CHAPTER 71: POST APPROVAL MONITORING OF ANIMAL DRUGS, FEEDS, AND DEVICES

SUBJECT:	**IMPLEMENTATION DATE:**
COMPREHENSIVE ANIMAL FOOD INSPECTION	02/08/2021

DATA REPORTING

PRODUCT CODES	**PRODUCT/ASSIGNMENT CODES (PAC)**
USE APPROPRIATE PRODUCT CODES	**REPORT PROGRAM ACTIVITIES UNDER THE FOLLOWING PAC CODES:**
	FDA PACs **71004** MEDICATED FEED MANUFACTURING CGMP INSPECTIONS - LICENSED FACILITIES **71009** BSE INSPECTIONS **71012** MEDICATED FEED MANUFACTURING CGMP INSPECTIONS – NON-LICENSED FACILITIES **71014** PART 507 CGMP INSPECTIONS **71015** PART 507 CGMP/PC INSPECTIONS **71016** MODIFIED REQUIREMENTS INSPECTIONS AT ANIMAL FOOD QUALIFIED FACILITIES **71017** MODIFIED REQUIREMENTS INSPECTIONS AT ANIMAL FOOD STORAGE FACILITIES SOLELY ENGAGED IN UNEXPOSED PACKAGED FOOD THAT REQUIRE TIME/TEMPERATURE CONTROLS FOR SAFETY **71018** ANIMAL FOOD SANITARY TRANSPORTATION INSPECTIONS **71023** VETERINARY FEED DIRECTIVE INSPECTIONS **71030** ANIMAL FOOD FD&C ACT INSPECTIONS **71R894** ANIMAL FOOD RISK-DATA FORM

	STATE PACs **71S004** STATE CONTRACT MEDICATED FEED MANUFACTURING CGMP INSPECTIONS – LICENSED FACILITIES **71S011** STATE CONTRACT BSE INSPECTIONS **71S012** STATE CONTRACT MEDICATED FEED MANUFACTURING CGMP INSPECTIONS – NON-LICENSED FACILITIES **71S014** STATE CONTRACT PART 507 CGMP INSPECTIONS **71S015** STATE CONTRACT PART 507 CGMP/PC INSPECTIONS **71S016** STATE CONTRACT MODIFIED REQUIREMENTS INSPECTIONS AT ANIMAL FOOD QUALIFIED FACILITIES **71S017** STATE CONTRACT MODIFIED REQUIREMENTS INSPECTIONS AT ANIMAL FOOD STORAGE FACILITIES SOLELY ENGAGED IN UNEXPOSED PACKAGED FOOD THAT REQUIRE TIME/TEMPERATURE CONTROLS FOR SAFETY **71S018** STATE CONTRACT ANIMAL FOOD SANITARY TRANSPORTATION INSPECTIONS **71S023** STATE CONTRACT VETERINARY FEED DIRECTIVE INSPECTIONS **71S894** STATE CONTRACT ANIMAL FOOD RISK-DATA FORM

FIELD REPORTING REQUIREMENTS:

Establishment inspection reports (EIRs) must be completed in eNSpect per Investigations Operations Manual (IOM) subchapter 5.11 *Establishment Inspection Report (EIR)*. Investigational reports must be prepared per IOM subchapter 8.10 *General Investigation Reporting*. Corrective actions taken during an inspection must be documented in the Observations and Corrective Action Reporting (OCAR) system – Corrective Action Report (CAR) within eNSpect. Compliance activities must be performed as outlined in the Regulatory Procedures Manual (RPM). Division recommendations coupled with their supporting evidence for a compliance action or actions should only be submitted to the Center for Veterinary Medicine (hereafter CVM or the Center) using Compliance Management Services (CMS) database.

Contents

Change History
Description of the initial issuance and changes to the compliance program.

Item	Change	Date
Issuance	CPGM 7371.000 initial issuance. This is the original version of the compliance program.	02/08/2021

Glossary

Inspectional Terms

Comprehensive Inspection - inspection covering everything in the facility subject to FDA jurisdiction to determine the facility's compliance status (IOM Subchapter 5.1.2 *Inspectional Approach*).

Directed Inspection – inspection with coverage directed to specific areas to the depth described in the program, assignment, or as instructed by your supervisor (IOM Subchapter 5.1.2 *Inspectional Approach*).

For-cause (Compliance) Inspection - An inspection that is carried out in response to specific information that raises questions, concerns, or problems associated with an FDA regulated firm or commodity. This information could come to the attention of FDA from any source, and includes, but is not limited to, the following: the results of a sample analysis, observations made during prior inspections, recall or market withdrawal, consumer or employee complaint, adverse reaction report, or suspicion of fraud. (RPM Chapter 11 *Glossary*).

Routine Inspection – surveillance inspection performed at the normal frequency (IOM Subchapter 5.2.3.1.1 *Individual Headings*).

Follow-up Inspection – inspection conducted in follow-up to a violative inspection (IOM Subchapter 5.2.3.1.1 *Individual Headings*).

Field Inspection Staff – FDA and State staff performing inspections on behalf of FDA.

Facility Terms

Facility – all animal food establishments that are subject to any requirements covered by this comprehensive animal food compliance program. When information in this compliance program is linked to registered food facilities, we use the phrase "registered food facility," or a "facility that must register as a food facility."

Registered food facility – A subset of the term "facility" that manufactures, processes, packs, or holds animal food and is required to register as a food facility under 21 CFR part 1, subpart H.

Retail Food Establishment – A subset of "facility" that is exempt from food facility registration as defined in 21 CFR §1.227. Note, that some animal food facilities that retail do not meet the definition of a retail food establishment because they sell more animal food to farms, which are considered businesses, than to consumers. See Appendix A section 1.A. *Food Facility Registration (21 CFR part 1, subpart H)* – for a full discussion of retail feed stores.

Licensed medicated feed mill – A "facility" that manufactures, processes, packs, or holds medicated feed that requires a medicated feed mill license and drug establishment registration as required by 21 CFR §558.4.

Non-licensed medicated feed mill - A subset of the term "facility" that manufactures, processes, packs or holds medicated feed that does not require a medicated feed mill license.

Animal Food Terms

Animal Food – means food for animals other than man and includes pet food, animal feed, and raw materials and ingredients as defined in 21 CFR §507.3.

Feed – This term is historically used to describe animal food in statutory and regulatory requirements related to medicated feed, veterinary feed directive, and prohibited materials (i.e., the bovine spongiform encephalopathy (BSE) requirements). In this compliance program we have used this term when referencing the language of these statutory and regulatory requirements; however, feed is synonymous with animal food.

PART I – BACKGROUND

Historically, FDA's inspection of animal food facilities was limited to inspections of licensed medicated feed mills under the medicated feed current good manufacturing practice (CGMP) requirements in 21 CFR part 225 and inspection of animal food facilities for compliance with the Bovine Spongiform Encephalopathy (BSE) regulation found in 21 CFR §§589.2000-2001. FDA's regulation of animal food has changed significantly in recent years due to two key regulatory changes: (1) the implementation of the Food Safety Modernization Act (FSMA) and it's implementing regulations; and (2) the voluntary effort of drug sponsors to switch medically important antimicrobials administered in animal feed from an over-the-counter marketing status to a veterinary feed directive (VFD) marketing status.

This comprehensive animal food compliance program incorporates and replaces the following compliance programs: 7371.004 Medicated Feed Manufacturing Compliance Program and 7371.009 BSE/Ruminant Feed Ban Inspections. In addition to incorporating those compliance programs (now subprograms), this comprehensive animal food compliance program also covers the following subprograms: (1) the Current Good Manufacturing Practice, Hazard Analysis and Risk-Based Preventive Controls Food for Animals requirements, hereinafter referred to as the Preventive Controls for Animal Food (PCAF) requirements; (2) the Veterinary Feed Directive (VFD) requirements; and (3) the Sanitary Transportation (ST) requirements. This compliance program also covers a discussion of several topics that are ancillary to these inspections, including food facility registration, medicated feed mill licensing and drug establishment registration, and VFD distributor notification requirements. In addition, this compliance program provides direction regarding inspections of animal food facilities not subject to any of these specific regulations (e.g., under statutory adulteration or misbranding standards).

1. Summary of Comprehensive Inspection Model

As a result of the recent regulatory changes, the Center has been moving towards a compliance program model that encompasses all of the regulatory requirements that may be applicable to a particular animal food facility. The comprehensive inspection approach serves two purposes: (1) implement a systems-based approach to evaluate whether a facility is implementing practices necessary to meet all the animal food safety regulatory requirements that apply at their facility; and (2) efficiently utilize inspectional resources.

This compliance program lays out the approach for the Divisions and commissioned State agencies conducting contract work to conduct a comprehensive animal food inspection by assessing the following applicable subprograms:

- Food Facility Registration (21 CFR part 1, subpart H), Medicated Feed Mill Licensing and Registration (21 CFR §558.4) and Veterinary Distributor Notification requirements (21 CFR §558.6(c)(5))
- Current Good Manufacturing Practice, Hazard Analysis, and Risk Based Preventive Controls for Food for Animals (PCAF) requirements (21 CFR part 507)
- Current Good Manufacturing Practice for Medicated Feeds requirements (21 CFR part 225)
- Veterinary Feed Directive (VFD) requirements (21 CFR §558.6)
- Prohibited Materials in Ruminant Animal Food (BSE) requirements (21 CFR §§589.2000-2001)
- **DIRECTED ONLY:** Sanitary Transportation (ST) requirements (21 CFR part 1, subpart O)
- Animal Food Subject to FD&C Act Adulteration Provisions (21 U.S.C. 342)

As a result, this comprehensive animal food compliance program is organized as follows:

- Parts II-V cover the areas that are common across all subprogram areas. These sections are important for understanding how the subprograms interact under one comprehensive inspection approach.
- Each subprogram's appendix covers the details for inspectional approach and compliance information related to each subprogram. These appendices are important for understanding how to appropriately inspect a facility's compliance with the subprogram's regulatory requirements.

