AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

21- CFR: An Important Concept Of Pharma Industry

Gaurav Kale*, A. M. Bhagwat, Manish Pujari, Resham Ingawale
YSPM'S YTC Faculty of Pharmacy, Satara

ABSTRACT

21 CFR is the code of federal Regulation. It is the regulation which gives by the USA/America for the pharma Industries. It is started in 1935 by the America's 32nd President (Franklil. D. Roosevlt). It is very useful for pharma Industries in future for the Manufacturing processing packaging or holding of drug and finish pharmaceutical's. It is the regulation for the food and drugs. This paper explores Title 21 of the Code of Federal Regulations (21 CFR), highlighting its essential role in regulating various aspects of the pharmaceutical industry in the United States. It emphasizes 21 CFR's impact on ensuring the safety, efficacy, and quality of pharmaceuticals and biologics. The paper also examines its relevance in modern regulatory practices and its global influence on regulatory compliance and good manufacturing practices (GMP).It will most useful guidelines for new Pharmacists. It is the future of the pharma Industries. Which is trying to get approval from USFDA?

Keyword: 21 CFR, Manufacturing, Processing, Packaging, USFDA

*Corresponding Author Email: mukeshshukla6122@gmail.com
Received 22 November 2024, Accepted 07 December 2024

Please cite this article as: Kale G *et al*., 21- CFR: An Important Concept Of Pharma Industry. American Journal of PharmTech Research 2024.

INTRODUCTION

Title 21 of the Code of Federal Regulations (21 CFR) serves as a critical regulatory framework for the pharmaceutical industry in the United States. Enforced by the U.S. Food and Drug Administration (FDA), 21 CFR encompasses a comprehensive set of rules governing the development, manufacturing, distribution, and approval of drugs, biologics, and medical devices. It includes standards for Good Manufacturing Practices (GMP), quality control, investigational new drugs (INDs), and new drug applications (NDAs), among others .CFR give the 50 titles in the federal register. [1, 2]

Title 1: General Provision
Title 2: Grants and Agreements
Title3: The President
Title 4: Accounts
Title 5: Administrative Personnel
Title 6: Domestic Security
Title 7: Agriculture
Title 8: Aliens and Nationality
Title 9: Animals and Animal Products
Title10: Energy
Title 11: Federal Elections
Title 12: Banks and Banking
Title 13: Business Credit and Assistance
Title 14: Aeronautics and Space
Title 15: Commerce and Foreign Trade
Title 16: Commercial Practices
Title 17: Commodity and Securities Exchanges
Title 18: Conservation of Power and Water Resources
Title 19: Customs Duties
Title 20: Employees' Benefits

Title 21: Food and Drugs

21 is come from the Title 21: Food and Drugs. Which title include the all guidelines of the manufacturing, packaging or holding of drug and finish Pharmaceutical's. The 21 CFR are divided in the two parts:

Part 210: GMP for manufacturing, processing, packing, or holding of drugs.

Part 211: GMP for finished pharmaceuticals

21 CFR-Parts 210 And 211

PART-210.1: Status of current good manufacturing practices.

PART-210.2: Applicability of current Good manufacturing practices

PART-210.3: Definitions.

PART-211: Sub part: A- General Provisions

PART -211; Subpart: B -Organization and pergsennol

PART-211: Subpart: C -Buildings and facilities,

PART-211: Subpart: D -Equipment.

PART-211: Subpart: E - Control of equipment and drug product containers and closures,

PART -211: Subpart: F - Production and Process Controls.

PART-211: Subpart: G -Packing and Labelling Control

PART -211: Subpart: H -Holding and Distribution

PART -211: Subpart: I -Laboratory Control

PART -211: Subpart: J - Records and Controls

PART-211: Subpart: K-Returned and salvaged Drug products

This regulatory structure ensures the safety, efficacy and quality of pharmaceutical products, thereby protecting public health and maintaining trust in the pharmaceutical industry. Compliance with 21 CFR is mandatory for companies seeking FDA approval to market drugs or devices in the U.S., and adherence to these regulations minimizes the risk of contamination, data integrity issues, and product recalls. Moreover, 21 CFR has significant global influence, serving as a model for regulatory standards worldwide and foundation promoting consistency in drug safety and quality. In this way, 21 CFR is more than a set of regulations it is a for ethical and safe pharmaceutical practices that impact every aspect of drug development and patient care. [1, 2]

History of the 21 CFR:

Code of federal Regulation (CFR) it is gives by the USA/America. It is started in 1935ByAmericas32ndpresident Franklin D. Roosevelt. 1935- Instrumental in passing the federal Register Act empowered the National Achiever of the US to form an Administrative Committee publishes the federal as Register. The federal Register Act- Amended in1937 to provide "codification" of all Regulation every five years known of code of federal Regulation The first edition in 1938 and included all finalized Regulations that were published in the federal Register From march 14, 1936 to June 1, 1938.Beginning in 1963 for some titles and for all titles in 1967, the office of the federal Register began publishing yearly revision. Beginning in 1972- published revision was conducted in staggered quarters.[1,2]

Parts of the 21CFR:

21 CFR Parts 210: Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs.

21 CFR Parts 211: Current Good Manufacturing Practice for Finished Pharmaceuticals.

PART 210- CURRENT GOOD MANUFACTURING PRACTICES IN MANUFACTURING, PROCESSING, PACKING, OR HOLDING OF DRUGS

210.1: General Status of current Good manufacturing practice Regulation:

(a) The regulations set forth in this part and in parts 211, 225, and 226 of this chapter contain the minimum current good manufacturing practice for methods to be used in, and the facilities or

controls to be used for, the manufacture, processing, packing, or holding of a drug to assure that such drug meets the requirements of the act as to safety, and has the identity and strength and meets the quality and purity characteristics that it purports or is represented to possess. Enhanced Content - Paragraph Tools.

