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A REVIEW ON DOCUMENTATION IN PHARMACEUTICAL INDUSTRY

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ABSTRACT

In the pharmaceutical industry, documentation is critical for ensuring product quality, regulatory compliance, and operational efficiency. This process involves the creation, management, and storage of various documents, such as Standard Operating Procedures (SOPs), batch records, validation protocols, and reports. Pharmaceutical documentation serves as the foundation for traceability and transparency across all phases of drug development, manufacturing, and distribution. Effective documentation practices help prevent errors, facilitate audits, and ensure adherence to Good Manufacturing Practices (GMP). Regulatory authorities such as the FDA and EMA require accurate and up-to-date documentation to evaluate compliance with safety and quality standards. The industry relies on a structured approach to documentation, incorporating both manual and electronic systems, to manage the vast amount of data and ensure the integrity of the information recorded. This abstract discusses the importance of proper documentation management and the challenges faced by the industry in maintaining accuracy, consistency, and compliance.

KEYWORDS: *Documentation in pharmaceutical industry, Good documentation practices (GDP), Quality control Documentation in pharmaceutical industry*

1.INTRODUCTION

Effective documentation of these elements ensures regulatory adherence, smooth audits, and the safeguarding of product quality. The transition from manual to electronic systems, while improving data management, brings challenges in maintaining accuracy, security, and real-time updates. This abstract explores the integral components of documentation in the pharmaceutical industry, focusing on DMF, CTD/eCTD, BMR, MFR, audit plans, and reports, and their importance in maintaining a high standard of compliance and operational excellence.

Documentation plays a pivotal role in the pharmaceutical industry to ensure product quality, regulatory compliance, and operational efficiency. Key documents include Drug Master Files (DMFs), which provide confidential information about the manufacturing process and facilities, and are critical for regulatory approval. The industry also follows structured audit plans and reports to ensure adherence to Good Manufacturing Practices (GMP), allowing for regular assessments of compliance with both internal standards and regulatory requirements.

1.1 History of documentation In the pharmaceutical industry:

The history of documentation In the pharmaceutical industry is deeply intertwined with the development of the industry itself, particularly in terms of regulations, quality control, and the need for safety and efficacy in medicines. Below is an overview of the evolution of pharmaceutical documentation:

1.1.1 Early Practices (Pre-19th Century)

• Ancient Civilizations: Pharmaceutical documentation began with ancient medical texts such as the Ebers Papyrus (1500 BCE, Egypt), which recorded medicinal recipes. Similarly, Indian Ayurveda texts and Chinese Materia Medica contained medicinal records.
• Middle Ages and Renaissance: European apothecaries and pharmacists kept detailed handwritten records of medicinal preparations to ensure consistency. Herbal books (herbals) were widely used.

1.1.2 Industrial Revolution and 19th Century

• 1800s: The advent of large-scale drug manufacturing highlighted the need for standardized processes and record-keeping.

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• 1848: The United States passed the Drug Importation Act, marking an early regulatory requirement for drug purity, indirectly emphasizing the importance of documentation.
• Pharmacopoeias: National pharmacopoeias (e.g., the British Pharmacopoeia, 1864) formalized standards for drug composition, requiring detailed documentation of formulations.

1.1.3 20th Century: Birth of Modern Pharmaceutical Documentation

• 1906: The U.S. Pure Food and Drug Act required manufacturers to ensure accurate labeling, necessitating batch records and documentation of ingredients.
• 1938: The U.S. Food, Drug, and Cosmetic Act (FDCA) was enacted following the 1937 Elixir Sulfanilamide tragedy. It required safety data to be submitted to the FDA, introducing systematic clinical trial documentation.
• 1940s-1950s: World War II and the post-war boom in antibiotics (e.g., penicillin) led to the need for quality assurance documentation in mass production.
• 1970s-1990s: Global Harmonization and Electronic Records
• 1976: The Medical Device Amendments extended documentation requirements to medical devices.
• 1980s: Computerized systems began to replace paper documentation, leading to the introduction of electronic records in pharmaceutical manufacturing and clinical trials.
• 1995: The establishment of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) led to harmonized documentation standards across regions.
ICH Guidelines: Key guidelines include ICH E6 (Good Clinical Practice) and ICH Q7 (GMP for APIs).
• 1997: The FDA introduced the 21 CFR Part 11 regulation, setting standards for electronic records and signatures.

1.1.4 21st Century: Digital Transformation and Advanced Standards

• 2000s: The pharmaceutical industry saw widespread adoption of electronic document management systems (EDMS) and enterprise resource planning (ERP) tools to manage documentation more efficiently.
• 2010s: Regulatory agencies increasingly emphasized data integrity, requiring detailed documentation of raw data, metadata, and audit trails.
• 2020s: Emerging technologies such as blockchain, artificial intelligence, and electronic batch records (EBR) are revolutionizing documentation, ensuring real-time tracking, transparency, and compliance.

1.2 Key Milestones in Pharmaceutical Documentation

• 1848: U.S. Drug Importation Act
• 1906: U.S. Pure Food and Drug Act
• 1938: Food, Drug, and Cosmetic Act
• 1963: GMP regulations introduced
• 1995: ICH established
•1997: FDA 21 CFR Part 11 implemented
The evolution of pharmaceutical documentation reflects a continuous effort to ensure drug safety, efficacy, and quality through meticulous record-keeping and compliance with global standards.

2.RETENTION AND RETRIEVING OF RECORDS

Retention and retrieval of documentation are critical processes in ensuring information is properly stored, organized, and accessible when needed.

2.1 RETENTION

INTRODUCTION
Records are information (stored in any form or medium) that are an important Part of the functioning of an organization and are an essential aspect in fulfilling Its legal obligations. It is therefore imperative to give due care to the maintenance Of this vital resource.

2.1.2 DEFINITION

The Biopharmaceutical Development Program(BDP) Records Retention Standard operating Procedure (SOP) defines the period of time during which records are maintained And specifies the disposition of records.

2.1.3 OBJECTIVE

Over time, offices generate numerous records, including files, registers, and dossiers. Ensuring the relevance and quick retrieval of these records is crucial. This Record Retention and Disposal Manual aims to provide guidelines for the Personnel Department to retain official records in compliance with applicable laws and to dispose of redundant records at the appropriate time. By following these guidelines, operations can become more efficient, and valuable office space can be freed up for better utilization.

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2.1.4 RETENTION PERIOD

Records must be retained according to operational, legal, regulatory, and fiscal requirements. The BDP maintains records for at least ten years, unless otherwise specified in writing for certain documents or categories of documents.

