

# Food & Drug Administration's Current Good Manufacturing Practice Regulations for Feeds

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## **Part 210 – Current Good Manufacturing Practice in Manufacturing, Processing, Packing or Holding of Drugs; General**

Part 210 is amended by revising the part heading as set out above.

In § 210.3 by revising paragraph (b)(13) and (14), to re read as follows:

### **§ 210.3 Definitions**

(b)\*\*\*

(13) The term “medicated feed” means any Type B or Type C medicated feed as defined in § 558.3 of this chapter. The feed contains one or more drugs as defined in section 201(g) of the act. The manufacture of medicated feeds is subject to the requirements of Part 225 of this chapter.

(14) The term “medicated premix” means a Type A medicated article as defined in § 558.3 of this chapter. The article contains one or more drugs as defined in section 210(g) of the act. The manufacture of medicated premixes is subject to the requirements of Part 226 of this chapter.

## **Part 225 – Current Good Manufacturing Practice for Medicated Feeds**

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## **Subpart A – General Provisions**

### **§ 225.1 Current good manufacturing practice**

- (a) Section 501 (a) (2) (B) of the Federal Food, Drug & Cosmetic Act provides that a drug (including a drug contained in a medicated feed) shall be deemed to be adulterated if the methods used in or the facilities or controls used for its manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirement 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.
- (b) (1) The provisions of this part set forth the criteria for determining whether the manufacture of a medicated feed is in compliance with current good manufacturing practice. These regulations shall apply to all types of facilities and equipment used in the production of medicated feeds and they shall also govern those instances in which failure to adhere to the regulations has caused nonmedicated feeds that are manufactured, processed, packed or held to be adulterated. In such cases, the medicated feed shall be deemed to be adulterated within the meaning of section 501(a)(2)(B) of the act and the nonmedicated feed shall be deemed to be adulterated within the meaning of section 402(a)(2)(D) of the act.

(2) The regulations in § 225.10 through 225.115 apply to facilities manufacturing one or more medicated feeds for which an approved medicated feed application is required. The regulations in § 225.120 through 225.202 apply to facilities manufacturing solely medicated feeds for which an approved license is not required.

(c) In addition to the recordkeeping requirements in this part, Type B and Type C medicated feeds made from Type A medicated articles or Type B feeds under approved NADA's and a medicated feed mill license are subject to the requirements of Sec. 510.301 of this chapter.

### **§ 225.10 Personnel**

(a) Qualified personnel and adequate personnel training and supervision are essential for the proper formulation, manufacture and control of medicated feeds. Training and experience lead to proper use of equipment, maintenance of accurate records and detection and prevention of possible deviations from current good manufacturing practices.

(b) (1) All employees involved in the manufacture of medicated feeds shall have an understanding of the manufacturing or control operation(s) which they perform, including the location and proper use of equipment.

(2) The manufacturer shall provide an on-going program of evaluation and supervision of employees in the manufacture of medicated feeds.

### **Subpart B – Construction and Maintenance of Facilities and Equipment**

#### **§ 225.20 Buildings**

(a) The location, design, construction and physical size of the buildings and other production facilities are factors important to the manufacture of medicated feed. The features of facilities necessary for the proper manufacture of medicated feed include provision for ease of access to structures and equipment in need of routine maintenance; ease of cleaning of equipment and work areas; facilities to promote personnel hygiene; structural conditions for control and prevention of

vermin and pest infestation; adequate space for the orderly receipt and storage of drugs and feed ingredients and the controlled flow of these materials through the processing and manufacturing operations and the equipment for the accurate packaging, and delivery of a medicated feed of specified labeling and composition.

(b) The construction and maintenance of buildings in which medicated feeds are manufactured, processed, packaged, labeled or held shall conform to the following:

(1) The building grounds shall be adequately drained and routinely maintained so that they are reasonably free from litter, waste, refuse, uncut weeds or grass, standing water and improperly stored equipment.

(2) The building(s) shall be maintained in a reasonably clean and orderly manner.

(3) The building(s) shall be of suitable construction to minimize access by rodents, birds, insects and other pests.