(b) The failure to comply with any regulation set forth in this part and in parts 211, 225, and 226 of this chapter in the manufacture, processing, packing, or holding of a drug shall render such drug to be adulterated under section 501(a)(2)(B) of the act and such drug, as well as the person who is responsible for the failure to comply, shall be subject to regulatory action.[9]

210.2: Application of current good manufacturing practice regulation:

(a) The regulations in this part and in parts 211, 225, and 226 of this chapter as they may pertain to a drug; in parts 600 through 680 of this chapter as they may pertain to a biological product for human use; and in part 1271 of this chapter as they are applicable to a human cell, tissue, or cellular or tissue-based product (HCT/P) that is a drug (subject to review under an application submitted under section 505 of the act or under a biological product license application under section 351 of the Public Health Service Act); shall be considered to supplement, not supersede, each other, unless the regulations explicitly provide otherwise. In the event of a conflict between applicable regulations in this part and in other parts of this chapter, the regulation specifically applicable to the drug product in question shall supersede the more general.

(b) If a person engages in only some operations subject to the regulations in this part, in parts 211, 225, and 226 of this chapter, in parts 600 through 680 of this chapter, and in part 1271 of this chapter, and not in others, that person need only comply with those regulations applicable to the operations in which he or she is engaged.

(c) An investigational drug for use in a phase 1 study, as described in § 312.21(a) of this chapter, is subject to the statutory requirements set forth in 21 U.S.C. 351(a) (2) (B). The production of such drug is exempt from compliance with the regulations in part 211 of this chapter. [9]

210.3:

Definitions:

(a) The definitions and interpretations contained in section 201 of the act shall be applicable to such terms when used in this part and in parts 211, 225, and 226 of this chapter.

(b) The following definitions of terms apply to this part and to parts 211, 225, and 226 of this chapter.

(1) Act means the Federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 301 et seq.).

(2) Batch means a specific quantity of a drug or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.

(3) Component means any ingredient intended for use in the manufacture of a drug product, including those that may not appear in such drug product. Drug product means a finished dosage form, for example, tablet, capsule, solution, etc., that contains an active drug ingredient generally, but not necessarily, in association with inactive ingredients. The term also includes a finished dosage form that does not contain an active ingredient but is intended to be used as a placebo.

(4) Fiber means any particulate contaminant with a length at least three times greater than its width.

(5) Nonfiber releasing filter means any filter, which after appropriate pretreatment such as washing or flushing, will not release fibers into the component or drug product that is being filtered.

(6) Active ingredient means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.

(7) Inactive ingredient means any component other than an active ingredient.

(8) In-process material means any material fabricated, compounded, blended, or derived by chemical reaction that is produced for, and used in, the preparation of the drug product.

(9) Lot means a batch, or a specific identified portion of a batch, having uniform character and quality within specified limits; or, in the case of a drug product produced by continuous process, it is a specific identified amount produced in a unit of time or quantity in a manner that assures its having uniform character and quality within specified limits.

(10) Lot number, control number, or batch number means any distinctive combination of letters, numbers, or symbols, or any combination of them, from which the complete history of the manufacture, processing, packing, holding, and distribution of a batch or lot of drug product or other material can be determined. [9]

PART 211—CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS

Part 211 Current Good Manufacturing Practice for Finished Pharmaceuticals

Subpart A—General Provisions:

211.1: Scope:

(a) The regulations in this part contain the minimum current good manufacturing practice for preparation of drug products (excluding positron emission tomography drugs) for administration to humans or animals.

(b) The current good manufacturing practice regulations in this chapter as they pertain to drug products; in parts 600 through 680 of this chapter, as they pertain to drugs that are also biological products for human use; and in part 1271 of this chapter, as they are applicable to drugs that are also human cells, tissues, and cellular and tissue-based products (HCT/Ps) and that are drugs (subject to review under an application submitted under section 505 of the act or under a biological product license application under section 351 of the Public Health Service Act); supplement and do not supersede the regulations in this part unless the regulations explicitly provide otherwise. In the event of a conflict between applicable regulations in this part and in other parts of this chapter, or in parts 600 through 680 of this chapter, or in part 1271 of this chapter, the regulation specifically applicable to the drug product in question shall supersede the more general.[10,3]

211.3: **Definitions:**

The in 210.3 of this chapter apply in this part.

Subpart B—Organization and Personnel

211.22: Responsibilities of quality control unit:

(a) There shall be a quality control unit that shall have the responsibility and authority to approve or reject all components, drug product containers, closures, in- process materials, packaging material, labelling, and drug products, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated. The quality control unit shall be responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another company.

(b) Adequate laboratory facilities for the testing and approval (or rejection) of components, drug product containers, closures, packaging materials, in-process materials, and drug products shall be available to the quality control unit.

(c) The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product.

(d) The responsibilities and procedures applicable to the quality control unit shall be in writing; such written procedures shall be followed. [10, 4]

211.25: **Personnel qualifications:**

(a) Each person engaged in the manufacture, processing, packing, or holding of a drug product shall have education, training, and experience, or any combination thereof, to enable that person to

perform the assigned functions. Training shall be in the particular operations that the employee performs and in current good manufacturing practice (including the current good manufacturing practice regulations in this chapter and written procedures required by these regulations) as they relate to the employee's functions. Training in current good manufacturing practice shall be conducted by qualified individuals on a continuing basis and with sufficient frequency to assure that employees remain familiar with CGMP requirements applicable to them.

(b) Each person responsible for supervising the manufacture, processing, packing, or holding of a drug product shall have the education, training, and experience, or any combination thereof, to perform assigned functions in such a manner as to provide assurance that the drug product has the safety, identity, strength, quality, and purity that it purports or is represented to possess.

(c) There shall be an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of each drug product.[10,4]

211.28: Personnel responsibilities:

(a) Personnel engaged in the manufacture, processing, packing, or holding of a drug product shall wear clean clothing appropriate for the duties they perform. Protective apparel, such as head, face, hand, and arm coverings, shall be worn as necessary to protect drug products from contamination.

(b) Personnel shall practice good sanitation and health habits.

(c) Only personnel authorized by supervisory personnel shall enter those areas of the buildings and facilities designated as limited-access areas.