2.1.5 RECORDS RETENTION POLICY & SCHEDULE(MANAGE THE ORGANISATION)

Global policy references for record management, detailing various record categories, their descriptions, examples, and retention periods as per the proposed India SOP. Below is a consolidated overview:

1. Accounting Records (GRS042)

Documentation of payment and receipt transactions, such as account reconciliation files, bank statements, and purchase orders.
Retention Period: Minimum 8 years.

2. Audit Records and Audit Schedules (GRS043, GRS077)

Records related to compliance examinations, audit schedules, findings, and recommendations for internal and external suppliers or contractors.
Retention Period: 7 years after the audit is closed.

3.Benefits Programme Records (GRS044)

Covers documentation for benefit programs, including pension funds, retirement savings, and health insurance plans.
Retention Period: 12 years after the program ends.

Likewise the retention of records are done

Global policy Ref. #	Record Category	Description	Examples	Retention Period as per Proposed India SOP
GRS042	Accounting Records	Documentation detailing payment / receipt transactions within the Company or between the Company and others.	Account Analysis: Account Reconciliation Files: Accounts Payable Batch Files: Accounts Receivable Files: Balance Sheets Bank Statements Cash Receipts Cheque Registers Cheque Requests Credit Cardholder Files Credit Case Files Education Reimbursement Forms Expense Reports Invoices Monthly Account Control Reports Purchase Orders Purchase Requisitions Travel & Entertainment Files Voided Cheques	For not less than 8 years immediately preceding current year
GRS043,GRS 077	Audit Records, Audit Schedules	a) Documentation relating to the examination of compliance with internal and external controls, policies and procedures, laws and regulations, by the Company and its external suppliers and contractors; and improved process recommendations. b) Audit schedules for internal (Company) and external suppliers and contractors.	a) Action Plan & Resolution Records: Audit Findings: Audit Plans: Audit Reports: Audit Schedules Audit Timetables Compliance Overview Documents Self-Assessments of Compliance required by the Company and its Regulators b) Audit Plans: Audit Timetables	7 Years after Audit is Closed
GRS044	Benefits Programme Records	Documentation detailing the Company's various benefit programmes including pension fund membership, retirement savings plans, health and life insurance plans.	Benefit Plan Documents: Cash Balance Plan Documents: Employee Assistance Programme Files: Matching Gift Programme Files: Pension Files Retirement Savings Plan Files	12 Years after Life of Programme
GRS045	Business Continuity Planning Records	Documentation detailing plans and preparations necessary to minimise loss and maximise the continuity of critical business functions in the event of an unforeseen business interruption.	Business Impact Analysis Documents: Contingency Resource Information: Disaster Recovery Plans: Emergency Response Plans: Findings Reports Mock Disaster Project Files	Until Superseded by New Version
GRS046	Communication Records – External	Communication materials prepared by or for the Company for external use with investors, stock analysts, corporate regulators and the general public.	Briefing Books: Company Promotional Information: Executive Biographies : Government Relations Files: Investor Relations Files Lobbying Records Press Releases / Kits Product Information Public Relations Records Request / Reply Letters Speeches – External Submissions to Corporate Regulators	5 Years
GRS047	Communication Records – Internal	Internal Company communication materials that are widely distributed throughout the organisation or within large business areas.	Bulletins / Announcements: Company Newsletter / Publications: Employee Communications	3 Years
GRS048	Compensation Programme Records	Documentation detailing terms and conditions of the Company's various compensation programmes.	Bonus Programme Records: Compensation Surveys: Salary Range History Records Sales Incentive Programme Records Special Incentive Programme Records Stock Option Programme	10 Years after Superseded by New Programme

Fig.GlaxoSmithKline Pharmaceuticals Limited,Records Retention Policy & ScheduleTable of documents Retention

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2.2 RETRIEVAL MAINTAINING

2.2.1 DEFINITION

The process of locating and accessing specific information or data from a system, database, or set of records. This can involve searching through various formats, such as text, images, or databases, to find relevant content or resources needed for reference or use.

Retrieving in documentation involves the systematic process of finding and accessing specific information stored in various types of documents, such as manuals,reports,databases, or digital archives.

2.2.2 DATA RETRIEVAL PROCESS

Identification: Determining what information is needed.
Locating: Finding the documents that contain the required information.
Extraction: Accessing and pulling the relevant content from those documents.

2.2.3 CHALLENGES

Volume of Information: Large datasets can make retrieval time-consuming.
Quality of Metadata: Poorly tagged documents can hinder effective searching.

2.2.4 APPLICATIONS

Legal and Compliance: Retrieving documents for audits or investigations.
Business Operations: Accessing policies, procedures, or records for decision-making

3. STANDARD OPERATING PROCEDURE (SOP)

A Standard Operating Procedure (SOP) is a set of written instructions that outline routine or repetitive tasks followed by an organization. SOPs play a key role in ensuring the success of a quality system, as they provide essential information for individuals to perform tasks correctly. Furthermore, they promote consistency in the quality and integrity of products or end-results.
The term “SOP” is sometimes used interchangeably with terms like protocols, instructions, and worksheets. The definition of SOPs can vary depending on the area in which they are applied.

3.1 OBJECTIVES

The task involves developing explanatory texts for a pharmacy curriculum and reference textbook, as well as creating model standard operating procedures (SOPs) for key quality and operational activities in the pharmaceutical file

3.2 PURPOSE

Standard Operating Procedures (SOPs) define the recurring work processes within an organization. They are designed to ensure that activities are performed consistently and in compliance with both technical and quality system requirements. Additionally, SOPs support data quality by documenting the proper methods to be followed.

Standard operating procedures (SOPs) outline fundamental programmatic and technical actions, such as analytical processes and procedures for maintaining, calibrating, and using equipment. They are designed to be specific to the organization or facility conducting the activities, helping to maintain quality control and quality assurance processes while ensuring compliance with governmental regulation

3.3 BENEFITS OF SOP

1.To ensure that processes continue uninterrupted and are completed on a Described Schedule. Ensure against process shut-downs caused by equipment failure or other Facility damage.
2.To ensure that approved procedures are followed in compliance with company and Government regulations. Well-written SOPs help ensure that government regulations Are satisfied. They also demonstrate a company good-faith intention to operate properly.
3. To serve as a checklist for auditors. Auditing job performance is a process similar to Observation mentioned in the previous item only it usually involves record keeping. SOPs should serve as a strong basis when detailed audit checklists are developed. [DMPI]

3.4 METHOD

3.4.1 Design

Follow the general directions of SOP F08-1 ‘Capsules, design composition´ if it concerns a new Preparation. The solvent method is preferably used for mixtures with very unfavourable mixing ratios(< 5 mg active substance). The method needs careful testing and validation.