(4) The buildings shall provide adequate space and lighting for the proper performance of the following medicated feed manufacturing operations:

(i) The receipt, control and storage of components.

(ii) Component processing.

(iii) Medicated feed manufacturing.

(iv) Packaging and labeling.

(v) Storage of containers, packaging materials, labeling and finished products.

(vi) Routine maintenance of equipment.

#### **§ 225.30 Equipment**

(a) Equipment which is designed to perform its intended function and is properly installed and used is essential to the manufacture of medicated feeds. Such equipment permits production of feeds

of uniform quality, facilitates cleaning and minimizes spillage of drug components and finished product.

- (b) (1) All equipment shall possess the capability to produce a medicated feed of intended potency, safety and purity.
- (2) All equipment shall be maintained in a reasonably clean and orderly manner.
- (3) All equipment, including scales and liquid metering devices, shall be of suitable size, design, construction, precision and accuracy for its intended purpose.
- (4) All scales and metering devices shall be tested for accuracy upon installation and at least once a year thereafter or more frequently as may be necessary to insure their accuracy.
- (5) All equipment shall be so constructed and maintained as to prevent lubricants and coolants from becoming unsafe additives in feed components or medicated feed.
- (6) All equipment shall be designed, constructed, installed and maintained so as to facilitate inspection and use of cleanout procedure(s).

**§ 225.35 Use of work areas, equipment and storage areas for other manufacturing and storage purpose**

- (a) Many manufacturers of medicated feeds are also involved in the manufacture, storage or handling of products which are not intended for animal feed use, such as fertilizers, herbicides, insecticides, fungicides, rodenticides and other pesticides. Manufacturing, storage or handling of nonfeed and feed products in the same facilities may cause adulteration of feed products with toxic or otherwise unapproved feed additives.
- (b) Work areas and equipment used for the manufacture or storage of medicated feeds or components thereof shall not be used for and shall be physically separated from, work areas and equipment used for the manufacture of fertilizers, herbicides, insecticides, fungicides, rodenticides and other pesticides unless such articles are approved drugs or approved food additives intended for use in the manufacture of medicated feed.

**Subpart C – Product Quality Control**

**§ 225.42 Components**

- (a) A medicated feed, in addition to providing nutrients, is a vehicle for the administration of a drug, or drugs, to animals. To ensure proper safety and effectiveness, such medicated feeds must contain the labeled amounts of drugs. It is necessary that adequate procedures be established for the receipt, storage and inventory control for all such drugs to aid in assuming their identity, strength, quality and purity when incorporated into products.
- (b) The receipt, storage and inventory of drugs, including undiluted drug components, medicated premixes and semiprocessed (i.e., intermediate premixes, in-plant premixes and concentrates) intermediate mixes containing drugs, which are used in the manufacture and processing of medicated feeds, shall conform to the following:
  - (1) Incoming shipments of drugs shall be visually examined for identity and damage. Drugs which have been subjected to conditions which may have adversely affected their identity, strength, quality or purity shall not be accepted for use.
  - (2) Packaged drugs in the storage areas shall be stored in their original closed containers.
  - (3) Bulk drugs shall be identified and stored in a manner such that their identity, strength, quality and purity will be maintained.
  - (4) Drugs in the mixing areas shall be property identified, stored, handled and controlled to maintain their integrity and identity. Sufficient space shall be provided for the location of each drug.
  - (5) A receipt record shall be prepared and maintained for each lot of drug received. The receipt record shall accurately indicate the identity and quantity of the drug, the name of the supplier,