(d) Any person shown at any time (either by medical examination or supervisory observation) to have an apparent illness or open lesions that may adversely affect the safety or quality of drug products shall be excluded from direct contact with components, drug product containers, closures, in-process materials, and drug products until the condition is corrected or determined by competent medical personnel not to jeopardize the safety or quality of drug products. All personnel shall be instructed to report to supervisory personnel any health conditions that may have an adverse effect on drug products. [10, 4]

211.34: Consultants:

Consultants advising on the manufacture, processing, packing, or holding of drug products shall have sufficient education, training, and experience, or any combination thereof, to advise on the subject for which they are retained. Records shall be maintained stating the name, address, and qualifications of any consultants and the type of service they provide. [10,4]

Subpart C—Buildings and Facilities

211.42: Design and construction features:

(a) Any building or buildings used in the manufacture, processing, packing, or holding of a drug product shall be of suitable size, construction and location to facilitate cleaning, maintenance, and proper operations.

(b) Any such building shall have adequate space for the orderly placement of equipment and materials to prevent mix up between different components, drug product containers, closures, labelling, in-process materials, or drug products, and to prevent contamination. The flow of components, drug product containers, closures, labelling, in process materials, and drug products through the building or buildings shall be designed to prevent contamination.[9,3]

(c) Operations shall be performed within specifically defined areas of adequate size

(d) Operations relating to the manufacture, processing, and packing of penicillin shall be performed in facilities separate from those used for other drug products for human user[10,4]

211.44: **Lighting:**

Adequate lighting shall be provided in all areas.

211.46: Ventilation, air filtration, air heating and cooling:

(a) Adequate ventilation shall be provided.

(b) Equipment for adequate control over air pressure, micro-organisms, dust, humidity, and temperature shall be provided when appropriate for the manufacture, processing, packing, or holding of a drug product.

(c) Air filtration systems, including prefilters and particulate matter air filters, shall be used when appropriate on air supplies to production areas. If air is recirculated to production areas, measures shall be taken to control recirculation of dust from production. In areas where air contamination occurs during production, there shall be adequate exhaust systems or other systems adequate to control contaminants. [10,4]

(d) Air-handling systems for the manufacture, processing, and packing of penicillin shall be completely separate from those for other drug products for human use. [10,4]

211.48: **Plumbing:**

(a) Potable water shall be supplied under continuous positive pressure in a plumbing system free of defects that could contribute contamination to any drug product. Potable water shall meet the standards prescribed in the Environmental Protection Agency's Primary Drinking Water Regulations set forth in 40 CFR part 141. Water not meeting such standards shall not be permitted in the potable water system.

(b) Drains shall be of adequate size and, where connected directly to a sewer, shall be provided with an air break or other mechanical device to prevent back-siphonage.[10,4]

211.50: **Sewage and refuse:**

Sewage, trash, and other refuse in and from the building and immediate premises shall be disposed of in a safe and sanitary manner. [10, 4]

211.52: **Washing and toilet facilities:**

Adequate washing facilities shall be provided, including hot and cold water, soap or detergent, air driers or single service towels, and clean toilet facilities easily accessible to working areas. [10, 4]

211.56: **Sanitation:**

(a) Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a clean and sanitary condition, Any such building shall be free of infestation by rodents, birds, insects, and other vermin (other than laboratory animals). Trash and organic waste matter shall be held and disposed of in a timely and sanitary manner G. [10, 4]

(b) There shall be written procedures assigning responsibility for sanitation and describing in sufficient detail the cleaning schedules, methods, equipment, and materials to be used in cleaning the buildings and facilities; such written procedures shall be followed.

(c) There shall be written procedures for use of suitable rodenticides, insecticides, fungicides, fumigating agents, and cleaning and sanitizing agents. Such written procedures shall be designed to prevent the contamination of equipment, components, drug product containers, closures, packaging, labeling materials, or drug products and shall be followed. Rodenticides, insecticides, and fungicides shall not be used unless registered and used in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act [9, 3]

(d) Sanitation procedures shall apply to work performed by contractors or temporary employees as well as work performed by full-time employees during the ordinary course of operation G.[10,4]

211.58: **Maintenance:**

Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a good state of repair.[10,4]

Subpart D—Equipment

211.63: Equipment design, size, and location:

Equipment used in the manufacture, processing, packing, or holding of a drug product shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.[10,5]

211.65: Equipment construction:

(a) Equipment shall be constructed so that surfaces that contact components, in-process materials, or drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity,

strength, quality, or purity of the drug product beyond the official or other established requirements.

(b) Any substances required for operation, such as lubricants or coolants, shall not come into contact with components, drug product containers, closures, in-process materials, or drug products so as to alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.[10,5]

211.67: **Equipment cleaning and maintenance:**

(a) Equipment and utensils shall be cleaned, maintained, and, as appropriate for the nature of the drug, sanitized and/or sterilized at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.

(b) Written procedures shall be established and followed for cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing, or holding of a drug product automatic, mechanical, and electronic equipment.

(a) Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily, may be used in the manufacture, processing, packing, and holding of a drug product. If such equipment is so used, it shall be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance. Written records of those calibration checks and inspections shall be maintained.

(b) Appropriate controls shall be exercised over computer or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel. Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system. A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data. Hard copy or alternative systems, such as duplicates, tapes, or microfilm, designed to assure that backup data are exact and complete and that it is secure from alteration, inadvertent erasures, or loss shall be maintained.[10,5]

211.72: **Filters:**

Filters for liquid filtration used in the manufacture, processing, or packing of injectable drug products intended for human use shall not release fibers into such products. Fiber-releasing filters may be used when it is not possible to manufacture such products without the use of these filters. If use of a fibre-releasing filter is necessary, an additional Nonfiber -releasing filter having a maximum nominal pore size rating of 0.2 micron (0.45 micron if the manufacturing conditions so dictate) shall subsequently be used to reduce the content of particles in the injectable drug product. The use of an asbestos-containing filter is prohibited.[10,5]

Subpart E—Control of Components and Drug Product Containers and Closures

211.80: General requirements:

(a) There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures; such written procedures shall be followed.