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Choice of a suitable organic solvent. In a suitable organic solvent the drug should dissolve easily. The solvent must …

Active substance and dose	Solvent and amount	Deposition and ratio	Diluent	Reference
.....	.....	.....	.....	.....

Determination of amount of diluent
[……]
Dissolving the active substance
[……]
Filling of the capsules
[……]
In process controls
[……]
Control checks
[……]
References
[……]

4. MASTER FORMULA RECORD AND BATCH FORMULA RECORD

4.1 MASTER FORMULA RECORD

A document or set of documents specifying the starting materials and their quantities, along with the packaging materials, the processing instructions (including in-process controls), and a description of the procedure and precautions required to produce a specified quantity of a finished product.

4.1.1 The master Formula shall include

1. The name of the product together with product reference code relating to its Specifications.
2. The patent or proprietary name of the product along with the generic name, a Description of the dosage form, strength, composition of the product and batch Size
3. Name, Quantity, and Reference Number of Starting Materials
4. List all starting materials to be used, including their names, quantities, and reference numbers Include any substances that may disappear during processing.
5. Detailed Stepwise Processing Instructions Provide step-by-step instructions for processing Include the time required for each step.

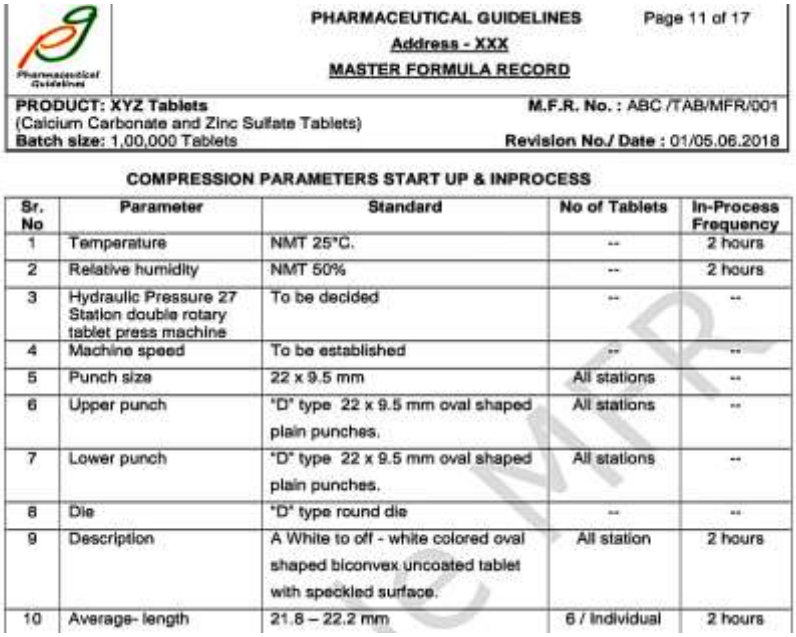
4.1.2 Example

Master Formula Record (MFR) used in pharmaceutical manufacturing for the compression process of XYZ Tablets (Calcium Carbonate and Zinc Sulfate). It outlines the standard operating parameters and in-process checks for a batch size of 1,00,000 tablet

This record ensures that the manufacturing process follows strict quality controls, and every critical parameter is monitored periodically during tablet production. It helps maintain consistency, ensures regulatory compliance, and ensures the quality of the final product.

Key Elements
. Product Details:Name: XYZ Tablets
Compression Parameters:Temperature and Humidity:

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Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal



PHARMACEUTICAL GUIDELINES Page 11 of 17
Address - XXX
MASTER FORMULA RECORD

PRODUCT: XYZ Tablets M.F.R. No. : ABC /TAB/MFR/001
(Calcium Carbonate and Zinc Sulfate Tablets)
Batch size: 1,00,000 Tablets Revision No./ Date : 01/05.06.2018

COMPRESSION PARAMETERS START UP & INPROCESS

Sr. No	Parameter	Standard	No of Tablets	In-Process Frequency
1	Temperature	NMT 25°C.	--	2 hours
2	Relative humidity	NMT 50%	--	2 hours
3	Hydraulic Pressure 27 Station double rotary tablet press machine	To be decided	--	--
4	Machine speed	To be established	--	--
5	Punch size	22 x 9.5 mm	All stations	--
6	Upper punch	"D" type 22 x 9.5 mm oval shaped plain punches.	All stations	--
7	Lower punch	"D" type 22 x 9.5 mm oval shaped plain punches.	All stations	--
8	Die	"D" type round die	--	--
9	Description	A White to off - white colored oval shaped biconvex uncoated tablet with speckled surface.	All station	2 hours
10	Average- length	21.8 – 22.2 mm	6 / Individual	2 hours

Fig.Master formula record of xyz tablet

4.2 BATCH FORMULA RECORD (BFR): DETAILED OVERVIEW

A Batch Formula Record (BFR) is a standardized document used in pharmaceutical, biotech, and food industries to outline detailed instructions and procedures for producin specific batch of a product. It is a vital part of Good Manufacturing Practices (GMP) and ensures consistency, quality, and compliance.

4.2.3 PURPOSE OF A BATCH FORMULA RECORD

- To provide step-by-step guidance for manufacturing a product batch.
- To ensure that every batch meets the quality standards and regulatory requirements.
- To document all processes and materials for traceability.
- Ensures that every batch of a product is manufactured using the same formula and process.

4.2.3 Benefits

Meets regulatory requirements set by agencies like the FDA, EMA, or other local authorities.
Demonstrates adherence to Good Manufacturing Practices (GMP) or ISO standards.
Provides a detailed record of all raw materials, quantities, and steps taken during production.

