



## Current Good Manufacturing Practices Checklist For Pharmaceutical Manufacturers

Current Good Manufacturing Practices (“cGMPs” or “GMPs”) for pharmaceutical manufacturers provide the methods and controls used for the manufacturing, processing, packaging or holding of a pharmaceutical to assure that the pharmaceutical meets the minimum safety requirements of the Federal Food, Drug and Cosmetic Act (“FDCA”) and that the pharmaceutical has the identity, strength, quality and purity characteristics required. The following checklist is intended to act as a reminder of some of the more significant requirements of cGMPs for pharmaceutical manufacturers and does not include all aspects of the detailed and extensive requirements of cGMPs regulations. As such, it is prudent to engage legal counsel to assist in meeting and complying with the requirements of cGMPs regulations. The failure to comply with cGMPs regulations may render a pharmaceutical to be considered adulterated and subject the manufacturer to the possibility of regulatory action.

### 1. General

- The key to all cGMPs is documentation - IF IT IS NOT DOCUMENTED THEN IT DID NOT HAPPEN OR DOES NOT EXIST!
- cGMPs require the maintaining of production, control and distribution records and the retention of these records for a minimum period of time after the expiration date of an active ingredient, a batch of a drug product, or other set marker.
- cGMPs require retained records be readily available for inspection during the retention period at the establishment where the activities described occurred.
- cGMPs require evaluation of records and data contained within, at least annually, to determine quality standards of each drug product to determine any need to alter drug product specifications.

### 2. Records and Reports

- Master Production Records – In order to assure uniformity from batch to batch cGMPs require the maintaining of master production and control records for each drug product which include: (i) name and strength of the product and a description of the dosage form; (ii) name and weight of each active ingredient per dosage unit and a statement of the total weight of any dosage unit; (iii) a complete list of components designated by names or codes sufficiently specific to indicate any special quality characteristics; (iv) an accurate statement of the weight of each component; (v) a statement concerning any calculated excess of component; (vi) a statement of theoretical weight at appropriate phases of processing; (vii) a statement of theoretical yield, including the maximum and minimum percentage theoretical yield beyond which investigation is required; (viii) a description of the drug product containers, closures, and packaging materials including a specimen or copy of each label and all other labeling; and (ix) complete manufacturing and control instructions, sampling and testing procedures, specifications, special notations, and precautions to be followed.



- Batch Records – cGMPs require the maintaining of batch production and control records which include: (i) a copy of the appropriate master production and control record; (ii) documentation that each significant step in the manufacturing, processing, packaging and holding of the batch was accomplished, including: dates, identity of major equipment and lines used, specific identification of each batch of component or in-process material used, weights of components used in the course of processing, in-process and laboratory control results, inspection of the packages and labeling area before and after use, statement of actual yield and a statement of percentage of theoretic yield at appropriate phases of processing, complete labeling records, including specimens or copies of all labeling, description of drug product containers and closures, any sampling performed, identification of the persons performing and directly supervising or checking significant step in the operation, any investigation, and results of examinations.
- Laboratory Records – cGMPs require the maintaining of all data derived from all tests necessary to assure compliance with established specifications, including: (i) a description of the sample received for testing with identification of source, quantity, lot number or other distinctive code, date sample was taken, and date sample was received for testing, a statement of each method used in the testing of the sample, a statement of the weight of sample used for each test, a complete record of all data secured in the course of each test, a record of all calculations performed in connection with the test, a statement of results of tests and how the results compare with established standards of identify, strength, quality, and purity for the component, drug product container, closure, in-process material, or drug product tested, the signature of the person who performed each test and the date the tests were performed, the signature of a second person showing the original records have been reviewed for accuracy, completeness, and compliance with established standards; (ii) any modifications of an established metric employed in testing; (iii) any testing and standardization of laboratory reference standards; (iv) periodic calibration of laboratory instruments, apparatus, gauges, and recording devices; and (v) all stability testing.
- Component, Container and Labeling Records – cGMPs require the maintaining of component, drug product container, closure and labeling records which include: (i) the identity and quantity of each shipment of each lot of components, drug product containers, closures, labeling, the name of the supplier, the supplier's lot number if known, the receiving code; and the date of receipt; (ii) the results of any test or examination performed and conclusions derived; (iii) an individual inventory record of each component, drug product container, and closure, and for each component, a reconciliations of the use of each lot of such component; (iv) documentation of the examination and review of labels and label conformity to established specifications; and (v) the disposition of rejected components, drug product containers, closure and labeling.
- Distribution Records – cGMPs require the maintaining of distribution records which include the name and strength of each product and describe the dosage form, name and address of the consignee, date and quantity shipped, and control number of the drug product.
- Complaint File – cGMPs require the establishment and following of written procedures for the handling of written and oral complaints. Complaint records must be maintained at the establishment where the drug product was manufactured, processed, or packed and must be maintained at least 1 year after the expiration of the drug product or one year after the complaint was received, whichever is longer.