(b) Components and drug product containers and closures shall at all times be handled and stored in a manner to prevent contamination.

(c) Bagged or boxed components of drug product containers, or closures shall be stored off the floor and suitably spaced to permit cleaning and inspection.

(d) Each container or grouping of containers for components or drug product containers, or closures shall be identified with a distinctive code for each lot in each shipment received. This code shall be used in recording the disposition of each lot. Each lot shall be appropriately identified as to its status (i.e., quarantined, approved, or rejected).[10]

211.82: Receipt and storage of untested components, drug product containers, and closures:

(a) Upon receipt and before acceptance, each container or grouping of containers of components, drug product containers, and closures shall be examined visually for appropriate labeling as to contents, container damage or broken seals, and contamination.

(b) Components, drug product containers, and closures shall be stored under quarantine until they have been tested or examined, whichever is appropriate, and released. Storage within the area shall conform to the requirements of 211.80 [10]

211.84: Testing and approval or rejection of components, drug product containers, and closures:

(a) Each lot of components, drug product containers, and closures shall be withheld from use until the lot has been sampled, tested, or examined, as appropriate, and released for use by the quality control unit.

(b) Representative samples of each shipment of each lot shall be collected for testing or examination. The number of containers to be sampled, and the amount of material to be taken from

each container, shall be based upon appropriate criteria such as statistical criteria for component variability, confidence levels, and degree of precision desired, the past quality history of the supplier, and the quantity needed for analysis and reserve where required by 211.170.

(c) Samples shall be collected.

(d) Samples shall be examined and tested.

(e) Any lot of components, drug product containers, or closures that meets the appropriate written specifications of identity, strength, quality, and purity and related tests under paragraph (d) of this section may be approved and released for use. Any lot of such material that does not meet such specifications shall be rejected.[10]

211.89: Rejected components, drug product containers, and closures:

Rejected components, drug product containers, and closures shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable.[10]

211.94: Drug product containers and closures:

(a) Drug product containers and closures s89 FR 5176hall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug beyond the official or established requirements.

(b) Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.

(c) Drug product containers and closures shall be clean and, where indicated by the nature of the drug, sterilized and processed to remove pyrogenic properties to assure that they are suitable for their intended use. Such depyrogenation processes shall be validated.

(d) Standards or specifications, methods of testing, and, where indicated, methods of cleaning, sterilizing, and processing to remove pyrogenic properties shall be written and followed for drug product containers and closures.[10]

Subpart F—Production and Process Controls

211.100: Written procedures deviations:

(a) There shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess. Such procedures shall include all requirements in this subpart. These written procedures, including any changes, shall be drafted, reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality control unit.

(b) Written production and process control procedures shall be followed in the execution of the various production and process control functions and shall be documented at the time of performance. Any deviation from the written procedures shall be recorded and justified. [10]

211.101: Charge-in of components:

Written production and control procedures shall include the following, which are designed to assure that the drug products produced have the identity, strength, quality, and purity they purport or are represented to possess:

(a) The batch shall be formulated with the intent to provide not less than 100 percent of the labelled or established amount of active ingredient.

(b) Components for drug product manufacturing shall be weighed, measured, or subdivided as appropriate. If a component is removed from the original container to another, the new container shall be identified

(c) Weighing, measuring, or subdividing operations for components shall be adequately supervised. Each container of component dispensed to manufacturing shall be examined by a second person to assure.

(d) Each component shall either be added to the batch by one person or verified by a second person or, if the components are added by automated equipment under 211.68, only verified by one person.[10]

211.103: Calculation of yield:

Actual yields and percentages of theoretical yield shall be determined at the conclusion of each appropriate phase of manufacturing, processing, packaging, or holding of the drug product. Such calculations shall either be performed by one person or independently verified by a second person, or, if the yield is calculated by automated equipment under be independently verified by one person.[10]

211.105: Equipment identification:

(a) All compounding and storage containers, processing lines, and major equipment used during the production of a batch of a drug product shall be properly identified at all times to indicate their contents and, when necessary, the phase of processing of the batch.

(b) Major equipment shall be identified by a distinctive identification number or code that shall be recorded in the batch production record to show the specific equipment used in the manufacture of each batch of a drug product. In cases where only one of a particular type of equipment exists in a manufacturing facility, the name of the equipment may be used in lieu of a distinctive identification number or code. [10]

211.110: Sampling and testing of in-process materials and drug products:

(a) To assure batch uniformity and integrity of drug products, written procedures shall be established and followed that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in process materials of each batch. Such control procedures shall be established to monitor the output and to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product. Such control procedures shall include, but are not limited.

(b) Valid in-process specifications for such characteristics shall be consistent with drug product final specifications and shall be derived from previous acceptable process average and process variability estimates where possible and determined by the application of suitable statistical procedures where appropriate. Examination and testing of samples shall assure that the drug product and in-process material confirm to specifications.[10]

211.111: Time limitations on production:

When appropriate, time limits for the completion of each phase of production shall be established to assure the quality of the drug product. Deviation from established time limits may be acceptable if such deviation does not compromise the quality of the drug product. Such deviation shall be justified and documented. [10]

211.113: Control of microbiological contamination:

(a) Appropriate written procedures, designed to prevent objectionable microorganisms in drug products not required to be sterile, shall be established and followed.

(b) Appropriate written procedures, designed to prevent microbiological contamination of drug products purporting to be sterile, shall be established and followed. Such procedures shall include validation of all aseptic and sterilization processes. [10]

211.115: Reprocessing:

(a) Written procedures shall be established and followed prescribing a system for reprocessing batches that do not conform to standards or specifications and the steps to be taken to insure that the reprocessed batches will conform with all established standards, specifications, and characteristics.

(b) Reprocessing shall not be performed without the review and approval of the quality control unit.[10]

Subpart G—Packaging and Labelling Control

211.122: Materials examination and usage criteria:

(a) There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labelling and packaging materials; such written procedures shall be followed. Labelling and packaging materials shall be representatively sampled, and examined or tested upon receipt and before use in packaging or labelling of a drug product.