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COMPANY NAME	BATCH MANUFACTURING RECORD			Page: 1 of 8
Department : Production	Title : Tongkat Ali Tablet			Batch Record : BMR-001
	Name	Signature	Date	Revision No. : 0
Prepared by :	Production Manager			
Approved by :	QA Manager			Effective Date : 1 January 2016

1. Product Details	
Description	Tongkat Ali 250mg Tablet Colour: Pale Shape: Round/ Biconvex
Batch Quantity	Batch size: 50 kg Approx No. tablets: _____
Packaging	Bottle of 60's
Storage Conditions	Ambient - conditions. store in tight container protected from light and moisture

2. Production Batch Record Issuance		
Issued By – Issuer has reviewed the Batch Record to ensure that the copy is a complete, accurate copy of the Master Batch Record.		
(Print) Issued By – Quality Assurance	Signature	Date
Issued To – Production has reviewed the Batch Record to ensure that the copy is a complete and correct. Production is responsible for the Batch Record following issuance.		
(Print) Issued By – Quality Assurance	Signature	Date

Fig. Batch Formula Record Table

4.2.4 KEY COMPONENTS OF A BATCH FORMULA RECORD

General Information

- Product Name: Full name of the product being manufactured.
- Product Code: Unique identifier for the product.
- Batch Number: Unique number assigned to the batch for traceability.
- Batch Size: Quantity to be manufactured, often specified in units, liters, or kilograms.
- Dosage Form: Tablet, capsule, syrup, cream, etc.

5. AUDIT PLANNING AND REPORT

5.1 Audit

An audit, in simple terms, can be described as the inspection of a process or system to ensure it meets the requirements for its intended use. According to the International Organization for Standardization (ISO), an audit is defined as a "systematic, independent, and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which the verification criteria are met."

In the pharmaceutical industry, audits are virtual means for Assessing compliance with the established objectives defined in the Quality system and thus paving the way for the continuous Improvement program by providing feedback to management .

5.2 GOALS OF AN AUDIT

The goal of this process is to evaluate existing activities and documentation to determine whether they meet established standards. An audit assesses the strengths and weaknesses of quality control and quality assurance processes. The results help improve these processes and create a better system for the benefit of the company. In the pharmaceutical industry, every product manufactured has specific characteristics that must be quantified or qualified through laboratory tests. Quality control and quality assurance serve as essential control and balance systems to ensure compliance and reliability.

5.3 AUDIT PLANNING PROCEDURES

To conduct an audit effectively and efficiently, the work must be properly planned and controlled. Audit planning involves formulating a general strategy that sets the direction of the audit, outlines its expected scope and conduct, and provides guidance for developing the audit program. The nature and extent of planning will vary based on factors such as the size and complexity of

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the enterprise, the commercial environment in which it operates, the methods used for processing transactions, and its reporting requirement.

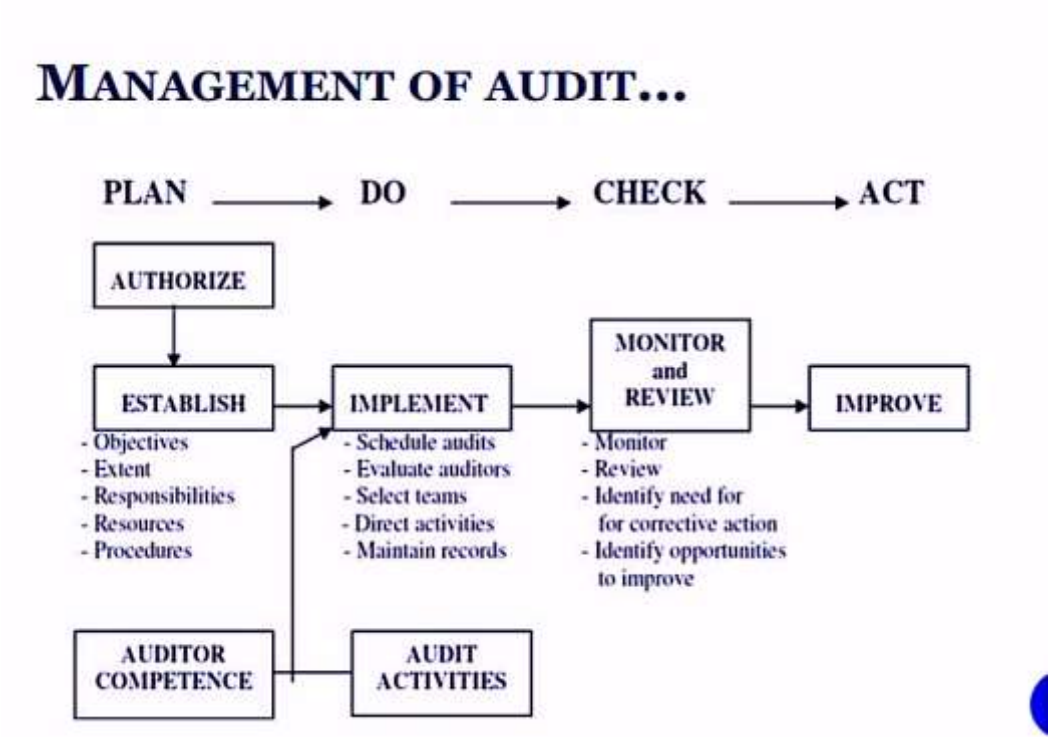


Fig.Management of Audit chart

5.4 AUDIT REPORT

The audit report is a key outcome of an audit, presenting the results of the auditor's investigation. It provides accurate and clear data, along with recommendations that outline corrective actions necessary for improvement.

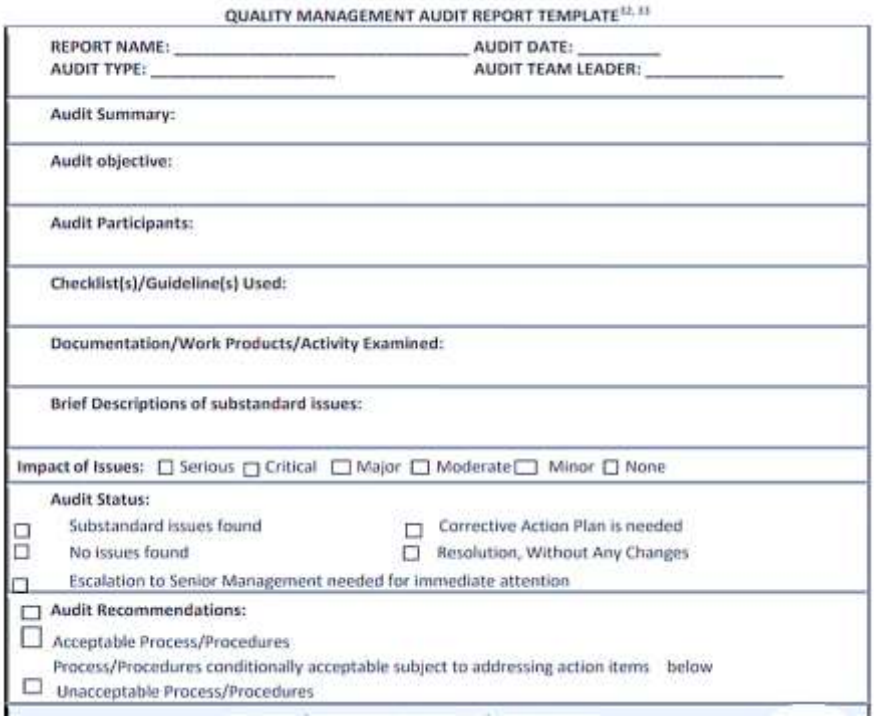
Nonconformities identified through audits can be classified into two types: major and minor, based on the severity of the infraction and the corrective actions required. A minor non-conformance indicates a system weakness that does not significantly impact the company's operations or quality control. It can typically be resolved quickly and with minimal effort.

