarded as the historical record of batch operations.
- Self-inspection of procedures [3].

- Good documentation practices are followed to safeguard the integrity and quality of all documents/records, both electronic and handwritten, utilized in various GMP operations and activities, ensuring these records are truthful, easily retrievable, and traceable [6].
- Proper documentation serves as the foundation of current good manufacturing practices (cGMP), and in the regulatory landscape, it is widely accepted that

"**If it isn't documented, it wasn't done!"[3].**

According to the WHO, Good Documentation Practices aim to:

- To outline the specifications and procedures for all materials and manufacturing and control methods,
- To guarantee that all personnel understand their responsibilities and the timing of their actions,
- To ensure that authorized individuals possess all necessary information for product release,
- To maintain documented evidence, traceability, and to provide records along with an audit trail for investigations, and
- To make data available for validation, review, and statistical analysis[7].

- **General Requirements for GMP Documentation:**
  - This encompasses various levels and types of GMP documentation, including both paper and electronic records related to the manufacturing, testing, and packaging of pharmaceutical products, APIs, and excipients.
  - These documents and records include raw data, reports, protocols, procedures, deviations, investigations, batch records, formats, and records pertaining to training, equipment, and retention for manufacturing and analytical controls.
  - Data integrity must always be prioritized, signifying the degree to which all data is complete, consistent, and accurate throughout its life cycle.
  - Controls must be established, and if any data integrity incident is observed, suitable corrective measures should be implemented to avert the recurrence of the same issue. Attempts to conceal errors are regarded as 'data integrity' problems and must be strictly forbidden at all levels.

- **Principles:**

Personnel should remain informed about the implementation of good documentation practices (GDP) to guarantee that the principles of ALCOA and ALCOA-plus are comprehended and applied to electronic data in the same way that has traditionally been applied to paper records. The requirements for good documentation for both manual and electronic records include the following, as relevant;

- **ALCOA:** An acronym widely used to signify that all records and data should be attributable, legible, contemporaneous, original, and accurate.
- **ALCOA-plus:** An acronym that expands on "attributable, legible, contemporaneous, original, and accurate" data, placing additional focus on the qualities of being complete, consistent, enduring, and accessible – fundamental principles of ALCOA.
  - **Attributable:** This term indicates that information is recorded in such a way that it can be uniquely identified as having been executed by the data's originator (e.g., an individual or a computer

system). Original data and any subsequent amendments should be traceable concerning the individual, date and time, reason, along with signatures and summarized audit trails.

- **Legible:** The term legible pertains to the necessity that data is clear, easily comprehensible, free from overwriting and unauthorized alterations, and allows for a clear depiction of the sequence of steps or events in the record, enabling all activities conducted to be fully reconstructed by individuals reviewing these records at any time during the designated records retention period.
- **Contemporaneous:** Data must be recorded simultaneously at the time the activity is performed, and recordings such as in-process and environmental data should be maintained as activities are carried out, along with signatures, date, and time.
- **Original**:Data must be recorded in its original form, rather than being noted on a rough piece of paper and subsequently copied, with no trial injections allowed. Out-of-Specification (OOS) results need to be reported without delay, and data should not be newly generated or rewritten following corrections and cancellations.
- **Accurate:** The definition of "accurate" indicates that data must be correct, truthful, complete, valid, and reliable. Data should never be falsified or fabricated[6].

4. HIERARCHICAL DOCUMENT SYSTEM :

Hierarchical filing systems are preferred by drug information departments due to their efficiency in processing and retrieving documents. It is advisable to implement strategies for maintaining current files and locating misplaced documents. The organization should create a structured document system, as illustrated in Figure no.:1

Figure no.: 1 Hierarchical document system

Level 1 documents (e.g., Quality Manual) under these regulations break them down into specific components relevant to the company's compliance. These documents outline the fundamental principles and guidelines for creating, documenting, and executing a compliant quality system that is applicable to all departments.

Level 2documents elaborate on regulations concerning specific subjects or topics (e.g., Company Policies), ensuring uniformity across departments by establishing guidelines for procedures at subordinate levels.

