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New Jersey State
Department of Health
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GOOD DRUG MANUFACTURING PRACTICES

The State Department of Health, pursuant to authority vested in it under the provisions of Chapter 2, Title 24 of the Revised Statutes, hereby promulgates the following regulations concerning "Good Drug Manufacturing Practices."

Roscoe P. Kandle, M.D.
State Commissioner of Health

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DRUGS; CURRENT GOOD MANUFACTURING PRACTICE IN MANUFACTURE, PROCESSING, PACKING, OR HOLDING.

DEFINITIONS

1. *Definitions*
   (a) "Act" means N.J.S.A. 24:1 et seq the Food, Drug and Cosmetic Law of New Jersey, and all amendments thereto.
   (b) The definitions and interpretations contained in the Food, Drug and Cosmetic Act shall be applicable to such terms when used in this regulation.

FINISHED PHARMACEUTICALS; MANUFACTURING PRACTICE

2. *Current good manufacturing practice*

   The criteria in 3-13, inclusive, shall apply in determining whether the methods used in, or the facilities or controls used for the manufacture, processing, packing, or holding of a drug conform to or are operated or administered in conformity with current good manufacturing practice to assure that a drug meets the requirements of the act as to safety, and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess. This regulation permits the use of precision automatic mechanical or electronic equipment in the production of drugs when adequate inspection and checking procedures are used to assure proper performance.*

3. *Buildings*

   Buildings in which drugs are manufactured, processed, packaged, labeled, or held shall be maintained in a clean and orderly manner and shall be of suitable size, construction, and location in relation to surroundings to facilitate maintenance and operation for their intended purpose. The buildings shall:

   (a) Provide adequate space for the orderly placement of equipment and materials used in any of the following operations for which it is employed, to minimize any risk of mix-ups between different drugs, their components, packaging, or labeling, and to control the possibility of cross-contamination of one drug by another drug that is manufactured, stored, or handled on the same premises:

   (1) The receipt, sampling, and storage of components.
   (2) Any manufacturing and processing operations performed on the drug.
   (3) Any packaging and labeling operations.
   (4) Storage of containers, packaging materials, labeling, and finished products.
   (5) Control and production-laboratory operations.

   (b) Provide adequate lighting and ventilation, and when necessary for the intended production or control purposes, adequate screening, filtering, dust, humidity, temperature, and bacteriological controls, as for example, to prevent contamination of products by extraneous adulterants (including the prevention of cross-contamination of one product by dust or particles of ingredients arising from the manufacture, storage or handling of another drug); to prevent the dissemination of micro-organisms from one area to another; to facilitate the sterilization of special work areas, such as those used for production of parenteral preparations; to provide suitable housing for any animals; and to avoid other conditions unfavorable to the safety and integrity of the product.

   (c) Provide for adequate washing, cleaning, toilet, and locker facilities.

4. *Equipment*

   Equipment used for the manufacture, processing, packaging, labeling, holding, or control of drugs shall be maintained in a clean and orderly manner and shall be of suitable design size, construction, and location in relation to surroundings to facilitate maintenance and operation for its intended purpose.

   The equipment shall:

   (a) Be so constructed that any surfaces that come into contact with drugs are suitable, in that they are not reactive, additive, or absorptive to an extent that significantly affects the identity, strength, quality, or purity of the drug or its components.
   (b) Be so constructed that any substances required for the operation of the equipment, such as lubricants or coolants, may be employed without hazard of becoming additive to drug products.
   (c) Be constructed to facilitate adjustment, cleaning and maintenance as necessary to assure the reliability of control procedures, to assure uniformity of production, and to assure the exclusion from drugs of contaminants, including

**It is recognized that some modification of these regulations may be indicated in connection with their application to the manufacture of chemicals and other raw materials used as components of finished drugs. Similarly these regulations relate to the manufacture of drugs in final dosage form and are inapplicable to the manufacture of medicated feeds and medicated premixes.*

those from previous and current manufacturing operations.

(d) Be of suitable size and accuracy for use in any intended measuring, mixing, or weighing operations.

5. *Personnel*

The key personnel involved in the manufacture and control of the drug shall have a background of appropriate education or appropriate experience or combination thereof for assuming responsibility to assure that the drug has the safety, identity, strength, quality, and purity that it purports to possess.

