CHAPTER 21A

GOOD DRUG MANUFACTURING PRACTICES

Authority

N.J.S.A. 24:5–1 et seq.

Source and Effective Date

R.1992 d.316, effective August 3, 1992.
See: 24 N.J.R. 2003(c), 24 N.J.R. 2729(a).

Executive Order No. 66(1978) Expiration Date

Chapter 21A, Good Drug Manufacturing Practices, expires on August 3, 1997.

Chapter Historical Note

Chapter 21A, Good Drug Manufacturing Practices, was filed as R.1979 d.453 and became effective November 13, 1979. Chapter 21A was readopted as R.1985 d.141, effective April 1, 1985. See: 16 N.J.R. 3248(a), 17 N.J.R. 815(a). Chapter 21A expired on April 1, 1990. Chapter 21A, unchanged from the expired version, was adopted as R.1992 d.316. See: Source and Effective Date. See also 23 N.J.R. 1252(b).

See section annotations for specific rulemaking activity.

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SUBCHAPTER 1. MANUFACTURING, PROCESSING, PACKING OR HOLDING OF DRUGS; GENERALLY

8:21A–1.1 Status of current good manufacturing practice regulations

(a) The regulations set forth in this subchapter and in subchapter 2 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.

(b) The failure to comply with any regulation set forth in this subchapter and in subchapter 2 of this chapter in the manufacture, processing, packing, or holding of a drug shall render such drug to be adulterated under N.J.S.A. 24:5–10 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.

8:21A–1.2 Applicability of current good manufacturing practice regulations

(a) In the event that it is impossible to comply with all applicable regulations in this chapter, the regulations specifically applicable to the drug in question shall supersede the more general.

(b) If a person engages in only some operations subject to the regulations in this subchapter and in subchapter 2 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.

8:21A–1.3 Definitions

(a) The definitions and interpretations contained in N.J.S.A. 24:1–1 shall be applicable to such terms when used in this chapter.

(b) The following words and terms, when used in this chapter, shall have the following meanings unless the context clearly indicates otherwise.

"Acceptance criteria" means the product specifications and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with an associated sampling plan, that are necessary for making a decision to accept or reject a lot or batch (or any other convenient subgroups of manufactured units). (See "Representative sample", this section.)

"Act" means the New Jersey Food, Drug, and Cosmetic Act, N.J.S.A. 24:1 et seq.

"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 of 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.

"Actual yield" means the quantity that is actually produced at any appropriate phase of manufacture, processing, or packing of a particular drug product. (See "Percentage of theoretical yield", this section.)

"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.

"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.

"Drug product salvaging" is the act of segregating drug products that may have been subjected to improper storage conditions such as extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation for the purpose of returning some or all of the products to the marketplace.

"Establishment" means a place of business under one management at one general physical location. The term includes, among others, independent laboratories that engage in control activities for registered drug establishments (e.g., "consulting" laboratories), manufacturers of vitamin products that are "drugs" within the meaning of N.J.S.A. 24:1–1e, and establishments engaged in drug product salvaging.

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

"Inactive ingredient" means any component other than an "active ingredient" (see definition, this section).

"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.

"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.

8:21A–2.20 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, as appropriate, and released. Storage within the area shall conform to the requirements of section 48 of this subchapter.

8:21A–2.21 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 section 45 of this subchapter.

(c) Samples shall be collected in accordance with the following procedures:

1. The containers of components selected shall be cleaned where necessary, by appropriate means.

2. The containers shall be opened, sampled, and resealed in a manner designed to prevent contamination of their contents and contamination of other components, drug product containers, or closures.

3. Sterile equipment and aseptic sampling techniques shall be used when necessary.

4. If it is necessary to sample a component from the top, middle, and bottom of its container, such sample subdivisions shall not be composited for testing.

5. Sample containers shall be identified so that the following information can be determined: name of the material sampled, the lot number, the container from which the sample was taken, the data on which the sample was taken, and the name of the person who collected the sample.

6. Containers from which samples have been taken shall be marked to show that samples have been removed from them.

(d) Samples shall be examined and tested as follows:

1. At least one test shall be conducted to verify the identity of each component of a drug product. Specific identity tests, if they exist, shall be used.

2. Each component shall be tested for conformity with all appropriate written specifications for purity, strength, and quality. In lieu of such testing by the manufacturer, a report of analysis may be accepted from the supplier of a component, provided that at least one specific identity test is conducted on such component by the manufacturer, and provided that the manufacturer establishes the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.

3. Containers and closures shall be tested for conformance with all appropriate written procedures. In lieu of such testing by the manufacturer, a certificate of testing by the manufacturer, a certificate of testing may be accepted from the supplier, provided that at least a visual identification is conducted on such containers/closures by the manufacturer and provided that the manufacturer establishes the reliability of the supplier's test results through appropriate validation of the supplier's test results at appropriate intervals.

4. When appropriate, components shall be microscopically examined.

5. Each of a component, drug product container, or closure that is liable to contamination with filth, insect infestation, or other extraneous adulterant shall be examined against established specifications for such contamination.

6. Each lot of a component, drug container, or closure that is liable to microbiological contamination that is objectionable in view of its intended use shall be subjected to microbiological tests before use.

(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 subsection (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.

8:21A–2.22 Use of approved components, drug product containers and closures

Components, drug product containers, and closures approved for use shall be rotated so that the oldest approved stock is used first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.

8:21A–2.23 Retesting of approved components, drug product containers and closures

Components, drug product containers, and closures shall be retested or reexamined, as appropriate, for identity,

strength, quality, and purity and approved or rejected by the quality control unit in accordance with section 21 of this subchapter as necessary, e.g., after storage for long periods or after exposure to air, heat or other conditions that might adversely affect the component, drug product container, or closure.

8:21A–2.24 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.

8:21A–2.25 Drug product containers and closures

(a) Drug product containers and closures shall 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.

(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.

8:21A–2.26 Written procedures; deviations

(a) There shall be written procedures for production and process control designated 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.

8:21A–2.27 Charge-in of components

(a) 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:

1. The batch shall be formulated with the intent to provide not less than 100 percent of the labeled or established amount of active ingredient.

2. 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 with the following information:

i. Component name or item code;

ii. Receiving or control number;

iii. Weight or measure in new container;

iv. Batch for which component was dispensed, including its product name, strength, and lot number.

3. 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 that:

i. The component was released by the quality control unit;

ii. The weight or measure is correct as stated in the batch production records;

iii. The containers are properly identified.

4. Each component shall be added to the batch by one person and verified by a second person.

8A:21–2.28 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 be performed by one person and independently verified by a second person.

8:21A–2.29 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 case 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.