Quality Management Audit Report Template

It is a form designed to document and standardize the process of conducting a quality management audit. Here's a breakdown of the sections in the template:

1. Header Information:Report Name: Title of the audit report.
2. Audit Summary: A concise summary of the audit findings.
3. Audit Objective: States the purpose or goal of the audit.
4. Audit Participants: Names of individuals involved in the audit process.
5. Checklist(s)/Guideline(s) Used: References to the checklists or standards followed during the audit.

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QUALITY MANAGEMENT AUDIT REPORT TEMPLATE[12, 13]

REPORT NAME: _____ AUDIT DATE: _____
AUDIT TYPE: _____ AUDIT TEAM LEADER: _____

Audit Summary:

Audit objective:

Audit Participants:

Checklist(s)/Guideline(s) Used:

Documentation/Work Products/Activity Examined:

Brief Descriptions of substandard issues:

Impact of Issues: ☐ Serious ☐ Critical ☐ Major ☐ Moderate ☐ Minor ☐ None

Audit Status:

☐ Substandard issues found ☐ Corrective Action Plan is needed
☐ No issues found ☐ Resolution, Without Any Changes
☐ Escalation to Senior Management needed for immediate attention

☐ Audit Recommendations:
☐ Acceptable Process/Procedures
Process/Procedures conditionally acceptable subject to addressing action items below
☐ Unacceptable Process/Procedures

Fig. Quality Management Audit Reports Template

This template is typically used in quality management systems to ensure consistency, identify areas for improvement, and document compliance or non-compliance with standards.

6. SUBMISSIONS DOCUMENTS TO DRUG MASTER FILES(DMF)

6.1 Drug Master File (DMF)

A Drug Master File (DMF) is a voluntary submission to the Food and Drug Administration (FDA) that provides confidential, detailed information about facilities, processes, or articles involved in the manufacturing, processing, packaging, and storage of human drugs. While not required by law or FDA regulation, a DMF may be submitted at the discretion of the holder. The information contained in a DMF can support various regulatory submissions, including an Investigational New Drug Application (IND), a New Drug Application (NDA), an Abbreviated New Drug Application (ANDA), another DMF, an Export Application, or amendments and supplements to any of these.

6.1.1 TYPES OF DRUG MASTER FILES

There are five types of DMF's:

- I Plant information (It has been discontinued)
- II Drug substance, drug product, intermediates and material used in Their manufacture
- III Packaging
- IV Excipients
- V FDA Accepted Reference Information (Not much in use)

By fulfilling these roles, DMFs contribute significantly to the pharmaceutical industry by ensuring drug quality, safety, and efficacy while protecting proprietary information.

6.1.2 SUBMISSIONS TO DRUG MASTER FILES(STEPS)

1.A DMF submission should include a transmittal letter, administrative information about the submission, and the specific details to be included in the DMF as outlined in this section.
2.The DMF must be in the English language. Whenever a submission contains information in another language, an accurate certified English translation must also be included.
3.Each page of each copy of the DMF should be dated and consecutively numbered. An updated table of contents should be included with each submission.

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4.This flowchart outlines the regulatory requirements for Drug Master Files (DMFs) across different markets, focusing on regulated and emerging markets. Here's the explanation:

6.1.3 DRUG MASTER FILE (DMF) REGULATORY REQUIREMENTS:

The chart begins with the general regulatory requirements for DMFs, which are detailed documents submitted to regulatory authorities to provide confidential information about manufacturing, processing, packaging, and storage of drugs.

• DMF related Regulated Market (USA):

For regulated markets like the USA, the DMF requirements are based on ICH-CTD (International Council for Harmonisation - Common Technical Document) guidelines.ICH-CTD serves as a harmonized framework for the preparation and submission of regulatory dossiers.

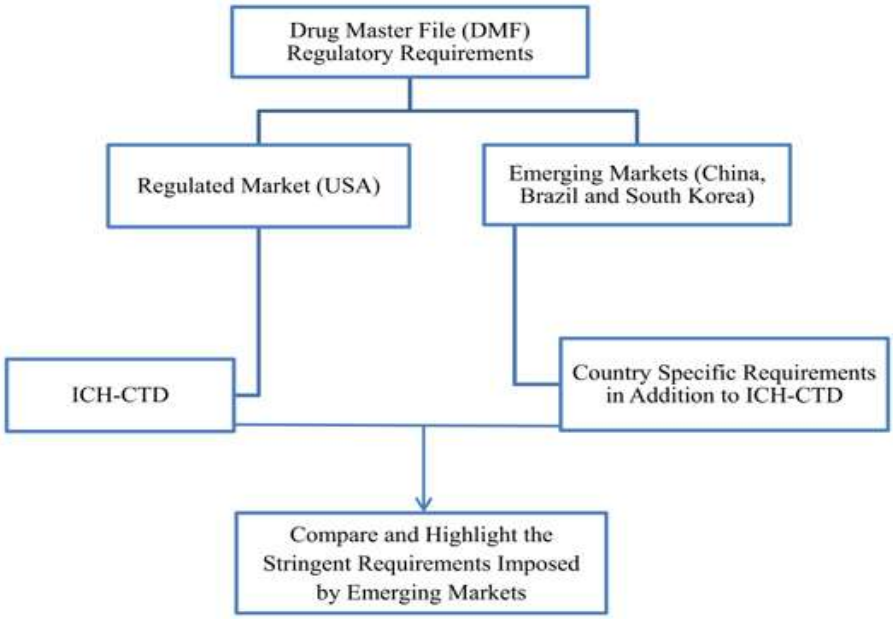


Fig. Drug Master File (Dmf) Regulatory Requirements

• Emerging Markets (China, Brazil, South Korea)

Emerging markets may follow ICH-CTD guidelines but often impose additional country-specific requirements. These unique regulations may reflect local standards, procedures, or legal frameworks, making compliance more challenging.