(b) Any labelling or packaging materials meeting appropriate written specifications may be approved and released for use. Any labelling or packaging materials that do not meet such specifications shall be rejected to prevent their use in operations for which they are unsuitable.

(c) Records shall be maintained for each shipment received of each different labelling and packaging material indicating receipt, examination or testing, and whether accepted or rejected.

(d) Labels and other labelling materials for each different drug product, strength, dosage form, or quantity of contents shall be stored separately with suitable identification. Access to the storage area shall be limited to authorized personnel.

(e) Obsolete and out dated labels, labelling, and other packaging materials shall be destroyed.

(f) Use of gang-printed labelling for different drug products, or different strengths or net contents of the same drug product, is prohibited unless the labelling from gang-printed sheets is adequately differentiated by size, shape, or colour.

(g) If cut labelling is used for immediate container labels, individual unit cartons, or multiunit cartons containing immediate containers that are not packaged in individual unit cartons, packaging and labelling operations. [10]

211.125: Labelling issuance:

(a) Strict control shall be exercised over labelling issued for use in drug product labelling operations.

(b) Labelling materials issued for a batch shall be carefully examined for identity and conformity to the labelling specified in the master or batch production records.

(c) Procedures shall be used to reconcile the quantities of labelling issued, used, and returned, and shall require evaluation of discrepancies found between the quantity of drug product finished and the quantity of labelling issued when such discrepancies are outside narrow present limits based on historical operating data. Such discrepancies shall be investigated in accordance with 211.192. Labelling reconciliation is waived for cut or roll labelling if a 100-percent examination for correct labelling is performed in accordance with 211.122(g)(2). Labelling reconciliation is also waived for 360° wraparound labels on portable cryogenic medical gas containers.[10]

(d) All excess labelling bearing lot or control numbers shall be destroyed.

(e) Returned labelling shall be maintained and stored in a manner to prevent mix-ups and provide proper identification.

(f) Procedures shall be written describing in sufficient detail the control procedures employed for the issuance of labelling. [10]

211.132: Tamper-evident packaging requirements for over-the-counter (OTC) human drug products:

(a) General. The Food and Drug Administration has the authority under the Federal Food, Drug, and Cosmetic Act (the act) to establish a uniform national requirement for tamper-evident packaging of OTC drug products that will improve the security of OTC drug packaging and help assure the safety and effectiveness of OTC drug products. An OTC drug product (except a dermatological, dentifrice, insulin, or lozenge product) for retail sale that is not packaged in a tamper-resistant package or that is not properly labeled under this section is adulterated under section 501 of the act or misbranded under section 502 of the act, or both.[10]

(b) Requirements for tamper-evident package.

(c) Labelling.

(1) In order to alert consumers to the specific tamper- evident feature(s) used, each retail package of an OTC drug product covered by this section (except ammonia inhalant in crushable glass ampules, containers of compressed medical oxygen, or aerosol products that depend upon the power of a liquefied or compressed gas to expel the contents from the container.

(2) If the tamper-evident feature chosen to meet the requirements in paragraph (b) of this section uses an identifying characteristic, that characteristic is required to be referred to in the labelling statement. For example, the labelling statement on a bottle with a shrink band could say “For your protection, this bottle has an imprinted seal around the neck.”

(d) Request for exemptions from packaging and labelling requirements. A manufacturer or packer may request an exemption from the packaging and labelling requirements of this section. A request for an exemption is required to be submitted in the form of a citizen petition under 10.30 of this chapter and should be clearly identified on the envelope as a “Request for Exemption from the Tamper-Evident Packaging Rule.”

(e) OTC drug products subject to approved new drug applications. Holders of approved new drug applications for OTC drug products are required under 314.70 of this chapter to provide the agency with notification of changes in packaging and labelling to comply with the requirements of this section. Changes in packaging and labelling required by this regulation may be made before FDA

approval, as provided under 314.70(c) of this chapter. Manufacturing changes by which capsules are to be sealed require prior FDA approval under 314.70(b) of this chapter.

(f) Poison Prevention Packaging Act of 1970. This section does not affect any requirements for "special packaging" as defined under 310.3(l) of this chapter and required under the Poison Prevention Packaging Act of 1970. [10]

211.134 Drug product inspection:

(a) Packaged and labeled products shall be examined during finishing operations to provide assurance that containers and packages in the lot have the correct label.

(b) A representative sample of units shall be collected at the completion of finishing operations and shall be visually examined for correct labelling.

(c) Results of these examinations shall be recorded in the batch production or control records.

211.137: Expiration dating:

(a) To assure that a drug product meets applicable standards of identity, strength, quality, and purity at the time of use, it shall bear an expiration date determined by appropriate stability testing described in 211.166.

(b) Expiration dates shall be related to any storage conditions stated on the labelling, as determined by stability studies described in 211.166.

(c) If the drug product is to be reconstituted at the time of dispensing, its labelling shall bear expiration information for both the reconstituted and under constituted drug products.

(d) Expiration dates shall appear on labelling in accordance with the requirements of 201.17 of this chapter. [10]

Subpart H—Holding and Distribution

211.142: Warehousing procedures:

Written procedures describing the warehousing of drug products shall be established and followed. They shall include:

(a) Quarantine of drug products before release by the quality control unit.

(b) Storage of drug products under appropriate conditions of temperature, humidity, and light so that the identity, strength, quality, and purity of the drug products are not affected. 211.150 Distribution procedures.

Written procedures shall be established, and followed, describing the distribution of drug products. They shall include:

(a) A procedure whereby the oldest approved stock of a drug product is distributed first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.

(b) A system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary. [10]

Subpart I—Laboratory Controls

211.160: General requirements:

(a) The establishment of any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this subpart, including any change in such specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms, shall be drafted by the appropriate organizational unit and reviewed and approved by the quality control unit. The requirements in this subpart shall be followed and shall be documented at the time of performance. Any deviation from the written specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms shall be recorded and justified.[10]

(b) Laboratory controls shall include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labelling, and drug products conform to appropriate standards of identity, strength, quality, and purity.[10]

211.165: Testing and release for distribution:

(a) For each batch of drug product, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release. Where sterility and/or pyrogen testing are conducted on specific batches of short lived radiopharmaceuticals, such batches may be released prior to completion of sterility and/or pyrogen testing, provided such testing is completed as soon as possible.