Level 3 documentsSOPs, which are the next level, deliver detailed step-by-step instructions for operational tasks referenced in the previous levels (e.g., SOP for Controlled Document Management). Level 3 documents (SOPs) are tailored to specific departments or functions.

Level 4 documents are the most detailed (e.g., batch records, test methods) and pertain to specific departments, products, equipment, or processes.

They provide comprehensive instructions and methods for documenting tasks, which may take precedence over instructions in higher-level documents. The document hierarchy pyramid presents a structured approach, adaptable to the company's requirements with the option for more or fewer levels as necessary[9].

- **In a standard pharmaceutical company, you will typically find different types of documents, such as:**
  - Technical agreements
  - Confidentiality agreements
  - Technical reports
  - Documents pertaining to the quality system
  - Quality Manual
  - Standard operating procedures (SOPs)
  - Validation protocols and reports
  - Deviation reports
  - Audit plans
  - Validation master plans and associated documents like the URS, DQ, FAT, IQ, OQ, PQ, and validation reports
  - Documents concerning test materials, which include product specifications, test material receipts, and reports
  - Personnel documents, including training records
  - Facility documents, such as floor plans, HVAC plans, and environmental specifications
  - Deviation forms that address unplanned deviations and investigations into system failures
  - Change control documents
  - Worksheets, notebooks, and logbooks.

These documents are crucial for ensuring clear, accurate records and are regularly reviewed and updated [5].

5. PREPARATION, ISSUANCE, AND UTILIZATION OF DOCUMENTS:

- Documents must be organized and presented logically to promote correct usage and facilitate easy verification.
- They should include all essential information while avoiding unnecessary data.
- Any headings, items, or spaces on a master document that are no longer in use should be eliminated promptly.
- Each document should specify or incorporate:
  - The user's company or trading name.
  - The document's purpose and title.
  - A unique document identity number that identifies the document and indicates any revisions.
  - The date of authorization.
  - The date of expiration or review (for SOPs, etc.).
  - The signatures of the authorizing individuals and, if different, the signature of the person who prepared the document.
  - The distribution list, indicating where copies are distributed (at least on the master copy), and page numbers (along with the total number of pages).
  - The intended use of the document and the individuals authorized to use it should be clearly evident from the document itself.
  - The rationale for any revisions should be documented.
  - Any references used in the preparation of the document, if applicable.
- Issued documents must not be handwritten.
- Reproductions of computer-printed documents should be clear and legible; in the case of batch documents, each must be initialed to signify a verified issue.
- Any corrections made to a document should be initialed or signed and dated
- The correction must allow for the original information to be read. When necessary, the rationale for the correction should be documented.
- Documents that necessitate the entry of a date or additional information should:
  - Provide ample space for the entry.
  - Ensure sufficient spacing between entries; and

- Clearly specify what needs to be entered.
- If any issued document requires the entry of data or additional information, entries must be handwritten clearly and legibly in permanent ink.
- In the event that a handwritten entry is corrected, the correction must allow for the original entry to be read and should be initialled by the individual making the correction.
- Documents that contain instructions should be phrased in the imperative, i.e., as direct commands in numbered steps.
- They should be clear, precise, unambiguous, and written in plain English that is understandable to the user. Such documents should be easily accessible to all individuals executing the instructions.
- Documents must be kept current. Any changes should be formally authorized before the document is utilized.
- For permanent amendments, the revised document should be replaced at the earliest opportunity with a newly prepared document, and the superseded document should be clearly marked and filed.
- Master Production and Control Records, Batch Production and Control Records, Standard Operating Procedures, and others.
- Master Documents that directly impact product quality must be authorized by the individual responsible for Quality Assurance or their delegate, as well as by a responsible Production or other relevant Manager[4].

6. QUALITY MANUAL:

A Quality Manual is a documented procedure for a quality system aimed at the comprehensive planning and management of activities that affect quality within an organization. It should encompass all relevant elements of the quality system standard necessary for the organization. The manual must adequately detail the control aspects of the organization's quality management system.