• Comparison and Highlighting of Stringent Requirements:

The chart emphasizes the importance of comparing the regulatory landscapes of emerging markets with the USA.It specifically focuses on identifying and highlighting stricter or more complex requirements imposed by emerging markets compared to those in regulated markets.

In summary, the flowchart provides a high-level comparison between the regulatory requirements in the USA (a regulated market) and emerging markets, with an emphasis on identifying the additional, more stringent requirements in the latter.

6.1.4 ROLE OF DMF

1.Confidentiality Protection:

A DMF allows manufacturers to maintain the confidentiality of their proprietary information (e.g., formulation, manufacturing process) while sharing necessary technical details with regulatory authorities.

2.Streamlining Regulatory Approvals:

DMFs support the regulatory review process by providing detailed information about specific components (e.g., active pharmaceutical ingredients (APIs), excipients, or packaging materials) to ensure compliance with quality and safety standards.

3.Facilitating Collaboration:

Contract manufacturers, suppliers, and pharmaceutical companies can use DMFs to share critical data without disclosing proprietary details to their partners, thus enabling smoother collaborations

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4.Ensuring Compliance:
By submitting a DMF, manufacturers demonstrate compliance with current Good Manufacturing Practices (cGMPs) and regulatory requirements, supporting the approval process for associated drug products.

5.Reducing Duplication of Effort:
A single DMF can be referenced in multiple applications by different pharmaceutical companies, reducing the need for redundant submissions and reviews.

6.2 COMMON TECHNICAL DOCUMENT (CTD)
The Common Technical Document (CTD) is a key project of the International Council for Harmonisation (ICH) designed to streamline the drug registration process by avoiding duplication and the need for translation into regional languages. Using this format, applicants can submit a single application simultaneously to multiple countries for the registration of their drug product. The CTD is an internationally accepted format for preparing applications for novel medications intended for submission to regional regulatory authorities in participating countries.

6.2.1 The Common Technical Document is organized into Five modules
- Module 1-Administrative and prescribing information
- Module 2-Overview and summary of modules 3 to 5
- Module 3- Quality (pharmaceutical documentation)
- Module 4-Non clinical document safety (toxicology studies)
- Module 5-Clinical document efficacy (Clinical studies)

6.2.2 CTD TRIANGLE
The CTD triangle refers to the structure of the Common Technical Document (CTD), a standardized format for submitting information to regulatory authorities for drug approval. It was established by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) to streamline and harmonize submissions across regions like the U.S., Europe, and Japan.

CTD TRIANGLE

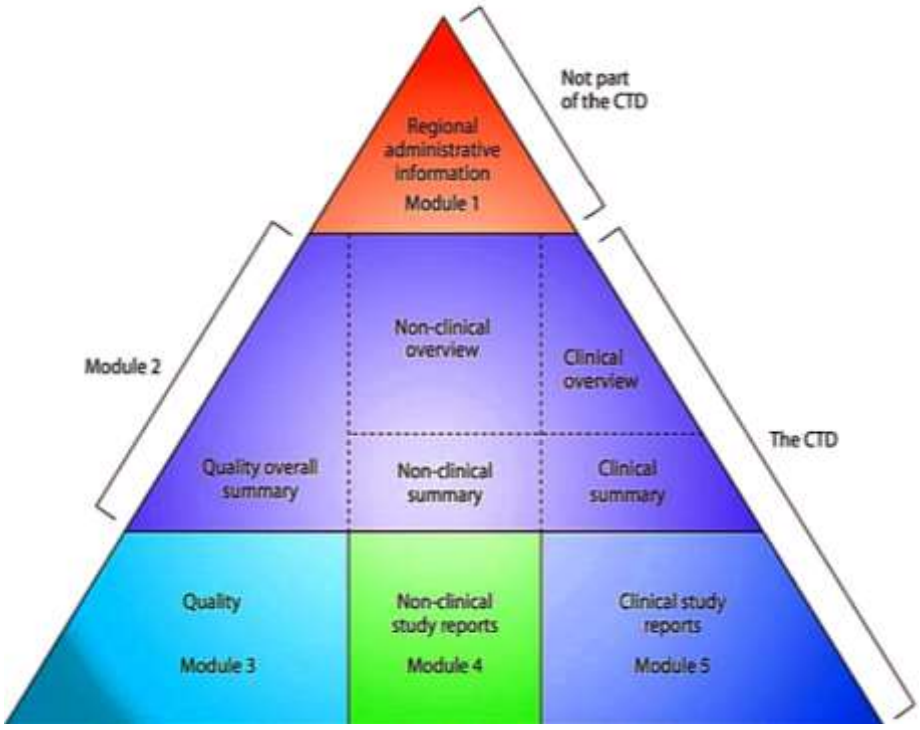


Fig. common technical Documentation Triangle including 5 module

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EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

6.2.3 CTD TRIANGLE: KEY COMPONENTS

The CTD is represented as a triangle to highlight its hierarchical structure, divided into five modules:

1. Module 1: Regional Administrative Information
2. Module 2: Common Technical Document Summaries
3. Module 3: Quality
4. Module 4: Nonclinical Study Reports
5. Module 5: Clinical Study Reports

6.2.4 Significance of the Triangle

• The base represents detailed data (Modules 3, 4, 5), which supports the submission.
• The middle (Module 2) summarizes and organizes the data for easier review.
• The top (Module 1) ensures region-specific compliance for submission.

This structured approach facilitates global regulatory harmonization, reduces duplication, and improves the efficiency of drug review processes.

6.3 eCTD

The eCTD is the standard format for submitting applications, amendments, supplements, and reports to FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER).