Complaint records must include: (i) the name and strength of the drug product; (ii) lot number; (iii) name of the complainant; (iv) nature of the complaint; and (v) reply to complainant. Complaint records must also indicate if an investigation was conducted, the results of investigation or, if no investigation, the reason so.

### 3. Production and Process Controls

- cGMPs require the establishment and following of written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality and purity they purport to possess.
- cGMPs require that the documentation of performance of compliance with established written procedures for production and process controls at the time of performance.
- Validation – cGMPs require the establishment and following of written procedures that detail in-process controls, tests, or examinations to be conducted to assure batch uniformity and integrity (i.e., identity, strength, quality and purity) of in-process materials of each batch and the final drug product. In-process controls can include, but are not limited to, the following: (i) tablet or capsule weight variation; (ii) disintegration time; (iii) adequacy of mixing to assure uniformity and homogeneity; (iv) dissolution time and rate; (v) clarity, completeness, or pH of solutions; (vi) bioburden testing. Rejected in-process materials must be identified to prevent use in manufacturing and processing operations.
- cGMPs require the establishment and following of written procedures of a system for reprocessing batches found not to conform to specifications and actions necessary to ensure that the reprocessed batch conforms to established specifications.

### 4. Laboratory Controls

- cGMPs require the establishment and following of scientifically sound and appropriate specifications, standards, sampling plans, and/or test procedures designed to assure identity, strength, quality and purity, including the following: (i) determination of conformance to applicable written specifications for the acceptance of each lot within each shipment of components, drug product containers, closures, and labeling used in the manufacture, processing, packing, or holding of drug products; (ii) determination of conformance to written specifications and a description of samples and testing procedures for in-process materials; (iii) determination of conformance to written descriptions of sampling procedures and appropriate specification for drug products; (iv) the calibration of instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in event accuracy and/or precision limits are not met.
- Testing and Release for Distribution – For each batch of drug product, there must 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. Any sampling and testing plans must be described in written procedures which include the method of sampling and the number of



units per batch to be tested. Drug products failing to meet established standards or specification and any relevant quality control criteria must be rejected.

- Stability Testing – The establishment and following of written testing program designed to assess the stability characteristics of drug products. The results of such stability testing must be used in determining appropriate storage conditions and expiration dates.
- Reserve Samples – An appropriately identified reserve sample that is representative of each lot in each shipment of each active ingredient must be retained. The reserve sample consists of at least twice the quantity necessary for all tests required to determine whether the ingredient meets its established specifications. For active ingredient in a drug product the reserve sample must be retained for 1 year after expiration date of the last lot of the drug product containing the active ingredient.

## 5. Quality Control Unit

- cGMPs require the establishment of a Quality Control Unit, as well as written procedures and responsibilities, with authority to approve or reject everything from drug components to the final drug product.
- Quality Control Unit must have adequate laboratory facilities for the testing and approval or rejection from drug components to the final drug product.
- Quality Control Unit is also responsible for approving or rejecting procedures or specifications impacting on the identity, strength, quality, and purity of the drug product.

