Food & Drug Administration's Current Good Manufacturing Practice For Type A Medicated Articles

Part 226 – Current Good Manufacturing Practice for Type A Medicated Articles

Authority: Secs. 501, 701, 52 Stat. 1049-1050 as amended; 1055-1056 as amended (21 U.S.C. 351, 371)

Subpart A – General Provisions

§ 226.1 Current good manufacturing practice

The criteria in § 226.10 through 226.115, inclusive, shall apply in determining whether the methods used in, or the facilities and controls used for the manufacture, processing, packing or holding of a Type A medicated article(s) conform to or are operated or administrated in conformity with current good manufacturing practice to assure that a Type A medicated article(s) 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, as required by section 501 (a)(2)(B) of the act. The regulations in this Part 226 permit the use of precision, automatic, mechanical or electronic equipment in the production of a Type A medicated article when adequate inspection and checking procedures or other quality control procedures are used to assure proper performance.

§ 226.10 Personnel

The key personnel and any consultants involved in the manufacture and control of the Type A medicated article(s) shall have a background of appropriate education or appropriate experience or combination thereof for assuming responsibility to assure that the Type A medicated article(s) has the proper labeling and the safety, identity, strength, quality and purity that it purports to possess.

Subpart B – Construction and Maintenance of Facilities and Equipment

§ 226.20 Buildings

Buildings in which Type A medicated articles 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 building shall:

(a) Provide adequate space for the orderly placement of equipment and materials used in any of the following operations for which they are employed to minimize risk of mix-ups between different Type A medicated articles, their components, packaging or labeling:
  (1) The receipt, sampling, control and storage of components.
  (2) Manufacturing and processing operations performed on the Type A medicated article.
  (3) Packaging and labeling operations.
  (4) Storage of containers, packaging materials, labeling and finished products.
  (5) Control laboratory operations.

(b) Provide adequate lighting and ventilation and when necessary for the intended production or control purposes, adequate screening, dust and temperature controls, to avoid contamination of Type A medicated articles and to avoid other conditions unfavorable to the safety, identity, strength, quality and purity of the raw materials and Type A medicated

articles before, during and after production.

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

Work areas and equipment used for the production of Type A medicated articles or for the storage of the components of Type A medicated articles shall not be used for the production, mixing or storage of finished or unfinished insecticides, fungicides, rodenticides or other pesticides or their components unless such materials are recognized as approved drugs intended for use in animal feeds.

§ 226.30 Equipment

Equipment used for the manufacture, processing, packaging, bulk shipment, labeling, holding or control of Type A medicated articles or their components shall be maintained in a clean and orderly manner and shall be of suitable design, size, construction and location to facilitate maintenance and operation for its intended purpose. The equipment shall:

(a) Be so constructed that any surfaces that come into contact with Type A medicated articles 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 Type A medicated article or its components.

(b) Be so constructed that any substance required for the operation of the equipment, such as lubricants and coolants, may be employed without hazard of becoming an unsafe additive to the Type A medicated article.

(c) Be constructed to facilitate adjustment, cleaning and maintenance and to assure uniformity of production and reliability of control procedures and to assure the exclusion from Type A medicated articles of contamination including cross-contamination from manufacturing operations.

(d) Be suitably grounded electrically to prevent lack of uniform mixing due to electrically charged particles.

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

Subpart C – Product Quality Control

§ 226.40 Production and Control Procedures

Production and control procedures shall include all reasonable precautions, including the following, to assure that the Type A medicated articles 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 measure of components; the addition of drug components during the process; weighing and measuring during various stages of the processing, and the determination of the finished yield, shall be performed by one or more competent, responsible individuals. If such steps in the processing are controlled by precision, automatic, mechanical or electronic equipment, their proper performance shall be adequately checked by one or more competent, responsible individuals.

(b) All containers to be used for undiluted drugs, drug components, intermediate mixtures thereof and Type A medicated articles shall be received, adequately identified and properly stored and handled in a manner adequate to avoid mix-ups and contamination.

(c) Equipment, including dust-control and other equipment, such as that used for holding and returning recovered or flush-out materials back into production, shall be maintained and operated in a manner to avoid contamination of the Type A medicated articles and to insure the integrity of the finished product.

(d) Competent and responsible personnel shall check actual against theoretical yield of a batch of Type A medicated article and, in the event of any significant discrepancies, key personnel shall prevent distribution of the batch in question and other associated batches of Type A medicated articles that may have been involved in a mix-up with it.

(e) Adequate procedures for cleaning of those pans of storage, mixing, conveying

and other equipment coming in contact with the drug component of the Type A medicated article shall be used to avoid contamination of Type A medicated articles.

(f) If there is sequential production of batches of a Type A medicated article containing the same drug component (or components) at the same or lower levels, there shall be sufficient safeguards to avoid any buildup above the specified levels of the drug components in any of the batches of the Type A medicated article.

(g) Production and control procedures shall include provision for discontinuing distribution of any Type A medicated article found by the assay procedures, or other controls performed, to fail to conform to appropriate specifications. Distribution of subsequent production of such Type A medicated article shall not begin until it has been determined that proper control procedures have been established.

§ 226.42 Components

(a) Drug components, including undiluted drugs and any intermediate mixes containing drugs used in the manufacture and processing of Type A medicated articles, shall be received, examined or tested, stored, handled and otherwise controlled in a manner to maintain the integrity and identification of such articles. Appropriate receipt and inventory records shall be maintained for two years and such records shall show the origin of any drug components, the manufacturer's control number (if any), the dates and batches in which they were used and the results of any testing of them.