As a result, first review Parts II-V to understand the overall comprehensive animal food inspection approach, and then review specific appendices, based on what subprograms apply at the facility, prior to conducting an inspection.

2. Summary of Food Facility Registration, Medicated Feed Mill Licensing and Registration, and Veterinary Feed Directive Distributor Notification Requirements

The activities an animal food facility is engaged in will determine if a facility is required to register, obtain a license, and/or submit notifications to the FDA. Examples relevant to animal food facilities that will be inspected under this compliance program include:

- Food Facility Registration (21 CFR part 1, subpart H)
- Medicated Feed Mill Licensing and Drug Establishment Registration (21 CFR §558.4)
- VFD Distributor Notification (21 CFR §558.6)

For simplicity, the terms "facility" or "facilities" will be utilized in this compliance program to generally refer to animal food businesses (see *Glossary*). When referring to facilities subject to a certain registration, license, or notification requirement, the compliance program will specifically use the language of that registration, licensure, or notification requirement, such as "registered food facility," "licensed medicated feed mill" or "VFD distributor."

For more information on these requirements, see *APPENDIX A – Registration, Licensing and Notification Requirements*.

3. Summary of PCAF Requirements (21 CFR part 507)

The Current Good Manufacturing Practice, Hazard Analysis, and Risk-based Preventive Controls for Food for Animals (PCAF) regulation has two primary components: (1) the current good manufacturing practice (CGMP) requirements; and (2) the hazard analysis and risk-based preventive controls (PC) requirements. Related personnel, training, and recordkeeping requirements are located in 21 CFR part 507, subparts A and F.

The CGMP requirements provide baseline safety and sanitation standards for the manufacturing, processing, packing, and holding of animal food. These CGMPs address general animal food safety and sanitation concerns. The CGMP requirements are located in 21 CFR part 507, subpart B. Additional information and guidance can be found in Guidance for Industry #235: Current Good Manufacturing Practice Requirements for Food for Animals.

The PC requirements provide a framework for facilities to assess the food safety hazards associated with their animal food and animal food facility. When appropriate, the facility must establish risk-based preventive controls designed to control their identified hazards. The PC requirements also include a

system of management components to verify that the hazards have been controlled in the animal food. Additional information and guidance can be found in Draft Guidance for Industry #245: Hazard Analysis and Risk-Based Preventive Controls for Food for Animals.

The PCAF CGMP and PC requirements generally apply to all facilities that are required to register as a food facility because they manufacture, process, pack, or hold animal food for consumption in the U.S. **Note: The PCAF CGMPs only apply to registered animal food facilities. This is a key difference between human and animal food CGMP requirements.** There are a number of exemptions and modified requirements for facilities based on their animal food, or the activities the facility is performing. These exemptions and modified requirements are found in 21 CFR §§ 507.5, 507.7, 507.10, and 507.12 and are explained in depth in Part III.1.A. *Inspections* and *APPENDIX B – PCAF Requirements (21 CFR part 507)*.

See *APPENDIX B – PCAF Requirements (21 CFR part 507)* for information on how to conduct these establishment inspections.

4. Summary of Medicated Feed Current Good Manufacturing Practice (CGMP) Requirements (21 CFR part 225)

The medicated feed CGMP requirements include the methods, facilities and equipment, or controls used for manufacturing, processing, packing, or holding a medicated feed to ensure the medicated feed meets the requirements for safety and has the identity, strength, quality and purity characteristics as identified in the new animal drug approval, conditional approval, or index listing.

The CGMPs in 21 CFR part 225 set forth the criteria for determining whether the manufacture of a medicated feed is in compliance with current good manufacturing practice for all types of facilities and equipment used in the production of medicated feeds (21 CFR §225.1(b)(1)). These CGMPs are divided into two sections and 21 CFR §225.1(b)(2) explains which section applies based on whether the facility is required to obtain a medicated feed mill license and register as a drug establishment.

- Facilities required to obtain a medicated feed mill license and register as a drug establishment must follow 21 CFR §225.10 through §225.115
- Facilities that are not required to obtain a medicated feed mill license and register as a drug establishment must follow 21 CFR §225.120 through §225.202.

The CGMPs in 21 CFR part 225 were implemented prior to the CGMPs in 21 CFR part 507. There is overlap between these CGMPs, especially with respect to building, grounds, employees, supervisors, management, equipment, and utensils requirements. However, the medicated feed CGMPs include requirements specific to the proper inclusion of drugs into the medicated feed and controls to ensure that drugs are not inadvertently included into other batches of animal food.

Information about how compliance with the medicated feed CGMPs in 21 CFR part 225 interacts with the CGMPs and PCs in 21 CFR part 507 is located in Part III.1.A.2 *Medicated Feed Inspection (21 CFR part 225, PACs 71004 and 71S004 or 71012 and 71S012)* and Appendix B.1.B.(2)(a) *Hazard Analysis*. In addition, the 21 CFR part 225 citation spreadsheet includes notes regarding areas of overlap between the medicated feed CGMPs found in 21 CFR part 225 and the CGMPs found in 21 CFR part 507. This spreadsheet can be located in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

See *APPENDIX C – Medicated CGMP Requirements (21 CFR part 225)* for information on how to conduct these facility inspections.

5. Summary of Veterinary Feed Directive Requirements (21 CFR §558.6)

The Veterinary Feed Directive (VFD) requirements provide a framework for the authorization, use, and distribution of medicated feeds with a veterinary feed directive marketing status. The requirements apply to the veterinarian authorizing the use of the VFD feed, the distributor of the VFD feed, and the client using the VFD feed. The regulation contains a set of general requirements in 21 CFR §558.6(a) that apply to all three roles, with more specific requirements for authorizing veterinarians in 21 CFR §558.6(b) and VFD distributors in 21 CFR §558.6(c).

See *APPENDIX D – VFD Requirements (21 CFR §558.6)* for information on how to conduct these establishment inspections.

6. Summary of Prohibited Materials in Ruminant Animal Food (BSE) Requirements (21 CFR §§589.2000 and 589.2001)

There are two regulations focused on preventing the spread of bovine spongiform encephalopathy (BSE) through animal food. These regulations are sometimes collectively referred to as the "feed ban."

The "Animal Proteins Prohibited From Use In Animal Feeds" regulation is located in 21 CFR §589.2000. This regulation was designed to prevent the establishment and amplification of BSE through animal food, by prohibiting the use of certain proteins derived from mammalian tissue in the feeding of ruminant animals (see Ruminant Feed Inspections).

A second regulation located in 21 CFR §589.2001 prohibits the use of brain and spinal cord from cattle 30 months of age and older from being used in any animal food. This includes all types of livestock and poultry feed, as well as pet food. In infected cattle, the brain and spinal cord contain approximately 85% of the potential infectivity. Therefore, the regulation requires the brain and spinal cord of cattle 30 months of age and older to be removed entirely from the animal food chain, to prevent cross-contamination or accidental or intentional misfeeding. Given the focus on removing the brain and spinal cord from the rendering stream, this regulation is directed towards renderers and slaughter facilities.

See *APPENDIX E – BSE Requirements (21 CFR §§589.2000 and 2001)* for information on how to conduct these establishment inspections.

7. DIRECTED ONLY: Summary of Sanitary Transportation Requirements (21 CFR part 1, subpart O)

Unless otherwise directed, routine surveillance inspections under this CP will not automatically include the ST sub-program. The ST sub-program should not be included as part of a routine surveillance animal food inspection unless specifically identified in the annual workplan and/or FSMA inventory.

When directed, for-cause ST inspections should be performed as part of a comprehensive animal food inspection at carriers or facilities subject to the ST transportation when they meet one of the factors identified in Part II.2.C.(4).(c). *DIRECTED ONLY*: Sanitary Transportation.

The Sanitary Transportation (ST) regulation establishes requirements for shippers, loaders, carriers by motor or rail vehicle, and receivers involved in transporting human and animal food to use sanitary practices to ensure the safety of that food. The purpose of these requirements is to prevent practices during transportation that create food safety risks, such as failure to properly refrigerate food, inadequate cleaning of vehicles between loads, and failure to properly protect food. This regulation applies to both human and animal food and contains sections including *General Provisions, Vehicles and Transportation Equipment, Transportation Operations, Training, Records, and Waivers.*

See *APPENDIX F – Sanitary Transportation Requirements (21 CFR part 1, subpart O)* for information on how to conduct these establishment inspections.

8. Summary of Adulteration and Misbranding Provisions for Facilities not Subject to Specific Animal Food Safety Regulations (21 U.S.C. §§342 and 343)

Some facilities are not subject to the specific regulatory requirements outlined in this comprehensive animal food compliance program because they are not required to register as a food facility and are manufacturing, processing, packing, or holding non-medicated animal food. Examples include, but are not limited to:

- pet food manufacturers that sell directly to consumers and therefore meet the definition of a retail food establishment (i.e., not required to register as a food facility or meet the 21 CFR part 507 requirements); and
- facilities that are exempt and/or under enforcement discretion from the requirements in 21 CFR part 507, such as facilities solely engaged in the holding of raw agricultural commodities.

However, these facilities are still subject to the adulteration and misbranding provisions in the FD&C Act. When performing a comprehensive animal food inspection at these facilities, all adulteration and misbranding provisions and the associated prohibited acts apply if evidence of interstate jurisdiction can be established.

See Part III.1.A.(6) *Adulteration and Misbranding Provisions for Facilities not Subject to Specific Food Safety Regulations (21 U.S.C. §§342 and 343, PAC 71030)* for information on how to conduct these establishment inspections.