- **The Purpose of the Quality Manual:**
- Communicating the organization's quality policy, procedures, and requirements.
- Describing and implementing an effective quality system.
- Enhancing control over practices and facilitating quality assurance activities.
- Providing a documented foundation for auditing the quality system.
- Ensuring the continuity of the quality system and its requirements amid changing circumstances.
- Presenting the quality system for external purposes, such as demonstrating compliance with national and international quality regulations.
- Training personnel on the quality system requirements and compliance methods.
- Demonstrating the quality system's compliance with quality requirements in contractual situations.

- **Structure and Format of the Quality Manual:**
- A model quality manual should include the following contents:
- Approval of the quality manual by top management, along with indications of any revisions made during its lifespan, including their approvals.
- A general introduction and statement of the organization's quality policy
- It should also explicitly mention what it does not encompass or for which it is not liable.
- A brief history of the company.
- Contact details of the company.
- An overview of the Quality Management System.
- Management's responsibility concerning quality systems.
- Policy on human resource management.
- Enhancement of the quality system through corrective and preventive actions [4].

7. SPECIFICATION:

Specifications can be defined as a collection of parameters that a specific material, piece of equipment, or similar object is expected to meet. For pharmaceutical products, specifications are required for:

a) Active and inactive starting materials.
b) Primary, printed, and other packaging materials.
c) Intermediate and bulk products and
d) Finished pharmaceutical products.

Each specification is a unique document for the company and must contain certain common elements, followed by specific contents for each document type.
Let us first examine the common elements found in any document. They are as follows:

- Company name and its address or location.
- Document title, e.g., "Specification."
- Date of issue and implementation, or effective date, preparation date, checking and authorization dates, and proposed review date.
- Names and signatures of individuals preparing, checking, and authorizing the specification.
- Unique Identification number of the specification.
- Pharmacopoeia or other references to the preparation of the specification.
- Circulation list of the specification.

Now, let us examine the specific contents of each type of specification.

(1) Specification for Active and Inactive Starting Materials:

These documents should include the following items, in addition to the previously mentioned common contents:

- Name of the material.
- Code number reference.
- Pharmacopoeial reference to the specific monograph if applicable.
- Qualitative and quantitative requirements, physical and chemical characterization, microbiological standards, and acceptance limits for assays, covering tests and limits for identity and purity.
- Names of approved suppliers and the original manufacturer.
- Directions for sampling and testing or references to the procedures.
- Storage conditions and any safety precautions.
- The maximum storage period before re-examination.
- Details of or references to the test method to be used for assessing compliance with the specification.

Format Title 1: Raw Material Specification

MAP PHARMACEUTICALS LTD.
RAW MATERIAL SPECIFICATION
(For Restricted circulation only)

Material:			Pages:
Code No.:		Shelf Life:	
Status:		Effective Date:	
Specification No.:		Review period:	
	Prepared by	Checked by	Approved by
Signature:			
Date:			

S. No.	Test	Specification

2)Specifications for Finished Products:

This document must include the following items, in addition to the standard contents mentioned earlier.

- Product name.
- Reference code number.
- Names of the active components.
- The formula or a reference to it.
- A description of dosage forms and packaging details.
- Instructions for sampling and testing or a reference to the procedures.
- The qualitative and quantitative criteria with acceptance limits.

- Storage conditions and precautions, if applicable, and
- Shelf life[4].

Format Title 2: Release Finished Product Specification

MAP PHARMACEUTICALS LTD.

RELEASE FINISHED PRODUCT SPECIFICATION

(For Restricted circulation only)

Product:			Pages:
Product Code:	Market:	Shelf Life:	
Stage: Release		Effective Date:	
Specification No.:		Review period:	
	Prepared by	Checked by	Approved by
Signature:			
Date:			

S. No.	Test	Specification

8. CERTIFICATE OF ANALYSIS:

A Certificate of Analysis (CoA) is a document that certifies the quality and compliance of a drug or formulation by testing a representative sample from a specific batch or lot of material. There is documented evidence of quality control testing conducted on the drug or formulation. The FDA declined to define CofAs in the preamble to the final rule regarding dietary supplements.

Manufacturers without a lab need a Certificate of Analysis to prove that their high standards are met when purchasing low-cost raw materials. The GMP applies to manufacturers, not farmers or raw material suppliers, so the question of what should be on a certificate of analysis should be directed inwards rather than outwards [10].

