Guidance for FDA Staff and Industry

Draft Compliance Policy Guides Manual

Sec. 6xx.yyy **VOLUNTARY SELF INSPECTION OF MEDICATED FEED MANUFACTURING FACILITIES**

Submit written comments on this draft compliance policy guide (CPG) identified with Docket No. 2007D-0027, to the Division of Dockets Management (HFA-305), 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Additional copies of this document may be obtained from the Internet at: http:www.fda.gov/ora/compliance_ref/cpg/default.htm, or http://www.fda.gov/OHRMS/DOCKETS/98fr/03d-0290-gd10001.pdf or by sending a request to the Division of Compliance Policy (HFC-230), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

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Guidance for FDA Staff and Industry

COMPLIANCE POLICY GUIDES MANUAL

Sec. 6xx.yy VOLUNTARY SELF INSPECTION OF MEDICATED FEED MANUFACTURING FACILITIES

This compliance policy guide is intended to provide guidance and instructions to Food and Drug Administration (FDA) staff. The compliance policy guide is the agency's current thinking on the topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations. It is intended for FDA personnel, industry, and the public and is available electronically to the public.

Background

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word "should" in Agency guidances means that something is suggested or recommended, but not required.

For many years, feed has served as a vehicle to deliver an oral dose of drugs to animals especially in situations that require dosing of multiple animals, multiple dosing regimens, or other situations where hands on administration may be difficult. Virtually all of these drugs intended for use in animal feed are "new animal drugs" as defined by the Federal Food, Drug, and Cosmetic Act (the act) that require FDA review and approval prior to their commercial manufacture, distribution, and use. Pre-market approval requires the submission by a sponsor and the evaluation by FDA of, among other things, safety and effectiveness data based on adequate and well-controlled studies, labeling, and manufacturing controls. [Section 512(b) of the Act {21 U.S.C. 360b(b)}]

When describing the requirements of new animal drugs intended for use in animal feed, the term "animal feed" is defined in the act as "an article which is intended for use for food for animals other than man and which is intended for use as a substantial source of nutrients in the diet of the animal, and is not limited to a mixture intended to be the sole ration of the animal." [Section 201(w) of the act]. Animal feed containing drugs is called "medicated feed."

Manufacturing of medicated feed typically takes place at commercial establishments and on-farm mixer/feeder operations. These firms receive drug ingredients of varying potencies and various amounts of carrier and/or nutritive ingredients.

Section 510 of the act requires producers of drugs, which means those engaged in the manufacture, preparation, propagation, compounding, or processing of drugs, to register with FDA once a year, unless exempt under section 510(g). However, in the case of establishments manufacturing medicated feed, typically only those firms that manufacture Type B or Type C medicated feed from Category II, Type A medicated articles are required to register under Section 510 of the act [21 U.S.C. 360]. (There are some exceptions. See 21 CFR 207.10(f)(3)) These firms must also be licensed by FDA, 21 CFR 558.4(a), and are referred to as "FDA-licensed feed mills." Feed mills manufacturing medicated feeds which are exempt from the section 510 registration requirements under 21 CFR 207.10(f) are not required to be licensed by FDA. 21 CFR 558.4(b). These firms are referred to as "non FDA-licensed feed mills". These firms are still subject to other applicable provisions of the act. [Definitions for the types and categories of medicated articles and feeds can be found in 21 CFR 558.3 and 558.4 and in Compliance Program 7371.004]

Manufacturing Controls - CGMP

Manufacturing controls for the production of medicated feed include compliance with Current Good Manufacturing Practice for Medicated Feeds regulations, published in Title 21, Code of Federal Regulations, Part 225 (CGMP). These regulations represent MINIMUM standards that must be met in the manufacture of medicated feed.

Medicated feed that is not produced in compliance with these regulations is adulterated under Section 501(a)(2)(B) of the act [21 U.S.C. 351(a)(2)(B)]. Section 501(a)(2)(B) provides that a drug (including a drug contained in a medicated feed) is 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 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. See 21 CFR 225.1(a).

Inspection of the Feed Manufacturing Industry

There are approximately 1,130 FDA-licensed feed mills, approximately 5,500 non FDA-licensed commercial feed mills, and an undetermined number of non FDA-licensed on-farm mixer/feeder operations. Although this inventory may vary from year to year, it still represents a significant number of establishments that are manufacturing medicated feeds. Many of these feeds are for use in food-producing animals. Oversight of these firms is essential to assuring that medicated feeds are properly manufactured so that edible products, including meat, milk, and eggs, from animals that consume these feeds are safe and do not contain potentially hazardous residues of drugs and other chemicals. In addition, proper production of medicated animal feed is essential to protecting the health and safety of the animal itself.

Section 704 of the act authorizes FDA to conduct inspections of firms that manufacture, process, pack, or hold drugs. Section 510(h) of the act requires inspection of every registered establishment at least once in the two-year period beginning with the date of registration and at least once in every successive two-year period. In the case of establishments manufacturing medicated feed, typically only those firms that manufacture Type B or Type C medicated feed from Category II, Type A medicated articles are required to register under Section 510 and be inspected at least once every two years. There are some exceptions as noted in the Background section of this CPG. [21 CFR 207.10 and 207.20(a)]

The mandatory two-year inspection of FDA-licensed feed mills is conducted by both FDA staff and individual state regulatory personnel commissioned by FDA. Information for FDA staff regarding these inspections is contained in Compliance Program 7371.004, Feed Manufacturing Compliance Program, found in FDA's Compliance Program Guidance Manual. Non FDA-licensed feed mills are also subject to inspection under section 704, but we are not required under the act to conduct inspections of these establishments every two years.