6. *Components*

Components used in the manufacture and process- of drugs, regardless of whether they are intended to appear in the finished product, shall be identified, stored, examined, tested, inventoried, handled and otherwise controlled in a manner to assure that they conform to appropriate standards of identity, strength, quality, and purity, and are free of contaminants at time of use, and are so stored and handled as to assure that dust or particles resulting from such storage or handling does not contaminate other substances or preparations on the premises, and to provide that appropriate records are maintained of their origin, receipt, examination, testing, disposition, and use in drug manufacture or processing.

7. *Master-Formula and batch-production records*

(a) For each drug product, master-formula records shall be prepared, endorsed, and dated by a competent and responsible individual and shall be independently checked, reconciled, endorsed and dated by a second competent and responsible individual. The record shall include:

(1) The name of the product, a description of its dosage form, and a specimen or copy of the label and each other portion of the labeling contained in a retail package of the drug.

(2) The weight or measure of each ingredient per dosage unit or per unit of weight or measure of the finished drug, and a statement of the total weight or measure of any dosage unit.

(3) A complete batch formula for each batch size to be produced from the master-formula record, including a complete list of ingredients designated by names or codes sufficiently specific to indicate any special quality characteristic; an accurate statement of the weight or measure of each ingredient, regardless of whether it appears in the finished product, except that reasonable variations may be permitted in the amount of components necessary in the preparation in dosage form, provided that the variations are stated in the master-formula; an appropriate statement concerning any calculated excess of an ingredient; appropriate statements of theoretical weight or measure at various stages of processing; and a statement of the theoretical yield.

(4) A description of the containers, closures, packaging, and finishing materials.

(5) Manufacturing and control instructions, procedures, specifications, special notations, and precautions to be followed.

(b) A separate batch-production and control record shall be prepared for each batch of drug produced and shall be retained for at least two years after distribution has been completed. The batch-production and control record shall include:

(1) An accurate reproduction of the appropriate master-formula record, checked and endorsed by a competent, responsible individual.

(2) Records of each step in the manufacturing, processing, packaging, labeling, and controlling of the batch, including dates, specific identification of each batch of compenents used, weights or measures of components and products in course of processing, in-process and laboratory-control results, and the endorsements of the individual actively performing or the individual actively supervising or checking each step in the operation.

(3) A batch number that permits determination of all laboratory-control procedures and results on the batch and all lot or control numbers appearing on the labels of drugs from the batch.

8. *Production and control procedures*

Production and control procedures shall include all reasonable precautions, including the following, to assure that the drugs produced have the identity, strength, quality, and purity they purport to possess.

(a) Each critical step in the process, such as the selection, weighing, and measuring of components; the addition of active ingredients during the process; weighing and measuring during various stages of the processing; and the determination of the finished yield shall be performed by a competent, responsible individual and checked by a second competent, responsible individual, or if such steps in the processing are controlled by precision automatic mechanical or electronic equipment their proper performance is adequately checked by one or more competent, responsible individuals.

(b) All containers and equipment used in producing a batch of drugs shall be clearly labeled at all times to identify fully and accurately their contents, the stage of processing, and the batch, and shall be stored and handled in a manner adequate to prevent mix-ups with other drugs.

(c) Equipment, utensils, and containers shall be thoroughly cleaned and previous identification removed between batches and in continuous batch operations at suitable intervals, to prevent contamination and mix-ups.

(d) Appropriate procedures to control the hazard of contamination with micro-organisms in the production of parenteral drugs, ophthalmic solutions, and any other drugs purporting to be sterile, and appropriate procedures to control the hazard of cross-contamination of non-penicillin products by penicillin in those establishments that manufacture, store, or handle penicillin products and nonpenicillin products.

(e) To assure the uniformity and integrity of products, there shall be adequate in-process controls, such as checking the weights and disintegration time of tablets, checking fill of liquids, and checking the adequacy of mixing, the homogeneity of suspensions, and the clarity of solutions.

(f) Competent and responsible personnel shall check actual against theoretical yield of a batch of drug, and in the event of any significant

unexplained discrepancies, key personnel shall prevent distribution of the batch in question and other associated batches of drugs that may have been involved in a mix-up with it.

9. *Product containers*

Suitable specifications, test methods, cleaning procedures, and, when indicated, sterilization procedures shall be used to assure that containers, closures, and other component parts of drug packages are suitable for their intended use, in that they are not reactive, additive, or absorptive to an extent that significantly affects the identity, strength, quality, or purity of the drug, and furnish adequate protection against its deterioration or contamination.