(b) Nondrug components shall be stored and otherwise handled in a manner to avoid contamination, including cross-contamination from manufacturing operations.

§ 226.58 Laboratory Controls

Laboratory controls shall include the establishment of adequate specifications and test procedures to assure that the drug components and the Type A medicated articles conform to appropriate standards of identity, strength, quality and purity. Laboratory controls shall include:

(a) The establishment of master records containing appropriate specifications and a description of the test procedures used to check them for each kind of drug component used in the manufacture of Type A medicated articles. This may consist of the manufacturer's or supplier's statement of specifications and methods of analyses.

(b) The establishment of specifications for Type A medicated articles and a description of necessary laboratory test procedures to check such specifications.

(c) Assays which shall be made of representative samples of finished Type A medicated articles in accordance with the following schedule:

(1) Each batch of a Type A medicated article manufactured from an undiluted drug shall be assayed for its drug component(s).

(2) In the case of Type A medicated articles which are manufactured by dilution of Type A medicated article(s) assayed in accordance with paragraph (c) (1) of this section, each batch shall be assayed for its drug component(s) with the first five consecutive batches assaying within the limitations, followed thereafter by assay of representative samples of not less than 5% of all batches produced. When any batch does not assay within limitations, each batch should again be assayed until five consecutive batches are within limitations.

(d) A determination establishing that the drug components remain uniformly dispersed and stable in the Type A medicated article under ordinary conditions of shipment, storage and use. This may consist of a determination on a Type A medicated article of substantially the same formula and

characteristics. Suitable expiration dates shall appear on the labels of the Type A medicated articles to assure that the articles meet the appropriate standards of identity, strength, quality and purity at the time of use.

(e) Adequate provision to check the reliability, accuracy and precision of any laboratory test procedure used. The official methods in "Methods of Analysis of the Association of Official Analytical Chemists," methods described in an official compendium and any method submitted as a part of a food additive petition or new-drug application that has been accepted by the Food & Drug Administration shall be regarded as meeting this provision.

(f) Provisions for the maintenance of the results of any assays, including dates and endorsement of analysts. Such records shall be retained in the possession of the manufacturer and shall be maintained for a period of at least two years after distribution by the manufacturer of the Type A medicated article has been completed.

Subpart D – Packaging and Labeling

§ 226.80 Packaging and Labeling

(a) Packaging and labeling operations shall be adequately controlled:

(1) To assure that only those Type A medicated articles that have met the specifications established in the master-formula records shall be distributed.

(2) To prevent mix-ups during the packaging and labeling operations.

(3) To assure that correct labeling is employed for each Type A medicated article.

(4) To identify Type A medicated articles with lot or control numbers that permit determination of the history of the manufacture and control of the batch of Type A medicated article.

(b) Packaging and labeling operations shall provide:

(1) For storage of labeling in a manner to avoid mix-ups.

(2) For careful checking of labeling for identity and conformity to the labeling specified in the batch-production records.

(3) For adequate control of the quantities of labeling issued for use with the Type A medical article.

(c) Type A medicated articles shall be distributed in suitable containers to insure the safety, identity, strength and quality of the finished product.

Subpart E – Records and Reports

§ 226.102 Master-Formula and Production Records

(a) For each Type A medicated article, 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 Type A medicated article and a specimen copy of its label.

(2) The weight or measure of each ingredient, adequately identified, to be used in manufacturing a stated weight of the Type A medicated article.

(3) A complete formula for each batch size, or of appropriate size in the case of continuous systems 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 characteristics; an accurate statement of the weight or measure of each ingredient, except that reasonable variations may be permitted in the amount of ingredients necessary in the preparation of the Type A medicated article, provided that the variations are stated in the master-formula; an appropriate statement concerning any

calculated excess of an ingredient and a statement of the theoretical yield.

(4) Manufacturing instructions for each type of Type A medicated article produced on a batch or continuous operation basis, including mixing steps and mixing times that have been determined to yield an adequately mixed Type A medicated article and in the case of Type A medicated articles produced by continuous production run, any additional manufacturing directions including, when indicated, the settings of equipment that have been determined to yield an adequately mixed Typed A medicated article of the specified formula.

(5) 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 or run of Type A medicated article produced and shall be retained for at least two years after distribution by the manufacturer has been completed. The batch-production and control record shall include:

(1) Product identification, date of production and endorsement by a competent and responsible individual.

(2) Records of each step in the manufacturing, packaging, labeling and controlling of the batch, including dates, specific identification of drug components used, weights or measures of all components, laboratory-control results, mixing times 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 the Type A medicated article.

226.110 Distribution Records

Complete records shall be maintained for each shipment of Type A medicated articles in a manner that will facilitate the recall, diversion or destruction of the Type A medicated article, if necessary. Such records shall be retained for at least two years after the date of the shipment by the manufacturer and shall include the name and address of the consignee, the date and quantity shipped and the manufacturing dates, control numbers or marks identifying the Type A medicated article shipped.

§ 226.115 Complain Files

Records shall be maintained for a period of two years of all written or verbal complaints concerning the safety or efficacy of each Type A medicated article. Complaints shall be evaluated by competent and responsible personnel and where indicated, appropriate action shall be taken. The record shall indicate the evaluation and action.