Table no. 1:Contents of the certificate of analysis[10].

Name/address/phone number of supplier and manufacturer	Test results—actual values as well as the pass/fail designation
Name of raw material/finished product	Acceptance Criteria—usually something along the lines of —not less than x, or not more than y
Category: (Component, ingredient, in-process, finished product)	Printed name(s) and signature(s) of analysts
Lot/Batch number	Printed name and signature of Approver
Date of manufacture (of material being certified)	Page number and total pages, e.g. page 1 of 5
Product Code or Number Ok	Date of manufacture of the material being certified
Expiration date of certified material (if applicable)	Expiration date (if applicable)
Re-evaluation date (if applicable)	Analysis date(s)
Stability statement (if required), e.g. Store at -80°K	Batch release date for the certified material. Test reference(s), e.g. USP 28/NF 34

Test name(s)—note may include physical descriptions, chemical tests for contaminants as well as desirable characteristics—chemicals like caffeine will require only a few specs and tests, botanicals and extracts will require more	Certification of compliance—something like ―this material complies with the specifications set forth in XXXX (e.g. USP 34/NF 28, In-House Specification) for the manufacture of Finished Product QQQQ as described in Master Batch Record VVVV‖

9.STANDARD OPERATING PROCEDURES (SOPs) :

Standard Operating Procedures (SOPs) are fundamentally a set of documented guidelines that detail the steps necessary for executing a routine or repeated task within an organization. The term "SOP" is sometimes used interchangeably with other terms such as protocols, instructions, and worksheets[11].

Purpose of SOPs:

- SOPs delineate the standard work processes carried out within an organization, guaranteeing consistent compliance with technical and quality standards while enhancing data accuracy.
- They encompass a range of activities, including essential programmatic tasks, technical procedures such as analytical processes, and the maintenance and calibration of equipment.
- SOPs are customized to fit the specific organization or facility, facilitating quality control, assurance, and adherence to regulations.
- The importance of well-crafted SOPs cannot be overstated; poorly constructed ones fail to serve their purpose. Even the most effective SOPs become irrelevant if not adhered to, highlighting the need for management oversight, ideally by direct supervisors.
- It is vital that current copies of SOPs are readily accessible to those executing the tasks, whether in printed form or electronically, to ensure their effectiveness[12].

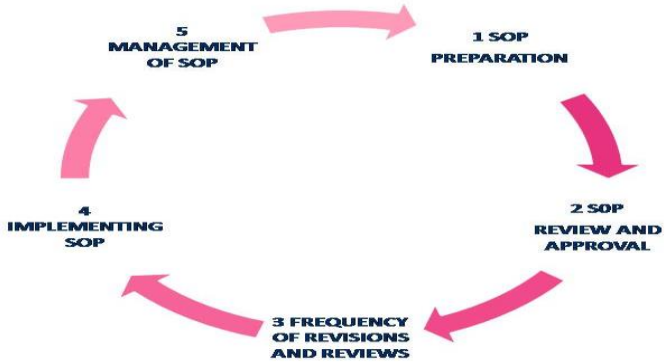

Figure no.:2 Process of SOP

10. DRUG MASTER FILE:

A Drug Master File (DMF) is a detailed and confidential document that API manufacturers present to the U.S. Food and Drug Administration (FDA). It encompasses extensive information regarding the chemistry, manufacturing, and controls of a drug component. Generally, a DMF is submitted when several companies work together on the development or production of a drug product[13].The DMF offers precise and comprehensive details about a drug product's chemistry, manufacturing process, stability, purity, impurity profile, packaging, and the current Good Manufacturing Practice (cGMP) status for any human drug product [14]. The application of DMFs differs by region, with varying procedures and requirements in the US, Canada, Europe, and Australia; however, the fundamental aim remains to meet regulatory standards and

demonstrate the quality, safety, and efficacy of medicinal products [15,16]. DMFs serve not only for regulatory submissions but also to enhance internal organization and support various IND-related protocols within a facility[17].Although creating a DMF can be resource-demanding, it is warranted by the specific information requirements of the medical center or pharmaceutical company[18, 19].