10. *Packaging and labeling*

Packaging and labeling operations shall be adequately controlled to assure that only those drugs that have met the specifications established in the master-formula records shall be distributed; to prevent mix-ups between drugs during the packaging and labeling operations; to assure that correct labeling is employed for the drug; and to identify finished products with lot or control numbers that permit determination of the history of the manufacture and control of the batch of drug. Packaging and labeling operations shall:

(a) Be performed with adequate physical segregation of such operations from operations on any other drugs to avoid mix-ups.

(b) Provide that each type of labeling used shall be stored in a mannner that avoids mix-ups between labelings and shall be carefully checked for identity and conformity to the labeling specified in the batch-production records.

(c) Provide adequate control of the quantities of labeling issued for use with the drug. (Competent, responsible personnel shall reconcile any discrepancy between the quantity of drug finished and the quantity of labeling issued. In the event of any significant unexplained discrepancy, key personnel shall prevent distribution of the batch in question and other associated batches of drugs that may have been involved in a mix-up.)

(d) Provide for an inspection of the facilities to be used prior to labeling a drug to assure that all the previously used labeling and other drugs have been removed.

(e) Provide for adequate examination or laboratory testing of adequately representative samples of finished products after packaging and labeling to safeguard against any error in the finishing operations, and to prevent distribution of any batch until all specified tests have been met.

11. *Laboratory controls*

Laboratory controls shall include the establishment of adequate specifications and test procedures to assure that components, drug preparations in the course of processing, and finished products conform to appropriate standards of identity, strength, quality, and purity. Laboratory controls shall include:

(a) The establishment of master records containing appropriate specifications for each component used in drug production and a description of the test procedures used to check them, including provisions for testing adequately representative samples. Such records shall also provide for appropriate retesting of materials subject to deterioration.

(b) The establishment of appropriate specifications, when needed, for drug preparations in the course of processing, and a description of the test procedures to check them, including provision for testing adequately representative samples.

(c) The establishment of appropriate finished-product specifications and a description of laboratory test procedures to check them including provision for testing adequately representative samples.

(d) Adequate provision for checking the identity and strength for all active ingredients of drugs, for assuring the sterility of articles purporting to be sterile, and the freedom from pyrogens of articles that should be tested for freedom from pyrogens.

(e) Adequate provision to check the reliability, accuracy, and precision of any laboratory test procedures used.

(f) A reserve sample of at least twice the quantity of drug required to conduct all the tests performed on the batch of drug shall be retained at least two years after distribution has been completed.

(g) Provision for complete records of all data concerning laboratory tests performed, including the dates and endorsements of individuals making the tests, and provision for specifically relating the tests to each batch of drugs to which they apply. Such records shall be retained for at least two years after distribution has been completed.

(h) Firms that manufacture nonpenicillin products, including certifiable antibiotic products, on the same premises or use the same equipment as that used for manufacturing penicillin products, or that operate under any circumstances that may reasonably be regarded as conducive to contamination of other drugs by penicillin, shall test such nonpenicillin products to determine whether any have become cross-contaminated by penicillin. Such products shall not be marketed if intended for use by man and the product is contaminated with an amount of penicillin equivalent to 0.05 unit or more of penicillin G per maximum single dose recommended in the labeling of a drug intended for parenteral administration, or an amount of penicillin equivalent to 0.5 unit or more of penicillin G per maximum single dose recommended in the labeling of a drug intended for oral use.

12. *Distribution records*

Complete records shall be maintained of the distribution of each batch of drug in a manner that will facilitate its recall if necessary. Such records shall be retained for at least two years after distribution has been completed, and shall include the name and address of the consignee, the date and quantity shipped, and the lot or control numbers identifying the batch of drug.

13. *Stability*

Adequate provision shall be made for testing the stability of components, drug preparations in the course of processing, when needed, and finished

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drugs. Such stability tests shall:

(a) Make adequate provision for determining the reliability and specificity of stability test methods employed.

(b) Make adequate provision to determine the stability of products in the containers in which they are marketed to assure, among other things, that the container is suitable, in that it is not reactive, additive, or absorptive to an extent that significantly affects the identity, strength, quality, or purity of the drug.

(c) Provide for stability studies of any solutions prepared as directed in the drug labeling at time of dispensing.

(d) Provide for suitable expiration dates to appear in the labeling of the drug when needed to assure that the drug meets appropriate standards of identity, strength, quality, and purity at time of use.

14. *Complaint files*

Records shall be maintained of all written or verbal complaints for each product. Complaints shall be evaluated by competent and responsible personnel and, where indicated, appropriate action taken. The record shall indicate the evaluation and action.

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