(b) There shall be appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable microorganisms.

(c) Any sampling and testing plans shall be described in written procedures that shall include the method of sampling and the number of units per batch to be tested; such written procedure shall be followed.

(d) Acceptance criteria for the sampling and testing conducted by the quality control unit shall be adequate to assure that batches of drug products meet each appropriate specification and appropriate statistical quality control criteria as a condition for their approval and release. The statistical quality control criteria shall include appropriate acceptance levels and/or appropriate rejection levels.[10]

211.166: Stability testing:

(a) There shall be a written testing program designed to assess the stability characteristics of drug products. The results of such stability testing shall be used in determining appropriate storage conditions and expiration dates.

(b) An adequate number of batches of each drug product shall be tested to determine an appropriate expiration date and a record of such data shall be maintained. Accelerated studies, combined with basic stability information on the components, drug products, and container-closure system, may be used to support tentative expiration dates provided full shelf life studies are not available and are being conducted. Where data from accelerated studies are used to project a tentative expiration date that is beyond a date supported by actual shelf life studies, there must be stability studies conducted, including drug product testing at appropriate intervals, until the tentative expiration date is verified or the appropriate expiration date determined.

(c) For homeopathic drug products, the requirements of this section are as follows:

(1) There shall be a written assessment of stability based at least on testing or examination of the drug product for compatibility of the ingredients, and based on marketing experience with the drug product to indicate that there is no degradation of the product for the normal or expected period of use.

(2) Evaluation of stability shall be based on the same container-closure system in which the drug product is being marketed.

(d) Allergenic extracts that are labeled "No U.S. Standard of Potency" are exempt from the requirements of this section. [10]

211.167: Special testing requirements:

(a) For each batch of drug product purporting to be sterile and/or pyrogen-free, there shall be appropriate laboratory testing to determine conformance to such requirements. The test procedures shall be in writing and shall be followed.

(b) For each batch of ophthalmic ointment, there shall be appropriate testing to determine conformance to specifications regarding the presence of foreign particles and harsh or abrasive substances. The test procedures shall be in writing and shall be followed.

(c) For each batch of controlled-release dosage form, there shall be appropriate laboratory testing to determine conformance to the specifications for the rate of release of each active ingredient.[10]

211.170: Reserve samples:

(a) An appropriately identified reserve sample that is representative of each lot in each shipment of each active ingredient shall be retained. The reserve sample consists of at least twice the quantity

necessary for all tests required to determine whether the active ingredient meets its established specifications, except for sterility and pyrogen testing. The retention time is as follows:

(1) For an active ingredient in a drug product other than those described in paragraphs of this section, the reserve sample shall be retained for 1 year after the expiration date of the last lot of the drug product containing the active ingredient.

(2) For an active ingredient in a radioactive drug product, except for nonradioactive reagent kits, the reserve sample shall be retained for:

(i) Three months after the expiration date of the last lot of the drug product containing the active ingredient if the expiration dating period of the drug product is 30 days or less; or

(ii) Six months after the expiration date of the last lot of the drug product containing the active ingredient if the expiration dating period of the drug product is more than 30 days.

(3) For an active ingredient in an OTC drug product that is exempt from bearing an expiration date under 211.137, the reserve sample shall be retained for 3 years after distribution of the last lot of the drug product containing the active ingredient.[10]

(b) An appropriately identified reserve sample that is representative of each lot or batch of drug product shall be retained and stored under conditions consistent with product labelling. The reserve sample shall be stored in the same immediate container- closure system in which the drug product is marketed or in one that has essentially the same characteristics. The reserve sample consists of at least twice the quantity necessary to perform all the required tests, except those for sterility and pyrogens. Except for those for drug products described in paragraph (b)(2) of this section, reserve samples from representative sample lots or batches selected by acceptable statistical procedures shall be examined visually at least once a year for evidence of deterioration unless visual examination would affect the integrity of the reserve sample. Any evidence of reserve sample deterioration shall be investigated in accordance with § 211.192. The results of the examination shall be recorded and maintained with other stability data on the drug product. Reserve samples of compressed medical gases need not be retained. The retention time is as follows:

(1) For a drug product other than those described in paragraphs (b) (2) and (3) of this section, the reserve sample shall be retained for 1 year after the expiration date of the drug product.

(2) For a radioactive drug product, except for nonradioactive reagent kits, the reserve sample shall be retained for:

(i) Three months after the expiration date of the drug product if the expiration dating period of the drug product is 30 days or less; or

(ii) Six months after the expiration date of the drug product if the expiration dating period of the drug product is more than 30 days.

(3) For an OTC drug product that is exempt for bearing an expiration date under 211.137, the reserve sample must be retained for 3 years after the lot or batch of drug product is distributed. 211.173[10]

211.173: Laboratory animals:

Animals used in testing components, in-process materials, or drug products for compliance with established specifications shall be maintained and controlled in a manner that assures their suitability for their intended use. They shall be identified, and adequate records shall be maintained showing the history of their use.[10]

Subpart J—Records and Reports

211.180: General requirements:

(a) Any production, control, or distribution record that is required to be maintained in compliance with this part and is specifically associated with a batch of a drug product shall be retained for at least 1 year after the expiration date of the batch or, in the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under § 211.137, 3 years after distribution of the batch.

(b) Records shall be maintained for all components, drug product containers, closures, and labelling for at least 1 year after the expiration date or, in the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under § 211.137, 3 years after distribution of the last lot of drug product incorporating the component or using the container, closure, or labelling.

(c) All records required under this part, or copies of such records, shall be readily available for authorized inspection during the retention period at the establishment where the activities described in such records occurred. These records or copies thereof shall be subject to photocopying or other means of reproduction as part of such inspection. Records that can be immediately retrieved from another location by computer or other electronic means shall be considered as meeting the requirements of this paragraph.