PART II - IMPLEMENTATION

1. Objectives

- Identify animal food facilities subject to the animal food safety regulations contained in this compliance program and conduct comprehensive inspections that cover, as applicable:
  - PCAF requirements in 21 CFR part 507
  - Medicated Feed CGMP requirements in 21 CFR part 225
  - VFD requirements in 21 CFR §558.6
  - BSE requirements in 21 CFR §§589.2000 and 589.2001
  - ST requirements in 21 CFR part 1, subpart O
  - Adulteration provisions for facilities not subject to specific food safety regulations (21 U.S.C. 342).
- Conduct inspections within mandated risk-based frequencies and enforcement follow-up timeframes.
- Encourage the timely implementation of voluntary corrective actions by facilities when applicable.
- Ascertain compliance and verify implementation of voluntary corrective actions taken during and after an establishment inspection.
- Document inspectional findings and initiate compliance action for conditions as warranted.

2. Program Management Instructions

A. Inspection Priorities

ORA Divisions will conduct annual animal food facility selection based on CVM's facility risk-ranking process which prioritizes multiple risk factors, including, but not limited to: food safety history (e.g., RFR, recall), time since last inspection, last inspection classification, and the risk level of the product and/or manufacturing process. In addition to these factors, Divisions should consider regional factors and institutional (both Division and State, if applicable) knowledge of inventory, when making final facility selections and assigning facilities to the States or ORA for inspection. Facilities selected should receive a comprehensive animal food inspection that covers all applicable regulations at the facility based on their current animal food activities.

In order to collect information to prioritize facilities by risk, it is important that the Animal Food Risk Data Form be completed for each comprehensive inspection under reporting PAC 71R894/71S894. This can be located in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States). In addition, it is vital that the Firm Management System (FMS) (electronic State Access to FACTS (eSAF) for states) is updated after each inspection with the facility's information (e.g., business name, gross annual sales, number of employees, etc.), appropriate industry codes, product codes, and any applicable District Use Codes (DUCs).

Field inspection staff **must** evaluate all applicable regulations associated with a facility's activities during a comprehensive animal food inspection, as described in this compliance program (e.g., Sanitary Transportation is directed only). As a result, it is important during workplanning that divisions assign work within the division and with their state partners so that facility selection is commensurate with field inspection staff's qualifications.

B. Comprehensive Inspection Priorities

The following types of inspections should receive priority for a comprehensive animal food inspection:

- Compliance (i.e., For-cause) Inspections: follow-up on specific information that raises questions, concerns, or problems associated with a facility, animal food or ingredient. Information includes, but is not limited to: results of sample analysis, observations made during a prior inspection (e.g., OAI follow-up), Center-directed follow-up, Center assignments (e.g., to assess a particular issue), Reportable Food Registry (RFR) reports, recalls, consumer or employee complaints, adverse reaction report (e.g., medicated feed), etc.
- Licensed Medicated Feed Mill Pre-Approval Inspections (must be conducted within 90 calendar days from original application).
- Routine (normal surveillance) of inspection facilities per the workplan inspection numbers, prioritizing:
    - Facilities that are likely subject to 21 CFR part 507, that have not been previously inspected under those applicable regulations.
    - Facilities with a high regulatory priority as designated in part II.2.C(1) *High Regulatory Priority* of this program.

C. Selection of High and Low Regulatory Priority Facilities

(1) High Regulatory Priority

While ORA and CVM continue gathering data for identifying and categorizing facility inventory by risk, inspections should be generally focused on the types of animal food facilities performing higher risk activities or handling higher risk animal foods. For example:

- Manufacturers of animal food that require pathogen controls (e.g., heat treatment, refrigeration, irradiation, environmental controls, etc.) to prevent the adulteration of animal food, such as pet food and treat manufacturers
- Multi-species feed mills that use drugs and micronutrients that may cause harm to some species through cross contamination or nutrient deficiencies and/or toxicities.
- Pre-mix ingredient manufacturers
- Facilities handling prohibited materials that also manufacture food for ruminants
- Medicated Feed facilities that manufacture both medicated articles (Type A) and medicated feed (e.g., there is a higher public health risk because of the potential for cross-contamination with highly concentrated medicated articles). Coordinate resources in the Division to perform an inspection under 21 CFR part 226 for medicated articles under Compliance Program 7371.005 Type A Medicated Articles see Part II.2.F. *Program Interactions*).

(2) Low Regulatory Priority

While ORA and CVM continue gathering data for identifying and categorizing our inventory by risk, some facilities are not currently a high regulatory priority because of enforcement discretion, or because they are not engaged in manufacturing activities or handle only low-risk animal food products. These facilities should not be prioritized until all other facilities in the inventory have received an initial inspection under this compliance program, unless a directed inspection is necessary due to a suspected or confirmed food safety issue. For example:

- Retail farm feed stores that are required to register as a food facility and thus subject to 21 CFR part 507 (See *APPENDIX A – Registration, Licensing and Notification Requirements* for additional discussion of whether a farm feed store would be required to register and Part III.1.A.(1)(b) *CGMP Only Inspection (PAC 71014 and 71S014)* for a discussion of inspectional scope for these facilities).

- Facilities where the only animal food/activities covered under this compliance program are: (1) human food by-products for use as animal food, and (2) the limited manufacturing/processing activities under enforcement discretion for PC requirements. The limited manufacturing/processing activities under enforcement discretion for PC requirements include activities typically performed to facilitate storage and transportation and are limited to the following activities and circumstances:
    - drying/dehydrating, evaporating, pressing, chopping, and similar activities to reduce weight, bulk, or volume, and/or
    - mixing (e.g., combining different vegetable culls and trimmings, combining juice and dairy by-products, stirring), centrifuging, and similar activities to combine ingredients or separate components (e.g., water and solids), and
    - these activities are not performed to prevent or significantly minimize animal food hazards and do not introduce animal food hazards.

  These facilities are subject to the CGMPs in 21 CFR part 507, subpart B, or the CGMPs in 21 CFR part 117, subpart B if they choose (see 21 CFR 507.1(d)). For more information, see Section D of Guidance for Industry: Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs.

- Facilities solely engaged in holding animal food (e.g., warehouses or retail farm stores that are required to register as food facilities).
- Facilities solely engaged in holding and repackaging animal food that will not be handled in the home (e.g., repackaging livestock mineral supplements).

(3) Exemption, Enforcement Discretion or Directed-Only Priority

These facilities should not be inspected under this comprehensive animal food program unless a for-cause (compliance) inspection is necessary due to a suspected or confirmed food safety issue.

- Facilities subject to only the Sanitary Transportation requirements (e.g., not also subject to 21 CFR part 507, 21 CFR part 225, etc.). All Sanitary Transportation inspections will be directed only.
- Facilities that are not subject to the subprograms in this comprehensive animal food inspection program, such as:
    - Facilities that meet the farm definition in 21 CFR 1.227 and do not manufacture medicated feed or distribute VFD drugs (e.g., on-farm mixing of non-medicated feed); or
    - Facilities that meet the definition of a retail food establishment because the majority of their sales are to end consumers instead of businesses (farms are considered businesses). Examples include pet food retail stores and retail feed stores that are not a VFD distributor.
      (See *APPENDIX A – Registration, Licensing and Notification Requirements* for additional discussion of whether a farm feed store would be required to register).
- Facilities with exemptions or enforcement discretion from 21 CFR part 507, such as:

- Cotton ginning operations;
- Silage operations at farm mixed-type facilities;
- Alcohol beverage manufacturers;
- Facilities whose only animal food is by-products of human food that they are not further manufacturing/processing, so it is inspected under the human food regulatory requirements (e.g., 21 CFR §§117.95/507.28 under PAC 71R909); or
- Facilities solely engaged in the holding and storage of raw agricultural commodities (e.g., grain elevators).

Divisions are requested to consult with CVM if questions arise when determining inspectional priorities and the applicability of any animal food regulations to a certain facility or facility type. See Part II.2.H.(1). *Notification of CVM*.

(4) Additional Subprogram Inspectional Priority Information

In addition to the inspection and facility priorities under the comprehensive inspection, there are a few sub-programs that have specific inspectional priorities. This includes inspection priorities that are statutorily required to be prioritized (e.g., medicated feed mill pre-approval inspections). It also includes situations where a sub-program will only be included during a comprehensive animal food inspection under certain circumstances (e.g., VFD trace-forward/back and directed Sanitary Transportation inspections).

(a) Licensed Medicated Feed Mill Pre-Approval Inspections

New licensed medicated feed mill applicants may be newly constructed or acquired facilities, or active medicated feed facilities that wish to secure a license. When a facility applies for a medicated feed mill license, CVM will send a pre-approval inspection request to the appropriate OHAFO Division. Field inspection staff performing these inspections determine whether the facility has the necessary knowledge of CGMP requirements, adequate equipment, drug receipt and inventory controls, formula and production instructions/records, and sampling and assay plans to demonstrate their ability to comply with the CGMP requirements for licensed feed mills (21 CFR §§225.10 - 225.115). This pre-approval inspection should be part of a comprehensive animal food inspection under this compliance program to fully assess all applicable regulations and subsequent compliance of the food facility. For more information on conducting pre-approval inspections see Appendix C.1.B. *Pre-approval Inspections*.

(b) VFD Trace-forward and Trace-back Priorities

For a subset of comprehensive animal food inspections at facilities that are VFD distributors field inspection staff will also conduct trace-forward (at the client) and trace-back (at the veterinarian) inspections. The number of trace-forward/trace-back inspections will be communicated to Divisions during the workplanning process. The Division will select which VFD distributors to conduct trace-forward/trace-back inspections from, based on the following criteria:

- Inspections at distributor that uncover issues with the VFDs as written;
- VFD distributors identified by the Division to best utilize agency resources (e.g., jurisdictional or logistical considerations)
- Client and veterinarian inspections initiated in conjunction with violative drug residue inspections (i.e., when the client is using VFD feed see Part II.2.F.(3). *Illegal Residues in Meat, Poultry, Seafood and Other Animal Derived Foods (CP 7371.006)*)

See *APPENDIX D – VFD Requirements (21 CFR §558.6)* for specifics on how to conduct these establishment inspections.