- the supplier's lot number or an identifying number assigned by the feed manufacturer upon receipt which relates to the particular shipment, the date of receipt, the condition of the drug when received and the return of any damaged drugs.
- (6) A daily inventory record for each drug used shall be maintained and shall list by manufacturer's lot number or the feed manufacturer's shipment identification number at least the following information:
- (i) The quantity of drugs on hand at the beginning and end of the work day (the beginning amount being the same as the previous day's closing inventory if this amount has been established to be correct); the quantity shall be determined by weighing, counting or measuring, as appropriate.
  - (ii) The amount of each drug used, sold or otherwise disposed of.
  - (iii) The batches or production runs of medicated feed in which each drug was used.
  - (iv) When the drug is used in the preparation of a semiprocessed intermediate mix intended for use in the manufacture of medicated feed, any additional information which may be required for the purpose of paragraph (b) (7) of this section.
  - (v) Action taken to reconcile any discrepancies in the daily inventory record.
- (7) Drug inventory shall be maintained for each lot or shipment of drug by means of a daily comparison of the actual

amount of drug used with the theoretical drug usage in terms of the semiprocessed, intermediate and finished medicated feeds manufactured. Any significant discrepancy shall be investigated and corrective action taken. The medicated feed(s) remaining on the premises which are affected by this discrepancy shall be detained until the discrepancy is reconciled.

- (8) All records required by this section shall be maintained on the premises for at least one year after complete use of a drug component of a specific lot number or feed manufacturer's shipment identification.

#### **§ 225.58 Laboratory Controls**

- (a) The periodic assay of medicated feeds for drug components provides a measure of performance of the manufacturing process in manufacturing a uniform product of intended potency.
- (b) The following assay requirements shall apply to medicated feeds:
  - (1) For feeds requiring a medicated feed mill license (Form FDA-3488) for their manufacture and marketing, at least three representative samples of medicated feed containing each drug or drug combination used in the establishment shall be collected and assayed by approved official methods, at periodic intervals during the calendar year, unless otherwise specified in this chapter. At least one of these assays shall be performed on the first batch using the drug. If a medicated feed contains a combination of drugs, only one of the drugs need be subject to analysis each time, provided the one tested is different from the one(s) previously tested.

- (2) (Reserved)
- (c) The originals or copies of all results of assays, including those from state feed control officials and any other governmental agency, shall be maintained on the premises for a period of not less than one year after distribution of the medicated feed. The results of assays performed by state feed control officials may be considered toward fulfillment of the periodic assay requirements of this section.
  - (d) Where the results of assays indicate that the medicated feed is not in accord with label specifications or is not within permissible assay limits as specified in this chapter, investigation and corrective action shall be implemented and an original or copy of the record of such action maintained on the premises.
  - (e) Corrective action shall include provisions for discontinuing distribution where the medicated feed fails to meet the labeled drug potency. Distribution of subsequent production of the particular feed shall not begin until it has been determined that proper control procedures have been established.

#### **§ 225.65 Equipment Cleanout Procedures**

- (a) Adequate cleanout procedures for all equipment used in the manufacture and distribution of medicated feeds are essential to maintain proper drug potency and avoid unsafe contamination of feeds with drugs. Such procedures may consist of cleaning by physical means; e.g., vacuuming, sweeping, washing. Alternatively, flushing or sequencing or other equally effective techniques may be used whereby the equipment is cleaned either through use of a feed containing the same drug(s) or through use of drug-free feedstuffs.
- (b) All equipment, including that used for storage, processing, mixing, conveying and distribution that comes in contact with the active drug component feeds in process or finished medicated feed shall be subject to all reasonable and effective procedures to prevent unsafe contamination of manufactured feed.

The steps used to prevent unsafe contamination of feeds shall include one or more of the following or other equally effective procedures:

- (1) Such procedures shall, where appropriate, consist of physical means (vacuuming, sweeping or washing), flushing and/or sequential production of feeds.
- (2) If flushing is utilized, the flush material shall be properly identified, stored and used in a manner to prevent unsafe contamination of other feeds.
- (3) If sequential production of medicated feeds is utilized, it shall be on a predetermined basis designed to prevent unsafe contamination of feeds with residual drugs.