Role of DMF:

- The Drug Master File (DMF) documents the purity, potency, and identification of drugs within the Chemistry, Manufacturing & Controls (CMC) domain.
- It assists in the preparation of registration or approval documentation for drugs.
- It protects confidential and proprietary information[20].

11. BATCH PRODUCTION RECORDS/BATCH PRODUCTION AND CONTROL RECORDS (BPCR)/BATCH MANUFACTURING RECORD (BMR):

Definition:

- A batch manufacturing record is a documented account of the batch, created during the pharmaceutical manufacturing process.
- It encompasses actual data and a detailed step-by-step procedure for producing each batch.
- The batch manufacturing record serves as evidence that the batches were correctly produced and verified by quality control personnel.
- Batch production records must be generated for every intermediate and API/formulation, including comprehensive information related to the production and control of each batch.
- Prior to issuance, the batch production record should be reviewed to confirm it is the correct version and a clear, accurate reproduction of the relevant master production instruction.
- If the batch production record is derived from a distinct section of the master document, that document must reference the current master production instruction in use.
- Before commencing any processing, a verification should be conducted and documented to ensure that the equipment and workstation are free from previous products, documents, or unnecessary materials for the intended process, and that the equipment is clean and fit for use.
- These records should be assigned unique batch or identification numbers, dated, and signed upon issuance.
- In continuous production, the product code along with the date and time can act as the unique identifier until the final number is assigned.
- The batch number should be promptly recorded in a logbook or through an electronic data processing system.
- The record must include the date of allocation, product identity, and batch size.
- Documentation of the completion of each significant step in the batch production records (batch production and control records) should encompass:

- Dates and, when applicable, times.
- Identification of major equipment utilized (e.g., reactors, driers, mills, etc.)

- Specific identification of each batch, including weights, measures, and batch numbers of raw materials.
- Each batch must be specifically identified, detailing the weights, measures, and batch numbers of raw materials, intermediates, or reprocessed materials utilized during manufacturing.
- Actual results for critical process parameters must be documented.
- Any sampling that has been conducted should be noted.
- Signatures of individuals performing and directly supervising or verifying each critical step in the operation are required.
- Results from in-process and laboratory tests must be recorded.
- The actual yield should be documented at relevant phases or times.
- A description of the packaging and labeling is necessary.
- A representative label (for commercial supply) should be included.
- Any noted deviations, along with their evaluation and any investigations conducted (if applicable), or references to those investigations (if stored separately) must be documented.
- Results from release testing should be included.
- All analytical records pertaining to the batch, or a reference that allows for their retrieval, must be maintained.
- A decision regarding the release or rejection of the batch must be documented, including the date and signature of the individual responsible for that decision.
- The production record review[21].

12. MASTER FORMULA RECORD(MFR):

Definition:

A document or collection of documents that outlines the starting materials along with their quantities and the packaging materials, in addition to a description of the procedure and necessary precautions to produce a specified amount of a finished product, as well as the processing instructions, which include the in-process controls.

The MFR includes:

- Product Details: The name, logo, and address of the manufacturing company.
- Dosage form name, brand name, generic name, product code, and label claims for all ingredients.
- Product description: Batch size, pack size, and packaging style.
- Shelf life and storage conditions.
- MFR number and date: The superseded MFR number and date.
- Effective batch number.
- Authorization from the heads of production and quality assurance.
- Equipment: A comprehensive list of all necessary equipment and machines required for manufacturing, along with their capacities.

- Special instructions: Precautions and specific instructions to be adhered to during the manufacturing and packaging of the product.
- Calculations: Steps for calculating all active materials to achieve 100% potency, using water or Loss on Drying (LOD) methods.
- Manufacturing Process: Detailed documentation of all steps involved in the manufacturing process, including shifting, milling, lubricating, granulation, compression, and coating, along with process times and yields. It also specifies atmospheric conditions such as temperature, humidity, and storage conditions for each step.
- Packing Process: A comprehensive list of all packing materials along with their quantities is documented. Detailed line clearance and reconciliation of both printed and unprinted packing materials must be included.
- Yield: The theoretical yield, actual yield, and acceptance limits for the batch should be specified[21].