(c) **DIRECTED ONLY: Sanitary Transportation**

Do not conduct routine surveillance inspections for the Sanitary Transportation (ST) sub-program under this comprehensive animal food Compliance Program, unless specifically directed. Divisions will be notified of the need to perform routine surveillance ST inspections during the workplanning process, or as otherwise directed. If a surveillance inspection under this comprehensive animal food program is suspected to be classified OAI, contact CVM to determine whether the ST sub-program should be covered. See Part II.2.H.(1). *Notification of CVM*.

In addition, directed ST inspections should be performed as part of a comprehensive animal food inspection at carriers or facilities subject to the sanitary transportation rule when:

- an ongoing inspection reveals significant observations related to the transport of food;
- the carrier or facility is responsible for a Class I recall associated with inadequate controls during the transportation of food;
- the previous inspection at the carrier or facility was classified "OAI" and there were significant observations related to the receipt or transport of foods subject the ST Rule; or
- the carrier or facility is implicated in an event that may impact public health. The FDA may obtain this information from federal, state, local, or tribal partners; foreign competent authorities (e.g. the rapid alert system for food and feed (RASFF) or information shared by a foreign competent authority under a cooperative arrangement); from the RFR; from information collected during inspections of other facilities, or from consumer complaints.

As a reminder, the sanitary transportation requirements only apply at facilities that are performing transportation operations and not subject to an exemption or waiver. Generally, this means ST requirements will only apply at facilities that are: (1) distributing exposed (e.g., bulk) animal food; or (2) distributing food that requires a temperature control for safety (regardless of whether bulk or packaged). As a reminder, the ST requirements do not apply to facilities that are farms, retail food establishments, or by-products of human food facilities (unless further manufactured/processed). In addition, do not perform routine surveillance inspections for ST requirements at grain elevators.

D. Comprehensive Inspection Frequency

Ultimately, the goal is to inspect registered animal food facilities at a frequency as mandated by Congress in FSMA section 201 (3 years for high risk; 5 years for non-high risk). This inspection frequency also takes into account the requirement to visit licensed medicated feed mills in accordance with the criteria for a risk-based schedule (see section 510(h) of the FD&C Act). However, when inspectional resource constraints do not allow for such frequencies, the Division should consider these factors in determining inspectional frequency for animal food facilities:

- Use facility priority criteria identified in part II.2.B. *Comprehensive Inspection Priorities* and part II.2.C. *Selection of High and Low Regulatory Priority Facilities* to focus resources on facilities with prior significant observations, and facilities that have not yet been inspected in order to obtain information, allowing for an appropriate facility risk assessment;

- Do not inspect licensed medicated feed mills more frequently than every three years unless a for-cause situation arises; and
- BSE requirements should generally be covered only at facilities that use prohibited materials and come up for reinspection under other subprograms (unless follow-up is necessary from an inspection classified OAI or VAI related to significant BSE deviations).

E. Planning Instructions

(1) Inspections

Comprehensive animal food inspections are to be performed at prioritized facilities as indicated in Part II.2.B. *Comprehensive Inspection Priorities* and Part II.2.C. *Selection of High and Low Regulatory Priority Facilities* of this program.

Field inspection staff **must** evaluate all applicable regulations associated with a facility's activities during a comprehensive animal food inspection, as described in this compliance program (e.g., Sanitary Transportation is directed only). As a result, it is important facility assignments are commensurate with field inspection staff's qualifications.

Inspections must be performed by qualified field inspection staff. Refer to FDA training policies and/or the State Contract Statement of Work for specific training requirements. FSMA inspections under PAC 71014 and PAC 71015 must be conducted by field inspection staff that have successfully completed VM102 and VM220, including any required pre-requisite courses.

(2) Sampling

Compliance (for-cause) and surveillance samples may be collected during inspections covered by this compliance program. These samples may be collected in accordance with interacting compliance programs listed in Part II.2.F. *Program Interactions*

of this program, under routine surveillance sampling programs such as the CP 7371.003 Feed Contaminants Program, CVM or ORA directed field assignments, or as directed for compliance purposes.

If a facility is involved in ongoing compliance activities or the current inspection may be classified OAI due to egregious inspectional findings, the Division must consult with their Compliance Branch **and** CVM to determine whether collection of samples is appropriate. See Part II.2.H.(1). *Notification of CVM*. Likewise, States conducting contract inspections must work with their FDA Program Division Director or their designee and CVM to determine whether collection of samples is appropriate.

(3) Resources and Reporting

Divisions should make every effort to coordinate resources so that inspections conducted under this program cover all requirements a facility is subject to based on their activities. See *Table 1: Resources and Reporting* for additional resources and reporting information.

Table 1: Resources and Reporting

Table 1 - Resources and Reporting	
Reporting PAC*	**FDA PAC Codes** **71004** Medicated Feed Manufacturing CGMP Inspections - Licensed Facilities **71009** BSE Inspections **71012** Medicated Feed Manufacturing CGMP Inspections - Non-Licensed Facilities **71014** Part 507 CGMP Inspections **71015** Part 507 CGMP/PC Inspections **71016** Modified Requirements Inspections at Animal Food Qualified Facilities **71017** Modified Requirements Inspections at Animal Food Storage Facilities Solely Engaged in Unexposed Packaged Food that Require Time/Temperature Controls for Safety **71018** Animal Food Sanitary Transportation Inspections **71023** Veterinary Feed Directive Inspections **71030** Animal Food FD&C Act Inspections **71R894** Animal Food Risk-Data Form **State Contract PAC Codes** **71S004** State Contract Medicated Feed Manufacturing CGMP Inspections - Licensed Facilities **71S011** State Contract BSE Inspections **71S012** State Contract Medicated Feed Manufacturing CGMP Inspections - Non-Licensed Facilities **71S014** State Contract Part 507 CGMP Inspections **71S015** State Contract Part 507 CGMP/PC Inspections **71S016** State Contract Modified Requirements Inspections at Animal Food Qualified Facilities **71S017** State Contract Modified Requirements Inspections at Animal Food Storage Facilities Solely Engaged in Unexposed Packaged Food that Require Time/Temperature Controls for Safety **71S018** State Contract Animal Food Sanitary Transportation Inspections **71S023** State Contract Veterinary Feed Directive Inspections **71S894** State Contract Animal Food Risk-Data Form
Inspection Op. Code **Investigation Op. Code**	12 (domestic), 11 (foreign) 13 (domestic), 15 (foreign)

F. Program Interactions

Divisions should make every effort to coordinate resources so that inspections conducted under this compliance program also meet inspection obligations from additional regulations, compliance programs,

or interacting assignments. Additional inspection and reporting requirements should be covered per the respective interacting program.

Programs that interact with this compliance program include the following:

(1) Feed Contaminants Compliance Program (CP 7371.003)

During a comprehensive animal food inspection with an anticipated inspectional classification of NAI or VAI, consider sampling to meet work obligations under the Feed Contaminants Compliance Program. Feed contaminant samples may also be collected outside of the comprehensive inspection in accordance with the Feed Contaminants SCOPE document, which can be found on the ORA OHAFO Dashboard. **If a facility is involved in ongoing compliance activities or the current inspection may be classified OAI, the Division must consult with their Compliance Branch and CVM to determine whether collection of samples is appropriate.** See Part II.2.H.(1). *Notification of CVM*.

(2) Type A Medicated Articles (CP 7371.005)

It should be noted that facilities under this comprehensive animal food compliance program with a medicated feed subprogram may be interrelated with the Type A Medicated Articles compliance program when the facility is producing both products. Medicated feed inspections are conducted under a Federal/State program and subject to 21 CFR Part 225, while Type A medicated articles are inspected strictly under a Federal program and subject to 21 CFR Part 226. This program is also related to the New Animal Drug Application (NADA) Pre-Approval Inspections Compliance Program (CP 7368.001) since FDA approval is required for Type A medicated articles. As a result, it may be necessary to coordinate inspectional activities between OHAFO and Office of Pharmaceutical Quality Operations (OPQO).

(3) Illegal Residues in Meat, Poultry, Seafood and Other Animal Derived Foods (CP 7371.006)

If, during the inspection of a violative drug residue, it has been determined that the producer manufactured, received or used a VFD feed, a VFD inspection should be conducted regardless of whether or not the VFD feed caused the drug residue. The producer should be informed that in addition to determining the cause of the drug residue, the Agency is also conducting a comprehensive evaluation of all animal drugs used at the facility, including the use of VFD feeds.

(4) Preventive Controls and Sanitary Human Food Operations (CP 7303.040)

Some human food facilities also manufacture, process, pack or hold animal food. For example, some ingredient manufacturers may produce ingredients for both human and animal food. Other human food manufactures may have by-products of their manufacturing processes that are used as animal food. Some manufacturers may perform certain processes for both human and animal food, such as irradiators that irradiate both produce and pet treats.

Below are factors to consider in determining what type of inspection should be performed based on the facilities activities with respect to their human food by-products for use as animal food:

- If the facility is performing different manufacturing/processing activities on their animal food (e.g., not covered in the review of their human food safety plan) then perform an inspection as follows:

  - Perform an inspection of the CGMP requirements in 21 CFR part 507, subpart B under PAC 71014 if the facility is only performing manufacturing/processing activities consistent with the activities under enforcement discretion, see Section D of the Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs: Guidance for Industry;
  - Perform an inspection of the CGMP and PC requirements in 21 CFR part 507, subparts B, C, and E under PAC 71015 if the facility is performing manufacturing/processing activities beyond those under enforcement discretion, unless another exemption or set of modified requirements applies, such as those for a qualified facility (QF).
- If the facility is performing the same manufacturing/processing activities on their human and animal food, then do not perform a comprehensive animal food inspection unless there are food safety issues identified with their ingredients or practices that could impact the animal food (see 21 CFR 507.1(d)).
- If the facility is not further manufacturing/processing human food by-product for use as animal food, the facility would be inspected under 21 CFR §117.95, holding and distribution CGMPs, under PAC 71R909.