Voluntary Self Inspection

Many feed manufacturing operations do not routinely check for compliance with CGMP as part of their quality procedures. Instead, problems or potential problems are identified when FDA or state investigators conduct an inspection for compliance with CGMP. However, many FDA-licensed feed mills do conduct their own internal assessment to ensure they are complying with CGMP. They may have quality assurance programs in place that include some periodic audit or assessment provision, i.e., a "self inspection." The concept of medicated feed mill "self inspection" was incorporated in the Association of American Feed Control Officials (AAFCO) proposed Model National Medicated Feed Program, designed to: (1) provide a credible, visible and cost-effective method for ensuring the use of prudent feed manufacturing practices; (2) promote self-regulation and implementation of quality assurance principles by all sectors of the regulated industry; (3) enable FDA and State regulatory authorities to focus and prioritize regulatory, compliance, and inspection efforts to enhance efficiency and cost-effectiveness; (4) foster a uniform regulatory environment among the regulated industry; (5) enhance compliance by providing ongoing education for the regulated industry; (6) and, promote expeditious, equitable, and consistent application of enforcement of the regulated industry. It is referred to as "VSIP" for Voluntary Self Inspection Program in that Model.

We encourage the use of quality assurance programs that include internal audits or assessments for compliance with CGMP. When properly implemented, these measures can enhance public health by providing increased assurance of a medicated feed manufacturing establishment's compliance with CGMP through means that supplement FDA's inspectional program.

Policy

In determining inspectional priorities for CGMP inspections for medicated feed manufacturing

establishments, we intend to consider, among other factors, whether the establishments follow the approach outlined in the Section entitled "Voluntary Self Inspection Conduct and Reporting". We intend to give a higher priority to medicated feed manufacturing establishments that do not:

1. Promptly and completely correct CGMP violations after opportunity for correction; and/or

2. Conduct self inspections as described in the Section entitled "Voluntary Self Inspection Conduct and Reporting".

This action should allow us to:

1. More effectively focus and utilize available resources in monitoring and inspecting medicated feed manufacturing establishments that have a history of non-compliance with CGMP regulations or for which FDA has no information regarding their compliance.

2. Recognize the pro-active and successful efforts of those feed manufacturing establishments that have taken steps to assure compliance with CGMP.

Voluntary Self Inspection Conduct and Reporting

The self inspection approach described in this CPG is voluntary. FDA staff may advise an establishment about this approach during an inspection or other interaction with personnel from the establishment but you need to emphasize that participation is voluntary.

For medicated feed manufacturers wishing to participate, the voluntary self inspection program is as follows:

1. Notify the local FDA Field Office in writing of its intent to conduct self inspections for compliance with CGMP. The notification should include:

   - The name and address of the facility;
   - The name, title, and signature of the most responsible person at the facility;
   - A statement that the facility will operate in full compliance with CGMP in 21 CFR Part 225; and
   - A statement that the inspection will be conducted by a qualified responsible person(s).

2. The facility may request that FDA conduct an inspection to verify current compliance with CGMP if the facility has not had a "passed" CGMP compliance inspection within the previous two years, or if it "failed" (i.e., not in substantial compliance) the last inspection during this period.

3. Conduct a self inspection at least once a year beginning the year of the notification.

4. Review any previous self-inspections to ensure that all necessary corrective actions have been taken.

5. For FDA-licensed feed mills, report the results of the self inspection on FDA Form 3621, the "Voluntary Inspection Report for FDA Licensed Medicated Feed Establishments" (Attachment 1). If the facility is not licensed with FDA, report the results of the self inspection on FDA Form 3622, "Voluntary Inspection Report for FDA Non-Licensed Medicated Feed Establishments" (Attachment 2).

6. Have a responsible person from the facility review all observations on the inspection form, formulate corrective action to be taken if necessary, and establish a target date for resolution of any deficient areas. Deficiencies could fall into one or more of the following categories:

- Deficiencies correctable at the time of inspection;
- Deficiencies requiring changes in procedures to ensure compliance;
- Deficiencies requiring additional employee training or employee changes to ensure compliance; or
- Deficiencies that have been ongoing and continue to occur.

7. If there were deficiencies that have been ongoing and continue to occur, self reinspect within ninety (90) days to ensure they have been corrected.

8. Have a responsible person from the facility submit a written report to the local FDA Field Office within sixty (60) days of self inspection. The report should include the following:

a. The name and title of the person(s) who conducted the self inspection;
b. The date(s) of the inspection;
c. A copy of the completed inspection report. If deficiencies are found, a report describing corrective action taken or to be taken; and
d. A report of any deficiencies that have been ongoing and continue to occur. The results of the ninety (90)-day follow-up inspection should be submitted as a supplement to this report.

9. The person(s) who conducted the self inspection should be available to answer FDA's questions about how the self inspection was conducted. This may be done by telephone.

Nothing in this guidance restricts FDA from conducting inspections or affects the legal responsibilities of medicated feed establishments (e.g., reporting under Title 21, Code of Federal Regulations, Section 510.301 for sponsors of new animal drugs used in feed). Even if the firm

conducts self inspections and provides the information described above, we do not intend to change our inspectional priority when we have information that a problem may exist. In addition, FDA intends to conduct random audits to verify the conduct and results of the self inspections.