#### **Subpart D – Packaging and Labeling** **§ 225.80 Labeling**

- (a) Appropriate labeling identifies the medicated feed and provides the user with directions for use which, if adhered to, will assure that the article is safe and effective for its intended purposes.
- (b) (1) Labels and labeling, including placards, shall be received, handled and stored in a manner that prevents labeling mix-ups and assures that correct labeling is employed for the medicated feed.
- (b) (2) Labels and labeling, including placards, upon receipt from the printer shall be proofread against the master record file to verify their suitability and accuracy. The proofread label shall be dated, initialed by the responsible individual and kept for one year after all the labels from that batch have been used.
- (b) (3) In those instances where medicated feeds are distributed in bulk, complete labeling shall accompany the shipment and be supplied to the consignee at the time of delivery. Such labeling may consist of a placard or other labels attached to the invoice or delivery ticket or manufacturer's invoice that identifies the medicated feed and includes adequate information for the safe and effective use of the medicated feed.

(b) (4) Label stock shall be reviewed periodically and discontinued labels shall be discarded.

## **Subpart E – Records and Reports**

### **§ 225.102 Master Record File and Production Records**

- (a) The master record file provides the complete procedure for manufacturing a specific product, setting forth the formulation, theoretical yield, manufacturing procedures, assay requirement(s) and labeling of batches or production runs. The production record(s) include(s) the complete history of a batch or production run. This record includes the amounts of drugs used, the amount of medicated feed manufactured and provides a check for the daily inventory record of drug components.
- (b) The master record file and production records shall comply with the following provisions:

(1) A master record file shall be prepared, checked, dated and signed or initialed by a qualified person and shall be retained for not less than one year after production of the last batch or production run of medicated feed to which it pertains. The master record file or card shall include at least the following:

- (i) The name of the medicated feed.
- (ii) The name and weight percentage or measure of each drug or drug combination and each nondrug ingredient to be used in manufacturing a stated weight of the medicated feed.
- (iii) A copy or description of the label or labeling that will accompany the medicated feed.
- (iv) Manufacturing instructions or reference thereto that have been determined to yield a properly mixed medicated feed of the specified formula for each medicated feed

produced on a batch or continuous operation basis, including mixing steps, mixing times, and, in the case of medicated feeds produced by continuous production run, any additional manufacturing directions including, when indicated, the setting of equipment.

- (v) Appropriate control directions or reference thereto, including the manner and frequency of collecting the required number of samples for specified laboratory assay.
- (2) The original production record or copy thereof shall be prepared by qualified personnel for each batch or run of medicated feed produced and shall be retained on the premises for not less than one year. The production record shall include at least the following:
- (i) Product identification, date of production and a written endorsement in the form of a signature or initials by a responsible individual.
  - (ii) The quantity and name of drug components used.
  - (iii) The theoretical quantity of medicated feed to be produced.
  - (iv) The actual quantity of medicated feed produced. In those instances where the finished feed is stored in bulk and actual yield cannot be accurately determined, the firm shall estimate the quantity produced and provide the basis for such estimate in the master record file.
- (3) In the case of a custom formula feed made to the specifications of a customer, the master record file and production records required by this section shall consist either of such records or of copies of

- the customer's purchase orders and the manufacturer's invoices bearing the information required by this section. When a custom order is received by telephone, the manufacturer shall prepare the required production records.
- (4) Batch production records shall be checked by a responsible individual at the end of the working day in which the product was manufactured to determine whether all required production steps have been performed. If significant discrepancies are noted, an investigation shall be instituted immediately and the production record shall describe the corrective action taken.
  - (5) Each batch or production run of medicated feed shall be identified with its own individual batch or production run number, code, date or other suitable identification applied to the label, package, invoice or shipping document. This identification shall permit the tracing of the complete and accurate manufacturing history of the product by the manufacturer.

#### **§ 225.110 Distribution Records**

- (a) Distribution records permit the manufacturer to relate complaints to specific batches and/or production runs of medicated feed. This information may be helpful in instituting a recall.
- (b) Distribution records for each shipment of a medicated feed shall comply with the following provisions:
  - (1) Each distribution record shall include the date of shipment, the name and address of purchaser, the quantity shipped and the name of the medicated feed. A lot or control number or date of manufacture or other suitable identification shall appear on the distribution record or the label issued with each shipment.