The Division should consider the following factors to determine how to coordinate an animal food and human food inspection (e.g., whether an animal food comprehensive inspection should be conducted in conjunction with the human food inspection, whether a separate animal food comprehensive inspection needs to be scheduled, or whether an animal food inspection can be held in conjunction with the next scheduled human food routine surveillance inspection):

- whether food safety issues are identified in the human food inspection that could impact the safety of the animal food;
- the food safety risk profile of the human food by-products for use as animal food and the activities the facility is performing (see Section II.2.C. *Selection of High and Low Regulatory Priority Facilities*); and
- availability of field staff qualified to complete animal food inspections under PACs 71014 and 71015 (e.g., if a state human food inspector that is not trained in animal food is performing the human food facility inspection a separate animal food comprehensive inspection may be necessary at a later date).

If an animal food inspection under PACs 71014 or 71015 is conducted, it must be accomplished by field inspection staff qualified to perform these inspections (e.g., trained in Preventive Controls for Animal Food). If field inspection staff are not trained to perform the applicable animal food inspection, they will need to coordinate with someone trained to lead the comprehensive animal food inspection.

If you have questions about what type of inspection should occur for human food by-products for use as animal food, or how to coordinate animal food inspectional activities with human food inspectional activities please contact CVM. See Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support.*

(5) CVM/ORA Field Assignments (CVM Field Assignments)

There are some interacting programs that are currently being implemented as assignments and will eventually be incorporated into this compliance program framework, such as foreign supplier verification programs (FSVP) inspections or sampling assignments (e.g., product or environmental sampling). When compliance programs covering these interacting programs are implemented, this compliance program will be updated with additional information.

CVM and ORA may occasionally issue field assignments to target a review of certain animal food facilities or sampling of certain animal food types in order to collect general surveillance data or to address specific emerging food safety issues.

Consider conducting a comprehensive animal food inspection in conjunction with the assignment if the facility is due for a comprehensive inspection, or when findings warrant a comprehensive inspection, and/or if required by the assignment.

(6) Food Facility Registration and Qualified Facility Attestation

Field inspection staff should confirm that each facility inspected under this program has a current food facility registration per the 2002 Bioterrorism Act and Section 415 of the FD&C Act. If registration information obtained during the inspection (foreign and domestic) is different from the information in the Food Facility Registration Module (FFRM), send an email to CFSANFoodFacilityRegistration@fda.hhs.gov in accordance with IOM Subchapter 5.4.1.5.2 *Food Facility Registration Resources*.

Qualified facility attestations are also submitted during the food facility registration process. A facility that meets the definition of a very small business and submits a qualified facility attestation should receive a qualified facility inspection. Prior to the inspection, field inspection staff must determine whether a facility submitted a qualified facility attestation and, if so, the attestation option they selected (i.e., in compliance with local regulations or controlling the hazard) by checking the Qualified Facility Attestation Module in the FDA Unified Registration and Listing System (FURLS) and in OSAR Firm 360.

G. Interactions with Federal Agencies, State and Local Counterparts, and Foreign Authorities

(1) Federal Agencies

Some facilities may also have dual jurisdiction with USDA. Refer to the USDA FSIS – FDA MOU 225-99-2001 when conducting inspections at dual jurisdiction facilities.

Follow IOM subchapter 3.1.3.2 *Discussion with Federal Inspector* when federal officials from other agencies are present during FDA inspections or investigations. See IOM Subchapter 3.2 *Federal Agency Interactions* for a list of Memorandums of Understanding (MOUs) between the FDA and other Federal agencies that may be applicable to inspections conducted under this program. A complete list of MOUs may be found at FDA's Memorandums of Understanding webpage.

(2) State and Local Agencies

(a) Animal Feed Regulatory Control Officials

The Statement of Work (SOW) included with animal food contracts identifies all available work and subsequent requirements for participating State agencies. The FDA Program Division Director or designee is responsible for issuing contract inspection assignments and monitoring performance. Work not conducted in conformance with this compliance program shall be returned, and when necessary discussed with the performing State agency and CVM.

States should work directly with the FDA Program Division Director or designee (e.g., state liaison) regarding questions related to contract SOW and work assigned. The FDA Program Division Director or designee is responsible for issuing contract inspection assignments and monitoring performance.

Divisions will collaborate with commissioned State agencies to make them aware of the requirements of this program and deadlines for deliverables under this compliance program. Divisions should follow procedures as outlined in IOM Subchapter 3.3.1.2 *Joint Inspections.* Divisions will offer State agencies opportunities to accompany FDA on inspections or assist as necessary. When possible and appropriate, the Division should coordinate routine surveillance or follow-up inspections with their respective State counterparts. Communication should be initiated as soon as possible and ideally no later than two weeks prior to the start of an inspection. CVM requests that State agencies offer ORA field inspection staff the same inspectional opportunities.

For inspections with an anticipated OAI classification, the Division should notify the State agency, when possible and appropriate, so coordination between agencies can occur at jointly regulated facilities (e.g., discussion of whether joint inspection is appropriate, coordination of Federal and State actions, etc.). In addition, the Division should notify the State of any administrative or judicial action taken at jointly regulated facilities. This information sharing shall be conducted in accordance with FDA disclosure requirements (shared only with commissioned state agency personnel or state agencies having a 20.88 agreement, depending on the state's purpose and use of that information). For additional guidance and/or clarification, please contact DIDP at ORAInfoShare@fda.hhs.gov.

State agencies must contact their respective ORA Division if the inspectional findings reveal violative conditions which may warrant case submission for potential compliance actions and must do so prior to closing the establishment inspection. When contacted, Divisions must follow inspectional procedures as required by the Agency and Center. See Part II.2.H.(1). *Notification of CVM – Violative Conditions*.

States should contact CVM via the rTAN when: violative conditions are observed, subsequent follow-up is required, or if questions regarding inspectional approach arise as outlined in Part II.2.H.(1). *Notification of CVM – Violative Conditions*.

Any joint inspection with violative findings which may warrant case submission for potential FDA compliance activities must be led by the ORA Division (e.g., sufficiently document evidence and observations in accordance with FDA procedures).

(b) State Veterinary Boards

While most FDA-State interactions for this comprehensive animal food compliance program will typically be held with State animal feed control officials, it may also be appropriate to collaborate with the State Veterinary Board when significant VFD issues are identified that relate to a veterinarian and their practice of veterinary medicine. For example, when inspections encounter significant VFD deviations related to the veterinarian's role result in a compliance action and/or OAI classification, Divisions should notify the State Veterinary Board when the information becomes public under the Freedom of Information Act (FOIA) (unless the State Veterinary Board is credentialed/commissioned). In an effort to maintain consistency in approach, Divisions must contact CVM prior to notifying the State Veterinary Board in order to obtain concurrence. See Part II.2.H.(1). *Notification of CVM – Violative Conditions.*

(3) Foreign Authorities

Follow ORA/Division of Foreign Human and Animal Food Operations (DFHAFO) procedures when foreign competent authorities are present during FDA foreign inspections or investigations.

H. FDA Notifications

(1) Notification of CVM – Violative Conditions

Division management must contact CVM:

- Prior to conducting compliance or directed inspections (i.e., follow-up to recalls, violative sample results, complaints, RFR, etc.); and
- During the course of a routine surveillance inspection, as soon as significant violative conditions that may result in an anticipated status of Official Action Indicated (OAI) are observed by field inspection staff (e.g., FDA or State Contract); and
- Prior to the close of the inspection to discuss observed conditions that may result in an anticipated status of OAI.

Contact CVM as soon as the possibility of an OAI classification arises and no later than one business day in advance of the closeout meeting with the facility. Early notification will allow CVM to identify and make available appropriate SMEs to address questions as the inspection progresses and to minimize the number of issues that will need to be discussed during the pre-closeout call. When necessary to support a compliance action, provide draft documents for CVM's review prior to the closeout meeting with the facility, preferably at least 24 hours prior to the meeting so CVM has time to review. Notify CVM via the CVMAnimalFoodPrograms@fda.hhs.gov inbox with the subject line; "**Potential OAI Case Review/(facility name) Pre-closeout Call**."

Upon notification, CVM will secure a Center Compliance Officer point of contact (POC) to aid the Division with policy and technical assistance. Once a POC has been assigned, the Division should utilize that POC for all pertinent questions and/or technical assistance related to the inspection. The POC will coordinate answers to questions and/or technical assistance in order to minimize duplication of correspondence while expediting information sharing (e.g., not required to use the rTAN process in Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support*). The POC may require the Division to set up additional calls as necessary to resolve inspectional and compliance questions or concerns. The Division shall work with their

respective Center POC to arrange a pre-closeout call as soon as reasonably possible (24 hours prior to the close-out) to allow for scheduling and preparation. CVM requests as much notification as possible but understands that all situations are on a case-by-case basis.

Depending on the egregiousness of the violative conditions encountered (i.e. totality of the specific facts and case circumstances) and when there is reasonable probability that an article of food has or will cause serious adverse health consequences, the Division and/or State should be prepared to discuss in detail draft copies of closing documents, when necessary, to support a compliance action including, but not limited to: Form FDA 483, Inspectional Observations; 463a, Affidavit; supporting evidence (if necessary); and other information that the Division deems essential for review (e.g., samples pending analysis, voluntary corrective actions, etc.). The Division shall work with the Center POC to determine what level of evidence, at minimum, of the elements of proof (Jurisdiction, Interstate Commerce, Violation and Responsibility (JIVR)) are required for the pre-closeout call. If the request occurs while field inspection staff are on official travel, CVM requests that Division management cancel subsequent inspections, as necessary, to ensure resources are prioritized to focusing on the OAI inspection.