6.3.1 Submissions Using the eCTD Specifications Guidance for Industry

• Under section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), sponsors and applicants must submit specified submission types to the Food and Drug Administration (FDA) electronically and in the format specified by the Agency. This requirement applies at least 24 months after the issuance of a final guidance document in which the FDA has defined the electronic format.
• This guidance document, along with the technical specification documents it incorporates by reference, outlines how sponsors and applicants must organize the content of their electronic submissions for all submission types under section 745A(a) of the FD&C Act. Additionally, more detailed technical instructions are provided in a separate eCTD technical conformance guide.
• In Japan And Canada DMF submissions in eCTD format are still not possible. In Europe and the USA, eCTD Is considered the preferred submission format. Furthermore, the EDQM offers alternative ways To submit DMFs in electronic format (NeeS, or single pdf for the whole submission), while this is Not foreseen for FDA and EMA
• When it Comes to eCTD submission, there continues to be Differences among different countrie and even ICH regions. For example, the FDA began Accepting eCTD submissions in 2003; Japan began accepting in 2004, yet the EU Heads of Medicines Agencies committed themselves, in 2005, to be ready for eCTD submissions by 2010.

6.3.2 Benefits of eCTD

• Efficiency: Faster submission preparation and review process.
• Standardization: Provides a uniform structure for submissions across regions.
• Lifecycle Tracking: Simplifies version control and document updates.
• Accessibility: Electronic format allows easy access, storage, and retrieval.

6.3.3 Challenges in Implementing eCTD

• Complexity: Requires training and expertise in XML and submission software.
• High Initial Costs: Investing in eCTD preparation tools and resources.
• Regulatory Variations: Module 1 is region-specific, requiring customization

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Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

6.3.2 eCTD STRUCTURE FOLDER

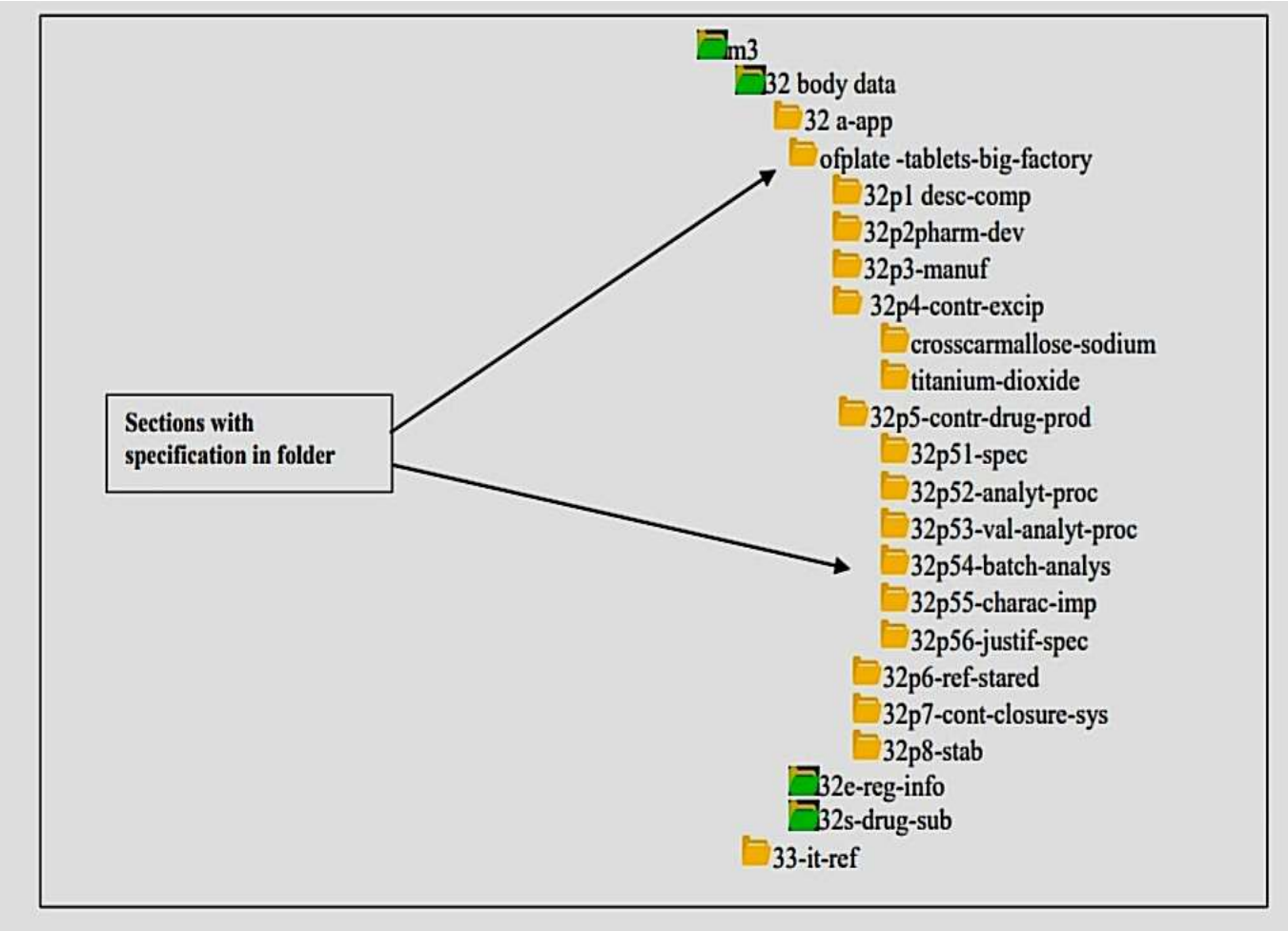


Fig.eCTD STRUCTURE FOLDER

7. REGULATED AND NON-REGULATED MARKETS

The pharmaceutical industry is among the most highly regulated industries, with the primary aim of protecting public health and well-being. The stringent drug approval system is designed to ensure that medicinal products are manufactured to meet acceptable standards of quality and efficacy. By law, all new drugs must be proven safe and effective before they can be approved for marketing. A regulated market refers to the provision of services overseen by a government-approved body.

7.1 REGULATED MARKET

A regulated market is governed by stringent rules and regulations enforced by governmental or international bodies. These regulations ensure the quality, safety, and efficacy of pharmaceutical products

A regulated market in the pharmaceutical industry refers to a region where stringent laws and guidelines govern the development, production, approval, marketing, and distribution of pharmaceutical products. These markets are overseen by regulatory authorities such as the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), or Japan's Pharmaceuticals and Medical Devices Agency (PMDA). The primary goal of regulation is to ensure drug quality, safety, and efficacy through rigorous standards like Good Manufacturing Practices (GMP), clinical trial approvals, and post-market surveillance (pharmacovigilance). Regulated markets typically require extensive documentation, clinical evidence, and compliance with international standards before a product can be approved for sale. While these regulations significantly increase development costs and time-to-market for pharmaceutical companies, they also provide high levels of consumer trust, minimized risks of counterfeit drugs, and a structured framework for innovation and competition.