(d) Records required under this part may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records. Where reduction techniques, such as microfilming, are used, suitable reader and photocopying equipment shall be readily available. [10,7]

(e) Written records required by this part shall be maintained so that data therein can be used for evaluating, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing or control procedures. Written procedures shall be established and followed for such evaluations and shall include provisions for:

(1) A review of a representative number of batches, whether approved or rejected, and, where applicable, records associated with the batch.

(2) A review of complaints, recalls, returned or salvaged drug products, and investigations conducted under 211.192 for each drug product. [10,7]

211.182: Equipment cleaning and use log:

A written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed. If equipment is dedicated to manufacture of one product, then individual equipment logs are not required, provided that lots or batches of such product follow in numerical order and are manufactured in numerical sequence. In cases where dedicated equipment is employed, the records of cleaning, maintenance, and use shall be part of the batch record. The persons performing and double checking the cleaning and maintenance (or, if the cleaning and maintenance is performed using automated equipment under 211.68, just the person verifying the cleaning and maintenance done by the automated equipment) shall date and sign or initial the log indicating that the work was performed. Entries in the log shall be in chronological order.[10,7]

211.184: Component, drug product container, closure, and labelling record:

(a) The identity and quantity of each shipment of each lot of components, drug product containers, closures, and labelling; the name of the supplier; the supplier's lot number(s) if known; the receiving code as specified in 211.80; and the date of receipt. The name and location of the prime manufacturer, if different from the supplier, shall be listed if known.

(b) The results of any test or examination performed (including those performed as required by 211.82(a), 211.84(d), or 211.122(a)) and the conclusions derived therefrom.

(c) An individual inventory record of each component, drug product container, and closure and, for each component, a reconciliation of the use of each lot of such component. The inventory record shall contain sufficient information to allow determination of any batch or lot of drug product associated with the use of each component, drug product container, and closure.

(d) Documentation of the examination and review of labels and labelling for conformity with established specifications in accord with 211.122 (c) and 211.130 (c).[10,7]

211.186: Master production and control records:

(a) To assure uniformity from batch to batch, master production and control records for each drug product, including each batch size thereof, shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person. The preparation of master production and control records shall be described in a written procedure and such written procedure shall be followed.

(b) Master production and control records shall include:

(1) The name and strength of the product and a description of the dosage form

(2) The name and weight or measure of each active ingredient per dosage unit or per unit of weight or measure of the drug product and a statement of the total weight or measure of any dosage unit;

(3) A complete list of components designated by names or codes sufficiently specific to indicate any special quality characteristic

(4) An accurate statement of the weight or measure of each component, using the same weight system (metric, avoirdupois, or apothecary) for each component. Reasonable variations may be permitted, however, in the amount of components necessary for the preparation in the dosage form, provided they are justified in the master production and control records [10,7]

(5) A statement concerning any calculated excess of component [10,7]

211.194: Laboratory records:

(a) Laboratory records shall include complete data derived from all tests necessary to assure compliance with established specifications and standards, including examinations and assays.as follows:

(1) A description of the sample received for testing with identification of source (that is, location from where sample was obtained), quantity, lot number or other distinctive code, date sample was taken, and date sample was received for testing.

(2) A statement of each method used in the testing of the sample. The statement shall indicate the location of data that establish that the methods used in the testing of the sample meet proper standards of accuracy and reliability as applied to the product tested. (If the method employed is in the current revision of the United States Pharmacopeia, National Formulary, AOAC INTERNATIONAL, Book of Methods,[1] or in other recognized standard references, or is detailed in an approved new drug application and the referenced method is not modified, a statement indicating the method and reference will suffice). The suitability of all testing methods used shall be verified under actual conditions of use.

(3) A statement of the weight or measure of sample used for each test, where appropriate.

(4) A complete record of all data secured in the course of each test, including all graphs, charts, and spectra from laboratory instrumentation, properly identified to show the specific component, drug product container, closure, in process material, or drug product, and lot tested.

(5) A record of all calculations performed in connection with the test, including units of measure, conversion factors, and equivalency factors.

(6) A statement of the results of tests and how the results compare with established standards of identity, strength, quality, and purity for the component, drug product container, closure, in-process material, or drug product tested.

(7) The initials or signature of the person who performs each test and the date(s) the tests were performed.

(8) The initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.

(b) Complete records shall be maintained of any modification of an established method employed in testing. Such records shall include the reason for the modification and data to verify that the modification produced results that are at least as accurate and reliable for the material being tested as the established method.

(c) Complete records shall be maintained of any testing and standardization of laboratory reference standards, reagents, and standard solutions.

(d) Complete records shall be maintained of the periodic calibration of laboratory instruments, apparatus, gauges, and recording devices required by 211.160(b)(4).

(e) Complete records shall be maintained of all stability testing performed in accordance wit 211.166. 211.196:[10,7]

Distribution records:

Distribution records shall contain the name and strength of the product and description of the dosage form, name and address of the consignee, date and quantity shipped, and lot or control number of the drug product. For compressed medical gas products, distribution records are not required to contain lot or control numbers. [10, 7]

211.198: Complaint files:

(a) Written procedures describing the handling of all written and oral complaints regarding a drug product shall be established and followed. Such procedures shall include provisions for review by the quality control unit, of any complaint involving the possible failure of a drug product to meet any of its specifications and, for such drug products, a determination as to the need for an investigation in accordance with 211.192. Such procedures shall include provisions for review to

determine whether the complaint represents a serious and unexpected adverse drug experience which is required to be reported to the Food and Drug Administration in accordance with §§ 310.305 and 514.80 of this chapter.