(2) Notification to CVM via the Case Management System (CMS)

Cases submitted to CVM via CMS should be assigned to teams as follows:

- Animal food compliance action cases (e.g., Warning Letters, Untitled Letters, etc.) - CVM Division of Compliance (HFV-230)
- Diversion and reconditioning requests for contaminated animal food (e.g., Reconditioning Proposal) - CVM Human & Animal Food Investigations Team (HFV-232)
- Import cases (e.g., Center review of detained shipment for refusal, import alert) - CVM Human and Animal Food Investigations Team (HFV-232)

(3) Regulator Technical Assistance Network (rTAN) and Inspectional Support

The rTAN is a resource for FDA and State field inspection staff and program management to request information assistance during inspections. It is not intended to replace the current enforcement communication mechanism between field inspection staff, supervisors and compliance officers or States.

The rTAN is an information assistance system designed to connect field inspection staff and Division/State management (e.g., Division Investigations and Compliance Branch) with SMEs to get answers and clarification on CVM programmatic approach and commodity specific questions as needed. Field inspection staff should submit inquiries through the Regulator TAN e-mail inbox at CVMAnimalFoodPrograms@fda.hhs.gov or phone (301-796-0001) and copy their supervisor. If a POC has not been assigned and an inspection is in-progress, or potentially OAI, and an answer is required as soon as possible, indicate that in the e-mail subject heading.

While the rTAN e-mail inbox is the preferred method of communication for ongoing routine surveillance inspections, if an SME or Center POC has already been assigned to a specific inspection, you may also contact that SME to request that they operate in a reasonable “on call” capacity during an inspection window. This will ensure that SMEs are available to answer questions during an inspection. If at any point during the inspectional process findings reveal

observations that may result in an anticipated status of OAI see Part II.2.H.(1). *Notification of CVM.*

(4) Ask CVM and FSMA Technical Assistance Network (TAN)

If a facility or other stakeholder has a question about CVM programs, guidance, policy, or other information not related to the inspection, then direct them to contact CVM directly through the e-mail askCVM@fda.hhs.gov. This mailbox is actively monitored and questions are directed to the appropriate SME based on the inquiry. Answers are developed by CVM SMEs and then returned to the facility or stakeholder. This response may take some time to develop, depending on current workload.

For questions related to the FSMA requirements, facilities or other stakeholders can be directed to the FSMA TAN.

(5) Medicated Feed Mill Licensing, Drug Establishment Registration and VFD Notification

Contact the Division of Animal Feeds' Program and Business Management Team, or provide their contact information to the facility, for anything related to:

- Medicated feed mill licenses, including applications, pre-approval inspections (including recommendations to approve or deny a license), approvals, withdrawals, and verification of the licensing status of a facility;
- Drug Establishment Registration, including information on how to register, how to change a registration, how to de-register, and information about registration status of a facility; and
- VFD Distributor Notification, including original notifications, changes to business information, removal from the notification list, and verification of the status of the facility.

All requests, forms, applications, and notifications can be sent by email to MedicatedFeedsTeamMail@fda.hhs.gov. Additional contact information for submission of paper or fax applications or notifications is:

Food and Drug Administration
Center for Veterinary Medicine, Division of Animal Feeds (HFV-220)
12225 Wilkins Avenue
Rockville, MD 20852
FAX: 240-453-6882

PART III - INSPECTIONAL

1. Operations

Inspections conducted under the comprehensive animal food program should: (1) identify what requirements a facility is subject to based on the activities they conduct; and (2) evaluate the facility's adherence to the relevant requirements. Field inspection staff **must** evaluate all applicable regulations associated with a facility's activities during a comprehensive animal food inspection, as described in this compliance program (e.g., Sanitary Transportation is directed only).

****Specifics on inspectional approach for each subprogram are contained in the associated appendix. Do not solely rely on the information contained in this section for specifics on how to conduct the establishment inspection for each subprogram.****

When applicable, all field inspection staff must adhere to biosecurity procedures as detailed in IOM, subchapter 5 Establishment Inspections. When warranted, field inspection staff are encouraged to maintain and have available appropriate personal protective equipment as to abide by the facility's biosecurity practices. For details regarding specific Agency approach see IOM Subchapter 5.2 – *Inspection Procedures* and IOM Subchapter 5.9 – *Veterinary Medicine* and review all relevant current field bulletins at the Field Bulletin Index.

For all inspections conducted under this program, the FDA Firms Resources Handout must be provided to the facility's management and discussed. During inspections at facilities that are also importers, Foreign Supplier Verification Programs: What Do Manufacturers/Processors Covered by the PC Supply-Chain Program Need to know about FSVP? should also be provided to the facility's management.

A. Inspections

The first step of any comprehensive inspection will involve determining the scope of requirements that apply to a particular animal food facility. *Table 2: Summary of Regulatory Precursors and the Applicable Requirements* provides a summary of what activities trigger a facility's requirement to comply with applicable regulations.

Table 2: Summary of Regulatory Precursors and the Applicable Requirements

If the facility …	**Applicable Requirements**
Manufactures, processes, packs, or holds animal food for consumption in the U.S. and is required to register as a food facility (i.e. do not meet any food facility registration exemptions). See the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States) for inspectional resources on exemptions and enforcement discretion.	• Current Good Manufacturing Practice requirements in 21 CFR part 507, subpart B • PCs in 21 CFR part 507, subparts C and E, or 21 CFR §507.7 QF modified requirements or 21 CFR § 507.51 Unexposed Packaged Animal Food Time/Temperature Modified Requirements
Manufactures medicated feed that requires a license and drug establishment registration.	Licensed Medicated Feed Mill CGMPs (21 CFR 225; 225.10 through 225.115)

If the facility …	Applicable Requirements
Manufactures only medicated feed that **DOES NOT** require a license and drug establishment registration.	Non-licensed Medicated Feed Mill CGMPs (21 CFR 225; 225.120 through 225.202)
Authorizes, Distributes, or Uses VFD feed (see Drugs with VFD Marketing Status)	VFD requirements in 21 CFR §558.6
Handles prohibited materials (surveillance inspections under this CP are only conducted for facilities that handle prohibited material, unless otherwise directed)	BSE requirements in 21 CFR §§589.2000 and 2001
Engages in Transportation Operations (Receiver, Shipper, Loader, Carrier).	Sanitary Transportation requirements in 21 CFR part 1, subpart O – DIRECTED INSPECTIONS ONLY
Manufactures, processes, packs, or holds animal food for consumption in the U.S., but is not required to register as a food facility because an exemption applies (e.g., retail food establishment)	Adulteration and Misbranding provisions in 21 U.S.C §§342 and 343 (section 402 and 403 of the FD&C Act)

Table 3: Examples of Facility Scenarios, Comprehensive Inspection Subprogram Applicable Requirements, and Related PAC Codes provides some examples of common animal food facility types and their activities with a summary of the requirements which must be covered under a comprehensive animal food inspection and associated subprogram PAC code/s that would apply.

Table 3: Examples of Facility Scenarios, Comprehensive Inspection Subprogram Applicable Requirements, and Related PAC Codes

Facility Example	Applicable Requirements	PAC Code
Multi-species non-licensed medicated feed mill required to register as a food facility that handles prohibited materials and VFD drugs and ships in bulk	• 21 CFR §§225.120 through 225.202 • 21 CFR part 507 • 21 CFR §§589.2000 and 2001 • 21 CFR §558.6 • DIRECTED ONLY - 21 CFR part 1, subpart O	• 71012/71S012 • 71015/71S015 • 71009/71S011 • 71023/71S023 • 71018/71S018
Feed mill that does not manufacture medicated feed (i.e., non-medicated feed mill) and is required to register as a food facility that handles prohibited material and ships in bulk	• 21 CFR part 507 • 21 CFR §§589.2000 and 2001 • DIRECTED ONLY - 21 CFR part 1, subpart O	• 71015/71S015 • 71009/71S011 • 71018/71S018

Facility Example	Applicable Requirements	PAC Code
Licensed medicated single-species feed mill, meets the definition of a farm so does not require food facility registration and does not handle prohibited material	• 21 CFR §§225.10 through 225.115	• 71004/71S004
Mineral pre-mix manufacturer that only ships fully enclosed packages of mineral	• 21 CFR part 507	• 71015/71S015
Mineral pre-mix and Type B medicated feed manufacturer (non-licensed) that ships both packaged and bulk minerals and Type B medicated feed	• 21 CFR §§225.120 through 225.202 • 21 CFR part 507 • DIRECTED ONLY - 21 CFR part 1, subpart O	• 71012/71S012 • 71015/71S015 • 71018/71S018
Pet food manufacturing facility that has submitted a qualified facility attestation, and ships only enclosed ambient packaged pet food	• 21 CFR part 507, subpart B and 21 CFR §507.7	• 71016/71S016
Pet food manufacturing facility that may meet the definition of a very small business, but has <u>not</u> submitted a qualified facility attestation and ships only enclosed ambient packaged pet food	• 21 CFR part 507	• 71015/71S015
Pet food retail facility (does not have to register as a food facility)	• 21 U.S.C. §§342 and 343 (section 402 and 403 of the FD&C Act)	• 71030/NA
Retail farm store (required to register because sales to farms exceed sales to consumers) that handles only packaged animal food and distributes medicated milk replacer requiring a VFD	• 21 CFR 507, subpart B • 21 CFR §558.6	• 71014/71S014 • 71023/71S023
Warehouse storing packaged animal food at ambient temperature	• 21 CFR part 507, subpart B	• 71014/71S014
Warehouse storing packaged animal food that is refrigerated for food safety	• 21 CFR part 507, subpart B and 21 CFR §507.51 • DIRECTED ONLY - 21 CFR part 1, subpart O	• 71017/71S017 • 71018/71S018
Rendering facility shipping bulk animal food	• 21 CFR §§589.2000 and 2001 • 21 CFR part 507 • DIRECTED ONLY - 21 CFR part 1, subpart O	• 71009/71S011 • 71015/71S015 • 71018/71S018

When possible, field inspection staff should attempt to identify all requirements the facility is subject to prior to performing the inspection. This may be conducted by a review of the facility's previous EIRs, reviewing the firm's information in FMS, and verifying information upon arrival at the facility. A business description is required in the Summary section of the EIR (See IOM 5.11.4.3.2 *Summary*). For animal food facilities this description must include a statement of the facility's activities sufficient to determine which requirements are applicable at the facility. Include a description of any activities that relate to exemptions or enforcement discretion applicable to the facility and the specific requirements that were applicable so that the scope of the inspection is clearly identified.