13. CHANGE CONTROL:

Today, change control systems are expected to be designed to not only document and approve changes but also to foresee changes within the quality organization."

The centralized change control system should clearly outline the change, specify documentation requirements, discuss change classifications, impact assessments, and the quality approval process for any changes encountered within the quality organization.

Change control can be defined as a set of procedures through which changes are reviewed, justified, documented, approved, and implemented in accordance with regulatory and corporate requirements.

In essence, change control is a system that manages change by:

- Identifying the ownership of the change.
- Facilitating the review and approval of the change.
- Preventing changes that could negatively impact product quality or conflict with registration or regulatory requirements.
- Providing an assessment of change and monitoring its impact[4].

14. Validation Master Plan (VMP):

A Validation Master Plan is a document that outlines how a company will function, identifies the responsible individual for various validation activities, and details how production, quality control, and personnel management will be organized. The VMP enables manufacturers to demonstrate their control over the overall quality system within the organization.

The VMP includes the following information, but is not limited to:

Title page and authorization – This section includes the title, document number, and version, along with necessary management approval signatures.

- **Table of contents** – This section lists all major areas of the VMP and their locations within the document.
- **Abbreviations and glossary** – This section defines technical or organizational terms.
- **Validation plan** – The VMP identifies what needs to be validated, as well as where, when, how, and why the validation is essential. The validation plan must pinpoint the processes that are critical to product quality and thus require validation.

- **Purpose and approach to validation** – This section summarizes each process and describes the validation approach, providing supporting rationale for what the document addresses.
- **Validation Scope** – The VMP encompasses all activities at the manufacturing site that pertain to equipment, utilities, processes, systems, and procedures potentially affecting product quality.
- **Roles and Responsibilities** – It outlines the primary duties of the validation department staff in creating validation protocols, change control documents, task reports, and validation Standard Operating Procedures, as well as the maintenance and storage of all documents related to validation.
- The manufacturing and engineering departments will review and approve the VMP along with all other documents such as validation protocols, protocol deviations, change control documents, and reports.
- The QA department will assess and approve the VMP, validation protocols, task reports, protocol deviations, change control documents, and SOPs to ensure alignment with cGMPs, adherence to policies and procedures, and authorization for implementation.
- **Outsourced Services** – This section pertains to the supplier responsible for conducting qualification activities or calibrations.
- **Deviation Management invalidation** – The VMP outlines the process for documenting deviations and conducting investigations as specified in validation protocols; corrective actions or plans must be reviewed and approved by authorized personnel prior to or alongside the validation report approval.
- **Change Control invalidation** – The VMP indicates that any changes with potential effects on validated systems and/or processes must be managed according to established change management procedures.
- **Risk Management Principles in Validation** – Risk management principles are essential to the validation process and should be included in the validation master plan as they relate to process validation, from the design and development phase through the entire lifecycle of the process.
- **Training** – The VMP specifies that all personnel involved in qualification and validation activities must receive appropriate training.
- **All validations** – This encompasses premises, central plant, manufacturing zones, material storage, as well as utilities, processes, qualifications, analytical methods, cleaning, equipment, revalidation, and computer validation.
- **Validation matrix** – The validation matrix outlines the necessary validations across the facility, arranged by their level of criticality.
- **References** – The VMP should include documents that offer guidance for the development and implementation of validation and qualification activities within the industries. [22].

15. SITE MASTER FILE:

The Site Master File (SMF) is a comprehensive document that provides accurate information about a pharmaceutical manufacturing facility. Although the structure of this document may differ from one country to another, the commonly recognized format includes the following topics.

This document should typically not be excessively lengthy, ideally not exceeding 100 pages, while also avoiding being overly concise. The M.H.R.A. (UK) has established specific guidelines regarding the length of the format, which are quite beneficial.

Now, let us take a brief look at the universally accepted contents of this document.

1.0 General Information

1.1Brief information about the organization.