7.1.1 Key characteristics include

• Regulatory Bodies: Agencies like the FDA (USA), EMA (Europe), and MHRA (UK) oversee these markets.

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• Stringent Standards: Compliance with Good Manufacturing Practices (GMP), Good Laboratory Practices (GLP), and Good Clinical Practices (GCP).
• High Costs and Time: Drug approval involves extensive clinical trials and documentation.
• Examples: USA, European Union, Canada, Japan, and Australia.

7.1.2 Countries and regulatory Authorities Considered in this review

Country	Regulatory authority	Website
Australia (17)	Therapeutic Goods Administration (TGA)	http://www.tga.gov.au/
Brazil (18)	National Health Surveillance Agency (ANVISA)	http://www.anvisa.gov.br/
Canada (19)	Health Canada	http://www.hc-sc.gc.ca/
China (20)	National Institute for the Control of Pharmaceutical and Biological Products	http://www.nicpbp.org.cn/cmsweb/
Europe (5)	European Medicines Agency (EMA)	http://www.ema.europa.eu/
India (21)	Central Drugs Standard Control Organization (CDSCO)	http://cdsco.nic.in/
Japan, (6,22–24)	Pharmaceuticals and Medical Devices Agency (PMDA)	http://www.pmda.go.jp/
Mexico (25)	Ministry of Health	http://www.salud.gob.mx/
Russia (5)	Ministry of Health	http://government.ru/
Thailand (26)	Ministry of Public Health	http://eng.moph.go.th/
Turkey (27)	Ministry of Health	http://www.saglik.gov.tr/
South Africa (28)	Medicines Control Council (MCC)	http://www.mccza.com/
South Korea (29)	Ministry of Food and Drug Safety (MFDS)	http://www.mfds.go.kr/
United States (4,14)	US Food and Drug Administration (FDA)	http://www.fda.gov/

Fig.Countries and regulatory Authorities Considered in this review

7.2 NON-REGULATED MARKET

A non-regulated market operates with relatively less stringent regulatory requirements. Oversight may be limited, and standards vary widely between countries.

A non-regulated market in the pharmaceutical industry refers to regions or markets where pharmaceutical production, distribution, and sales are subject to minimal or no oversight by governmental or regulatory agencies. Unlike regulated markets, which are governed by stringent standards for drug approval, manufacturing practices, and marketing (e.g., the U.S. FDA, EMA in Europe, or PMDA in Japan), non-regulated markets often lack uniform enforcement of such standards.

7.2.1 Key Characteristics Include

• **Minimal Regulations:** Lower requirements for clinical trials, quality control, and documentation.
• **Cost-Effective:** Easier and faster market entry due to less regulatory burden.
• **Market Diversity:** Standards differ significantly across regions.
• **Examples:** Many African, Asian, and Latin American countries fall under this category.

7.2.2 Here's a Table Comparing Regulated and non-regulated markets in the pharmaceutical industry:

S.NO	DIMENSIONS	REGULATED MARKETS	EMERGING MARKETS
1	Level of economic development	High	Medium/low
2	State of economy (and society)	Developed/stable	Transitional/ unstable (economic/ political reforms)
2.1	Macroeconomic frame work	Developed/stable	Undeveloped / being created
2.2	Market institutions	Developed	Undeveloped (being built)
2.3	Market conditions	Stable	unstable

Fig. **Regulated Vs Non Regulated Market Comparison**

7.2.3 RISKS AND CHALLENGES OF NON REGULATED MARKET

1. Patient Safety: Lack of regulation can lead to adverse health outcomes due to unsafe or ineffective drugs.
2. Market Dynamics: The proliferation of low-cost, low-quality drugs can undermine the value of genuine pharmaceutical innovation.

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3. Reputational Risks: Pharmaceutical companies operating in these markets may face ethical scrutiny if they are perceived as exploiting weaker regulations.

7.2.4 Generic Drugs Approved in the USA in the year 2017

Approval process for generic drugs in the United States is overseen by the U.S. Food and Drug Administration (FDA). This process ensures that generic drugs meet rigorous standards for safety, efficacy, and quality, while offering a cost-effective alternative to brand-name drugs.

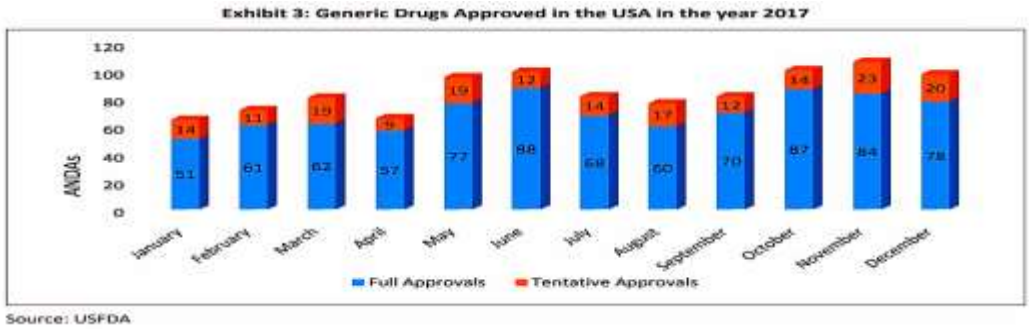


Fig.Generic Drugs Approved in the USA in the year 2017

• ROLE OF PHARMACEUTICAL COMPANIES

Pharmaceutical companies operating in or exporting to non-regulated markets must balance profitability with corporate social responsibility, ensuring they do not contribute to public health crises by prioritizing profits over safety and quality

8. CONCLUSION

In the pharmaceutical industry, robust documentation practices are essential for ensuring product quality, regulatory compliance, and operational efficiency. Proper retention and retrieval systems safeguard historical records, enabling quick access during audits, inspections, and reviews. Documents such as Standard Operating Procedures (SOPs), Manufacturing Formula Records (MFRs), and Batch Manufacturing Records (BMRs) ensure consistency, traceability, and adherence to Good Manufacturing Practices (GMP). Comprehensive audit documentation and reports demonstrate transparency and support continuous improvement. Regulatory submissions are streamlined through standardized formats like the Common Technical Document (CTD) and Electronic Common Technical Document (eCTD), while Drug Master Files (DMFs) provide detailed information for regulatory approval. Together, these practices uphold patient safety, facilitate regulatory approvals, and build trust among stakeholders, forming the foundation of a compliant and efficient pharmaceutical system.

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