(b) A written record of each complaint shall be maintained in a file designated for drug product complaints. The file regarding such drug product complaints shall be maintained at the establishment where the drug product involved was manufactured, processed, or packed, or such file may be maintained at another facility if the written records in such files are readily available for inspection at that other facility. Written records involving a drug product shall be maintained until at least 1 year after the expiration date of the drug product, or 1 year after the date that the complaint was received, whichever is longer. In the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under § 211.137, such written records shall be maintained for 3 years after distribution of the drug product.[10,7]

Subpart K—Returned and Salvaged Drug Products

211.204: Returned drug products:

Returned drug products shall be identified as such and held. If the conditions under which returned drug products have been held, stored, or shipped before or during their return, or if the condition of the drug product, its container, carton, or labeling, as a result of storage or shipping, casts doubt on the safety, identity, strength, quality or purity of the drug product, the returned drug product shall be destroyed unless examination, testing, or other investigations prove the drug product meets appropriate standards of safety, identity, strength, quality, or purity. A drug product may be reprocessed provided the subsequent drug product meets appropriate standards, specifications, and characteristics. Records of returned drug products shall be maintained and shall include the name and label potency of the drug product dosage form, lot number (or control number or batch number), reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned drug product. If the reason for a drug product being returned implicates associated batches, an appropriate investigation shall be conducted in accordance with the requirements of § 211.192. Procedures for the holding, testing, and reprocessing of returned drug products shall be in writing and shall be followed.[10,8]

211.208: Drug product salvaging:

Drug products that have been subjected to improper storage conditions including extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace. Whenever there is a question whether drug products have been subjected to such conditions, salvaging

operations may be conducted only if there is (a) evidence from laboratory tests and assays (including animal feeding studies where applicable) that the drug products meet all applicable standards of identity, strength, quality, and purity and (b) evidence from inspection of the premises that the drug products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident. Organoleptic examinations shall be acceptable only as supplemental evidence that the drug products meet appropriate standards of identity, strength, quality, and purity. Records including name, lot number, and disposition shall be maintained for drug products subject to this section [10, 8]

CONCLUSION:

The 21 CFR (Code of Federal Regulations) refers to Title 21 of the U.S. Code of Federal Regulations, which governs food and drug-related activities, including the regulation of pharmaceuticals, medical devices, food safety, and other related areas by the U.S. Food and Drug Administration (FDA). This title outlines the standards for manufacturing, labelling, and distribution of drugs and medical devices to ensure public safety and efficacy. Key sections within 21 CFR cover topics such as Good Manufacturing Practices (GMP), clinical trials, and labelling requirements for drugs and biologics. The regulations are critical for companies in the healthcare and pharmaceutical industries to ensure compliance with FDA standards. A review paper would likely conclude by discussing the balance that the FDA strives to maintain between protecting public health and encouraging innovation, emphasizing that while compliance with 21 CFR is complex, it is critical to ensuring the safety and efficacy of drugs, medical devices, and food products.

ACKNOWLEDGEMENT

At the very outset, I fail to find adequate words, with limited vocabulary at my Command, to express my emotions to “Dear God”, & Shree Ganesh whose eternal blessings, divine presence and masterly guidance helps me to fulfill all my goals. It’s not easy to express my emotions in words especially when I have to say thanks to my guide Dr. Avinash M. Bhagwat (Professor. Dept. of Pharmaceutical Chemistry Yspm,s YTC, Satara),Prof. Dasharath Sagare (President),Prof. Ajinkya Sagare (Vice President),Prof. (Dr. V.K. Redsani (Principal, Yspm,s YTC, Satara) for his constructive suggestions, meticulous support and constant motivation. Above all I would like to thank My Parents for showering their infinite bounty, clemencies and graces upon me. To them I owe a lifelong indebtedness. I am especially grateful to dear friends Resham Ingawale, Manish Pujari, Omkar Dadas. At last but not the least I am humbly grateful to all those peoples who directly or indirectly played role of a catalyst to bring out the lovely reaction of this research.

REFERENCES

1. Parks KC , Bernard B , Cogdill CB .The Evolution of 21 CFR Parts 210 & 211 for Drug Compounders : An Unspoken Opportunity For Pharmacist.2015(5).377-380
2. Allan L. Forsberg. Brief Remark on The Evolution of 21 CFR. Section 80.1.1973.1-111.
3. Graham PB. Good Laboratory Practice For Nonclinical Studies(Subpart A) , CRS Press , 2022.15-16
4. Bettina D.W , Denis R. Good Laboratory Practice For Nonclinical Studies(Subpart B) , CRS Press, 2022.20-30
5. William S. Good Laboratory Practice For Nonclinical Studies(Subpart C) , CRS Press , 2022.1-10
6. Graham P.B. Good Laboratory Practice For Nonclinical Studies(Subpart D) , CRS Press , 2022.1-12
7. Jennifer C. Good Laboratory Practice For Nonclinical Studies(Subpart J) , CRS Press , 2022.1-16
8. Jennifer C. Good Laboratory Practice For Nonclinical Studies(Subpart K) , CRS Press , 2022.1-45
9. Code of Federal Regulation.21-11-2024. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-210
10. Code of Federal Regulation. 21-11-2024. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211
11. Kolekar P.D, Prof. Bhagwat A. M. Good Documentation Practices: A Need of Pharmaceutical Industry. Asian J. Research Chem.2021.1-7
12. Chavan P. J, Chaudhari A. P, Bhagwat A. M.CAPA: An Important Concept of Pharmaceutical Industry. Asian J. Research Chem.2021.1-6
13. Chavan S. R, Bhagwat A. M, Rao M, Chaudhari A. P. Importance Of Force Degradation Study In Pharmaceutical Industry – A Review. World Journal of Pharmaceutical Research. 2019(8).639-652
14. Bhagwat A. M, Khadke A. P, Patil A. M, Shelar N. S. Essential Procedural Review On Cleaning Aspect Of Accessories Used In Industrial Laboratories. European Journal Of Biomedical And Pharmaceutical Sciences. 2017(4).179-187
15. Ingawale s. s, Bhagwat A. M, Khadke A. P, Khadke A. A. Data Integrity :A Need Of Pharmaceutical Industry. European Journal Of Biomedical And Pharmaceutical Sciences 2017(4).199-211

16. Bhagwat A. M, Khadke A.P, Patil A.M, Tarade S.V. Quality Preparatory Work : The Basic Analysis. European Journal Of Biomedical And Pharmaceutical Sciences. 2017(4).158-167