Unless directed by assignment or special circumstances, field inspection staff should not contact a facility to verify this information before the start of the inspection since this could pre-announce the inspection to the facility. Field inspection staff must adhere to IOM, Subchapter 5.2.1.1, *Pre-Announcements,* when deciding whether a facility qualifies for pre-announced inspection.

The CVM SMEs can be contacted before, during, and/or after the inspection to discuss questions field inspection staff may have when preparing, conducting, and/or closing out the inspection. The CVM SMEs can be contacted through the CVM email and/or rTAN telephone as provided in Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support*.

While preparing for the inspection, begin to think about the potential overlap and interdependencies of the applicable subprograms based on the facility's known activities. *Table 4: Example of Comprehensive Inspection Activities with Multiple Subprograms* illustrates, at high-level, a potential approach to a facility that is being inspected under multiple subprograms. The intent of this table is to help visualize how field inspection staff might cover multiple subprograms during a comprehensive inspection. Inspections are non-linear and fluid, so, as field inspection staff perform the inspection, these activities may occur concurrently or in a different order. While this table is not all inclusive, it provides an example of how to cover multiple subprograms during a comprehensive inspectional approach. Remember to ensure coverage of all applicable requirements and adjust the approach based on the facility's current activities, applicable requirements, inspectional findings and other factors.

Table 4: Example of Comprehensive Inspection Activities with Multiple Subprograms

Inspectional Step	**Example Comprehensive Activities**
Initial Interview & Walk-through	• Walk-through to determine the flow of the facility, while gaining familiarity with ingredients, equipment, and personnel activities • Determine personnel roles and responsibilities • Verify facility and animal food information such as types of micro-ingredients, vitamins, minerals, or drugs used and animal food produced (including species/life stage/etc.) • Verify scope of the comprehensive inspection based on facility's activities (i.e., what subprograms and applicable parts of the regulation to cover) • Assess general condition of facility and grounds (i.e., 21 CFR part 225 and 507 CGMPs) • Assess distribution practices and review suitability of transportation vehicles (e.g., 21 CFR part 225 and 507 CGMPs, ST requirements) • Select products to cover based on the applicable subprograms • Determine and request procedures and records to review

Inspectional Step	Example Comprehensive Activities
Review Written Procedures/Food Safety Plan Review	• Review food safety plan (e.g., hazard analysis, prerequisite program procedures, written PC and PC management component procedures, etc.) • Review medicated feed written procedures (e.g., master record file, formulation records, drug assays as necessary, etc.) • Review BSE procedures (e.g., segregation and cross contamination prevention procedures at facility handling prohibited material and animal food that may be used for ruminants)
Observe Implementation Practices	• Interview various facility employees to determine whether practices are consistently implemented and reflect written procedures • Observe general food safety practices (e.g., sanitation, housekeeping, ingredient storage, etc.) • Observe specific food safety practices (e.g., prerequisite program implementation, PC implementation, PC verification activities, medicated feed cleanout or sequencing, prohibited material cleanout or segregation practices, etc.)
Implementation Record Review	• Review food safety practice implementation records (e.g., PC monitoring and verification records, medicated feed inventory and production records, BSE segregation records, VFDs and distribution records, etc.) • Review prerequisite programs to ensure they are consistently implemented and effective • Review corrective action records (e.g., PC corrective actions, medicated feed assay corrective actions, etc.) • Review complaint file (e.g., required for licensed medicated feed, used to support food safety plan, etc.)
Other	• Review labeling (e.g., medicated feed, VFD and BSE caution statements, etc.) and any other relevant food safety documentation or practices.

Once the requirements that apply at the facility have been identified, field inspection staff should select the highest risk animal food product(s) to cover during the inspection. It may be necessary to look at activities related to other animal food products during a comprehensive inspection because the facility's highest risk animal food product may not be subject to all the requirements applicable at the facility. For example, if the highest risk products at a medicated feed mill are rations containing ionophores such as monensin and lasalocid because they make food for equines, but they also handle VFD feeds, then also cover VFD feeds.

(1) PCAF Inspection (21 CFR part 507, PACs 71014 – 71017 and 71S014-71S017)

If a facility is required to register as a food facility under section 415 of the FD&C Act because they are manufacturing, processing, packing or holding animal food for consumption in the U.S., they will likely require a 21 CFR part 507 inspection unless an exemption or enforcement discretion applies. However, the activities at the facility will determine whether all, or some of the requirements in 21 CFR part 507 apply.

NOTE: Facilities that are not required to register as a food facility are not subject to the requirements in 21 CFR part 507, (i.e., not subject to CGMPs or Preventive Controls), or other FSMA and Food and Drug Administration Amendments Act (FDAAA) authorities tied to facility

registration (e.g., reportable food registry notification, food facility registration suspension, mandatory recall authority, etc.). However, these facilities would still be subject to the adulteration and misbranding provisions of the FD&C Act. See Part III.8. *Summary of Adulteration and Misbranding Provisions for Facilities not Subject to Specific Animal Food Safety Regulations (21 U.S.C. §§342 and 343).*

There are several exemptions to food facility registration that commonly apply at animal food facilities. These are facilities that meet the definition of a farm and facilities that meet the retail food establishment definition, such as pet food manufacturers that primarily sell directly to consumers. The food facility registration guidance includes several frequently asked questions related to animal food facilities that may be exempt from registration - Guidance for Industry: Questions and Answers Regarding Food Facility Registration (Seventh Edition). For more information see *APPENDIX A – Registration, Licensing and Notification Requirements.*

See *APPENDIX B – PCAF Requirements (21 CFR part 507)* for information on how to conduct these establishment inspections.

(a) **Determining Scope of Applicable 21 CFR Part 507 Requirements and Reviewing 21 CFR part 507, subparts A and F**

Both the CGMP and PC requirements only apply to animal food facilities that are required to register as a food facility. This is a key difference from the human food regulations, where CGMPs apply regardless of whether the facility must register as a food facility. There are exemptions and enforcement discretion policies from the PCAF regulation for certain facilities and activities. As a result, in some circumstances, only certain subparts or modified requirements will be applicable at a facility.

Field inspection staff should first review the facility's activities before and during the start of the inspection to verify if a facility meets one of these exemptions in the PCAF regulation or meets any conditions described in FDA's enforcement discretion policy documents. See PCAF Exemption Table located in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States). See also Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs: Guidance for Industry.

For all facilities subject to 21 CFR part 507, review the requirements in 21 CFR part 507, subpart A and the recordkeeping requirements in 21 CFR part 507, subpart F for any required records. Field inspection staff should evaluate the relevant requirements under the corresponding reporting PAC applicable to that facility based on their size (e.g., small or very small business as defined in 21 CFR §507.3) and activities.

(b) **CGMP Only Inspection (*PAC 71014 and 71S014*)**

All registered food facilities must comply with the CGMP requirements unless they meet an exemption in 21 CFR 507.5. However, this PAC code applies when inspecting a facility only for the CGMP requirements. Thus, this PAC will apply when the facility is performing activities that exempt them from the PC requirements and they are not subject to modified requirements. For example, ambient warehouses and retail farm feed stores that must register as a food facility are facility types that would be inspected under this PAC. This PAC should not be used if a facility

is subject to the PC requirements, or modified requirements (e.g., qualified facility or warehouses that require time/temp control).

Some retail farm feed stores that are required to register as food facilities may hold food that is exposed to the environment (e.g., hay bales) and as a result do not meet the exemption from 21 CFR part 507, subparts C and E in 21 CFR part 507.10 because they are not solely engaged in the storage of unexposed packaged animal food. However, these facilities do not typically perform manufacturing/processing activities and typically sell low-risk animal food products such as shelf-stable packaged animal food, mineral mixes, hay, bird seed, and other similar types of animal food. As a result, these facilities are a low regulatory priority. **CVM requests that when these retail feed stores are inspected for routine surveillance inspections, perform a CGMP only (PAC 71014) inspection. Contact CVM prior to performing a for-cause inspection to discuss inspectional scope.** For more information on when retail farm feed stores may be required to register, see *APPENDIX A – Registration, Licensing and Notification Requirements*.

During a CGMP inspection, field inspection staff will review:

- The responsibility and training requirements in 21 CFR part 507, subpart A and associated recordkeeping requirements in subpart F; and
- Current Good Manufacturing Practice (CGMP) requirements in subpart B, including: personnel, plant and grounds, sanitation, water supply and plumbing, equipment and utensils, plant operations, holding and distribution.

(c) **CGMP/PC Inspection (*PAC 71015 and 71S015*)**

During a CGMP/PC inspection, field inspection staff will review the training, responsibility and associated recordkeeping requirements in 21 CFR part 507, subparts A and F, as well as the CGMP requirements as described previously in items Part III.1.A.(1).(a) and (b). Also, field inspection staff should review the hazard analysis and risk-based preventive controls requirements in 21 CFR part 507, subparts C and E, along with the associated recordkeeping requirements in subpart F. Facilities subject to subpart C are required to develop and maintain a written Food Safety Plan (FSP) that includes, at a minimum, a written hazard analysis (HA). The FSP must be developed and maintained or overseen by a Preventive Controls Qualified Individual (PCQI) and the plan must be reanalyzed, as a whole, every three years at a minimum.

If the hazard analysis reveals one or more hazards requiring a preventive control, then the facility must have and implement appropriate preventive controls and associated preventive control management components. Preventive controls may include process controls, sanitation controls, supply-chain-applied controls (subpart E), and other controls. When a hazard requiring a preventive control has been identified, a recall plan is required.