1.2 Pharmaceutical manufacturing activities.

1.3 Other manufacturing activities.

1.4 Name and address of the site.

1.5 Types of products manufactured at the site.

1.6 Description of the site.

1.7 Employees details.

1.8 External technical assistance.

1.9 Quality Management System.

2.0 Personnel

2.1 Organization chart.

2.2 Qualification, experience, and responsibilities of key personnel.

2.3 Training (Basic and in service).

2.4 Health requirements for personnel engaged in manufacturing.

2.5 Clothing.

3.0 Premises and Equipment

3.1 Description of manufacturing area.

3.2 Nature of construction and finish.

3.3 Brief description of ventilation system (H.V.A.C. system).

3.4 Special areas.

3.5 Water system.

3.6 Maintenance of premises.

3.7 Major production and laboratory equipment.

3.8 Maintenance of equipment.

3.9 Calibration system.

3.10 Sanitation.

4.0 Documentation

4.1 Preparation, Revision and Distribution of documents.

4.2 Other documents related to product quality.

4.3 Additional documents.

5.0 Production

5.1 Brief description of production operations.

5.2 Handling of materials.

5.3 Handling of rejected materials and products.

5.4 Brief description of general policy for process validations.

6.0 Quality Control

6.1 Quality Management System.

7.0 Contract Manufacture and Analysis and other services

7.1 Contract Manufacture.

7.2 Contract analysis.

7.3 Contract services.

8.0 Post Operational Activities

8.1 Product distribution.

8.2 Handling of product complaints.

8.3 Product recall.

9.0 Self inspection

9.1 Self inspection programme.

In addition to these points, Schedule-M has added following points in the guidelines for preparing the Site Master File, they are as follows:

10.0 Export of Drugs

10.1 Products exported to different countries

10.2 Complaints and product recalls if any[4].

16. STORAGE AND RETENTION OF DOCUMENTS AND RECORDS:

- Except where legislation mandates longer retention periods, all records related to each batch, including original data such as laboratory notebooks, must be kept for a minimum of one year after the batch's expiry date, or if there is no expiry date, for six years following the date of manufacture of the batch.
- Records of complaints should be maintained for the same duration.
- Master documents must be adequately secured to prevent theft, loss, or alteration of information.
- Records may be preserved on microfilms or microfiche. The responsibility for photo reduction should be assigned to a designated individual, and the following procedures and controls should be implemented.
- A verification should be conducted to confirm that all necessary documents have been photo reduced.
- All photo reduced documents must be reviewed to ensure they are clear and accurate reproductions, displaying all information found on the originals.
- Original documents associated with a batch should not be destroyed until the aforementioned checks have been completed.
- All photo reduced records should be accessible in a readable format. Provisions should be made on-site for producing legible copies.
- The photo reduced records for each batch should be retained for the specified duration.
- Paper or film records should be stored in a restricted access area. Records must be safeguarded against tampering and loss.
- Records may also be retained using a computer storage system, following established procedures and checks. Such records should be backed up progressively (e.g., daily), with backups stored in a location separate from the active files.

17. STORAGE AND RETRIEVAL OF DOCUMENTS:

- All documents must be organized within the department to facilitate easy retrieval. To achieve this, the following system may be implemented:
- A comprehensive list (which may be arranged alphabetically) of documents should be created. This list must include:
- The title of the document.
- The location where it can be found.
- The individual to contact for retrieval.
- Any document requested, if available, should be provided to the requesting authority within a reasonable timeframe.
- Completed B.P.C.R. documents must always be securely stored under lock and key, under the supervision of Q.A.

- The retrieval of any M.P.C.R. and other critical documents should only occur with proper authorization from Q.A.

18.DISPOSAL OF DOCUMENT:

The expired documents should be disposed of by Q.A. following appropriate record-keeping and authorization through an acceptable method, such as shredding or burning, etc. [4].

19. CONCLUSION:

Here by we conclude that documents made in industries are beneficial for further reference, auditing, review and others. Documents made in industries are well thoroughly written in the paper work or digitalised by e-documents and these are stored according to the requirement. All these guidelines for preparing specific type of document are mentioned in this article. Various types of documents like BFR, MFR, SOP, SMF,VMP and others, their making procedures are explained. Effective documents can help in error correction in the process hence preparation of documents is very necessary step in the pharmaceutical industries.

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