- (2) The originals or copies of the distribution records shall be retained on the premises for not less than one year after the date of shipment of the medicated feed.

#### **§ 225.115 Complain Files**

- (a) Complaints and reports of experiences of product defects relative to the drug's efficacy or safety may provide an indicator as to whether or not medicated feeds have been manufactured in conformity with current good manufacturing practices. These complaints and experiences may reveal the existence of manufacturing problems not otherwise detected through the normal quality control procedures. Timely and appropriate follow-up action can serve to correct a problem and minimize future problems.
- (b) The medicated feed manufacturer shall maintain on the premises a file which contains the following information:
  - (1) The original or copy of a record of each oral and written complaint received relating to the safety and effectiveness of the product produced. The record shall include the date of the complaint, the complainant's name and address, name and lot or control number or date of manufacture of the medicated feed involved and the specific details of the complaint. This record shall also include all correspondence from the complainant and/or memoranda of conversations with the complainant and a description of all investigations made by the manufacturer and of the method of disposition of the complaint.
  - (2) For medicated feeds whose manufacture require a medicated feed mill license (Form FDA-3448), records and reports of clinical and other experience with the drug shall be maintained and reported, under Sec. 510.301 of this chapter.

## **Subpart F – Facilities and Equipment**

### **§ 225.120 Buildings and Grounds**

Buildings used for production of medicated feed shall provide adequate space for equipment, processing and orderly receipt and storage of medicated feed. Areas shall include access for routine maintenance and cleaning of equipment. Buildings and grounds shall be constructed and maintained in a manner to minimize vermin and pest infestation.

### **§ 225.130 Equipment**

Equipment shall be capable of producing a medicated feed of intended potency and purity and shall be maintained in a reasonably clean and orderly manner. Scales and liquid metering devices shall be accurate and of suitable size, design, construction, precision and accuracy for their intended purposes. All equipment shall be designed, constructed, installed and maintained so as to facilitate inspection and use of cleanout procedure(s).

### **§ 225.135 Work and Storage Areas**

Work areas and equipment used for the production or storage of medicated feeds or components thereof shall not be used for and shall be physically separated from, work areas and equipment used for the manufacture and storage of fertilizers, herbicides, insecticides, fungicides, rodenticides and other pesticides unless such articles are approved for use in the manufacture of animal feed.

## **Subpart G – Product Quality Assurance**

### **§ 225.142 Components**

Adequate procedures shall be established and maintained for the identification, storage and inventory control (receipt and use) of all Type A medicated articles and Type B medicated feeds intended for use in the manufacture of medicated feeds to aid in assuring the identity, strength, quality and purity of these drug sources. Packaged Type A medicated articles and Type B medicated feeds shall be stored in designated areas in their original closed containers. Bulk Type A medicated articles and bulk Type B medicated feeds shall be identified and stored in a manner such that their identity, strength, quality and purity will be maintained. All Type A medicated articles and Type B medicated feeds shall be used in accordance with their labeled mixing directions.

### **§ 225.158 Laboratory assays**

Where the results of laboratory assays of drug components, including assays by state feed control officials, indicate that the medicated feed is not in accord with the permissible limits specified in this chapter, investigation and corrective action shall be implemented immediately by the firm and such records shall be maintained on the premises for a period of one year.

### **§ 225.165 Equipment Cleanout Procedures**

Adequate procedures shall be established and used for all equipment used in the production and distribution of medicated feeds to avoid unsafe contamination of medicated and nonmedicated feeds.

## **Subpart H – Labeling**

### **§ 225.180 Labeling**

Labels shall be received, handled and stored in a manner that prevents label mix-ups and assures that the correct labels are used for the medicated feed. All deliveries of medicated feeds, whether bagged or in bulk, shall be adequately labeled to assure that the feed can be properly used.

## **Subpart I – Records**

### **§ 225.202 Formula, Production and Distribution Records**

Records shall be maintained identifying the formulation, date of mixing and if not for own use, date of shipment. The records shall be adequate to facilitate the recall of specific batches of medicated feed that have been distributed. Such records shall be retained on the premises for one year following the date of last distribution.