## 6. Packaging and Labeling Controls

- Materials Examination and Usage Criteria – cGMPs require the establishment and following of written procedures describing the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling and packaging materials. Labeling and packaging materials must be representatively sampled, and examined or tested upon receipt and before use in packaging or labeling of a drug product. Records must be maintained for each shipment received of each different label and packaging material indicating receipt, examination or testing, and whether accepted or rejected.
- Labeling Issuance – cGMPs require the establishment and following of control procedures for the issuance of labeling. Labeling materials issued for a batch must be carefully examined for identity and conformity to the labeling specified in the master or batch production records. Procedures must be used to reconcile the quantities of labeling issued, used, and returned, and must require evaluation of discrepancies found between the quantity of drug product finished and the quantity of labeling issued when such discrepancies are outside narrow preset limits based on historical operating data.
- Packaging and Labeling Operations – cGMPs require the establishment and following of written procedures designed to assure that correct labels, labeling and packaging materials are used for drug products and incorporate the following features: (i) prevention of mix-ups and cross-contamination by physical or spatial separation from operations on other drug products; (ii) identification and handling of filled drug product containers that are set aside and held in unlabeled condition for future labeling operations to preclude mislabeling of individual containers, lots, or portions of lots; (iii) identification of



the drug product with a lot or control number that permits determination of the history of the manufacture and control of the batch; (iv) examination of packaging and labeling materials for suitability and correctness before packaging operations, and documentation of such examination in the batch production; (vii) inspection of the packaging and labeling facilities immediately before use to assure that all drug products have been removed from previous operations.

- Drug Product Inspection – cGMPs require the examination of packaged and labeled products during finishing operations to assure that containers and packages in the lot have the correct label. There must be collected a representative sample of units at the completion of finished operations and visual inspection. Also, required to maintain records of examinations and inspections.
- Expiration dating – cGMPs also require drug products to bear an expiration date determined by appropriate stability testing to assure it meets identity, strength, quality, and purity at the time of use. Expiration date must be related to any storage conditions stated on the labeling, as determined by stability testing. If drug product is reconstituted, labeling must bear expiration information for the reconstituted and unreconstituted drug product.

## **7. Holding and Distribution**

- Warehousing Procedures – cGMPs require the establishment and following of written procedures describing the warehousing of drug products, including description of procedures for: (i) quarantine of drug products before release by the quality control unit; and (ii) storage of drug products under appropriate conditions of temperature, humidity and light so that identity, strength, quality, and purity of the drug products are not affected.
- Distribution Procedures – cGMPs require the establishment and following of written procedures describing the distribution of products, including: (i) a procedure whereby the oldest approved stock of a drug product is distributed first and the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary.

## **8. Building and Facilities Controls**

- cGMPs require the maintaining of separately defined areas of operations within building or buildings to prevent contamination or mix-ups during the course of the following procedures: (i) receipt, identification, storage, and withholding from use of components, drug containers, closures, and labeling, pending the appropriate sampling, testing, or examination by the quality control unit before release for manufacturing or packaging; (ii) holding rejected components, drug product containers, closures, and labeling before disposition; (iii) storage of released components, drug product containers, closures, and labeling; (iv) storage of in-process material; (v) manufacturing and processing operations; (vi) packaging and labeling operations; (vii) quarantine storage before release of drug products; (viii) storage of drug products; (ix) control and laboratory operations; and (x) aseptic processing, which includes as appropriate: (a) floors, walls and ceilings of smooth, hard surfaces that are easily cleanable; (b) temperature and humidity controls; (c) an air supply filtered through high-efficiency particulate air filters under pressure, regardless of whether flow is laminar or nonlaminar; (d) a system



for monitoring environmental conditions; (e) a system for cleaning and disinfecting the room and equipment to produce aseptic conditions; and (f) a system for maintaining any equipment used to control the aseptic conditions

- Ventilation, Air Filters, Air Heating and Cooling – cGMPs require that there is equipment which provides for adequate control over air pressure, micro-organisms, dust, humidity and temperature for the manufacturing, processing, packing or holding of a drug product.

## 9. Equipment Controls

- cGMPs require the establishment and following of written procedures for cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing, or holding of a drug product.
- Equipment and utensils must be cleaned, maintained, and, as appropriate for the nature of the drug, sanitized and 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.
- Automatic, Mechanical, or Electronic Equipment – Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems used in the manufacture, processing, packing and/or holding of a drug product must be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance. Written records of those calibrations and inspections must be maintained.



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