The FSP shall be specific to the facility and animal food(s) they manufacture, process, pack, or hold. When reviewing the FSP and HA, field inspection staff should utilize inspectional resources to determine if the facility identified applicable known or reasonably foreseeable hazards. See the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States) for inspectional resources.

(d) **Qualified Facility Inspection (*PAC 71016 and 71S016*)**

A facility that meets the definition of a very small business and submits a qualified facility attestation should receive a qualified facility inspection. Prior to the inspection, field inspection staff must determine whether a facility submitted a qualified facility attestation and, if so, the attestation option they selected (i.e., in compliance with local regulations or controlling the hazard) by checking the Qualified Facility Attestation Module in the FDA Unified Registration and Listing System (FURLS) and in OSAR Firm 360.

If a facility asks about whether they are a qualified facility, or what they need to do to submit a qualified facility attestation, provide them the information located at FDA's Qualified Facility Attestation website. If a facility has not submitted an attestation, conduct a CGMP/PC inspection under reporting PAC 71015/71S015. If there are circumstances that exist where a full CGMP/PC inspection under PAC 71015/71S015 may not be warranted, contact your Division management prior to proceeding.

During a Qualified Facility inspection, field inspection staff must review the responsibility, training, recordkeeping, and CGMP requirements in 21 CFR part 507, subparts A, B, and F as described previously in items Part III.1.A.(1).(a) and (b). In addition, review the qualified facility requirements in 21 CFR §507.7, Requirements that apply to a qualified facility.

21 CFR part 507, Subpart D covers the procedures for withdrawing a qualified facility exemption and appealing an order to withdraw. See Part V.3.C.(3). *Withdrawal of Qualified Facility Exemption (21 CFR part 507, subpart D)*Withdrawal of Qualified Facility .Compliance Activities

(e) **Modified Requirement Inspections at Facilities Solely Engaged in Storage of Unexposed Packaged Food that Require Time/Temperature Controls for Safety (*PAC 71017 and 71S017*)**

A facility that is solely engaged in the storage of unexposed packaged animal food that requires time/temperature control, such as a cold storage warehouse, should receive an inspection under this reporting PAC.

When conducting the inspection, review the training, responsibility and associated recordkeeping requirements in 21 CFR part 507, subpart A and F, as well as the CGMP requirements as described above in items Part III.1.A.(1).(a) and (b). In addition, review the requirements in 21 CFR §507.51, Modified requirements that apply to a facility solely engaged in the storage of unexposed packaged animal food.

(2) Medicated Feed Inspection (21 CFR part 225, PACs 71004 and 71S004 or 71012 and 71S012)

The medicated feed current good manufacturing practice (CGMP) requirements in 21 CFR part 225 apply to any facility that manufactures, processes, packs or holds a medicated feed. The section of the CGMPs that applies depends on whether a facility holds a medicated feed mill license and drug establishment registration.

- The CGMPs in 21 CFR §§225.10 through 225.115 apply to licensed medicated feed mills, i.e., "facilities manufacturing one or more medicated feeds for which an approved medicated feed mill licensed is required." (21 CFR §225.1(b)(2)).

  - These regulatory requirements should be applied to a facility that is required to hold a medicated feed mill license.
  - If a medicated feed mill holds an active medicated feed mill license, but has not manufactured any medicated feed requiring such licensure and they have objectionable conditions that could result in a compliance action, contact CVM prior to closing out the inspection. See Part II.2.H.(1). *Notification of CVM – Violative Conditions*.
- The CGMPs in 21 CFR §§225.120 through 225.202 apply to non-licensed medicated feed mills, i.e., "facilities manufacturing solely medicated feeds for which an approved license is not required." (21 CFR §225.1(b)(2)).
  - These regulatory requirements should be applied to a feed mill that is not performing activities that require a medicated feed mill license (e.g., not manufacturing a medicated feed requiring licensure or maintaining drugs requiring licensure in their inventory).

Prior to the inspection, review the medicated feed facility's drug establishment registration and license status to determine what CGMP requirements may apply at a facility. A facility's drug establishment registration information may be found on the Drug Establishments Current Registration Site. A facility's medicated feed mill license status may be found on the Animal Drugs @FDA webpage.

Many medicated feed mills will also be subject to the CGMP and PC requirements in 21 CFR part 507. There are areas of these regulations that overlap, for example facilities will be using the same building, grounds, employees, supervisors, management, equipment, and utensils to perform operations under 21 CFR part 507, subpart B, and part 225. In instances where the facility is subject to both 21 CFR parts 225 and 507 and the CGMPs overlap, review the more specific requirements found in 21 CFR part 507. However, the CGMPs under 21 CFR part 507, subpart B do not address the use of animal drugs in the manufacturing of medicated animal feed. Therefore, also review the specific requirements in 21 CFR part 225 related to the use of drugs in the manufacture of medicated animal feed, such as provisions for the handling of drugs and medicated mixes and for laboratory controls.

For more details about the inspectional approach for facilities subject to both the CGMP requirements in 21 CFR part 507 and 21 CFR part 225 see Appendix C.1.C. *Inspection Approach*. In addition, see the 21 CFR part 225 Citation Spreadsheet in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

See *APPENDIX C – Medicated CGMP Requirements (21 CFR part 225)* for specifics on how to conduct these establishment inspections.

(a) **Pre-approval Inspections for Medicated Feed Mill License Applicants (*PAC 71004 and 71S004*)**

During a pre-approval inspection, determine whether the facility has the necessary knowledge of CGMP requirements, adequate equipment, drug receipt and inventory controls, formula and production instructions/records, sampling and assay plans to demonstrate their ability to comply with the CGMP requirements for licensed feed mills (21 CFR §§225.10 - 225.115). This pre-approval inspection should be part of a comprehensive animal food inspection under this

compliance program to fully assess the facilities compliance with all applicable regulations as required.

See *APPENDIX C – Medicated CGMP Requirements (21 CFR part 225)* for specifics on how to conduct a medicated feed mill license pre-approval inspection.

(b) **Licensed Medicated Feed CGMP Inspections *(PAC 71004 and 71S004*)**

The facility must follow the requirements in 21 CFR §§225.10- 225.115. Field inspection staff should review the building and grounds and overall operations (either under 21 CFR part 507 if applicable, or if not under 21 CFR part 225). This subprogram of the comprehensive inspection should focus on the drug receipt and storage, manufacturing processes (including flushing, sequencing, or physical cleanout), master record file (including formulation), production records, complaint records, assay results (including applicable root-cause investigations and corrective actions), labeling, and distribution records to ensure a safe and effective medicated feed has been manufactured and distributed. Finally, determine if the facility can (1) trace-forward and recall its product, and (2) trace-back the medicated article or the medicated feed received from its suppliers.

See *APPENDIX C – Medicated CGMP Requirements (21 CFR part 225)* for specifics on how to conduct these establishment inspections.

(c) **Non-licensed Medicated Feed CGMP Inspections (*PAC 71012 and 71S012*)**

Overall compliance is determined by review of certain portions of the facility's operations using the non-licensed medicated feed CGMPs (21 CFR §§225.120- 225.202). The non-licensed CGMP requirements are similar to the licensed CGMP requirements, but are more flexible. See *APPENDIX C – Medicated CGMP Requirements (21 CFR part 225)* which outlines the key differences between the requirements.

Field inspection staff should review the building and grounds and overall operations (either under 21 CFR part 507 if applicable, or, if not, under 21 CFR part 225). Review the facility's activities with respect to their medicated feed components and the resulting medicated feed. This subprogram of the comprehensive inspection should focus on the drug receipt and storage, manufacturing processes (including flushing, sequencing, or physical cleanout), formulations, production records, out-of-specification assay results (and if so, review the root-cause investigation and corrective actions), labeling, and distribution records to ensure the safe and effective production and distribution of medicated feed. Finally, determine if the facility can (1) trace-forward and recall its product, and (2) trace-back the medicated article or the medicated feed received from its suppliers.

See *APPENDIX C – Medicated CGMP Requirements (21 CFR part 225)* for specifics on how to conduct these establishment inspections.

(3) VFD Inspection (21 CFR §558.6, PAC 71023 and 71S023)

If a facility manufactures and/or distributes VFD feed (see Drugs with VFD Marketing Status), review the requirements for a VFD distributor during the comprehensive animal food inspection. VFD distributors are required to notify FDA of their intent to distribute VFD feed. Verify whether a distributor has submitted their notification using the VFD distributor list located on

Animal Drugs@FDA under the "Medicated Feeds" section. In addition, for a subset of VFD distributors identified by the Division (e.g., management or field inspection staff), conduct trace-forward (at the client) and trace-back (at the veterinarian) inspections. For information on how to select trace-forward/trace-back inspections, see Part II.2.C.(4).(b). *VFD Trace-forward and Trace-back Priorities*. Also, if field inspection staff observe issues related to a VFD reviewed at the distributor (e.g., improperly completed VFD or improper distribution), consider conducting a trace-forward or trace-back inspection to further investigate the root cause of the issue or contact CVM to discuss whether a trace-forward or trace-back inspection is warranted.

For each VFD distributor inspection and subsequent trace-forward/back inspection, conduct a separate inspection for each legal entity visited (e.g., distributor, client, and veterinarian). For example, if field inspection staff visit three different facilities for the distributor, client, and veterinarian, conduct three separate inspections and fully document findings under three different EIRs.

A single VFD operation can be categorized as more than one operation type. In these instances, review all applicable requirements for that entity. For example, a veterinarian may also be a distributor.

See *APPENDIX D – VFD Requirements (21 CFR §558.6)* for specifics on how to conduct these establishment inspections.

(a) **Review of VFD Requirements at Distributor (*PAC 71023 and 71S023*)**

Field inspection staff should review up to three VFDs at each inspection at a distributor, preferably from different clients and/or veterinarians when possible. If fewer than three VFDs are available, field inspection staff should review those that are available.

For facilities selected for a VFD trace-forward/back inspection, select one of the three VFDs to perform a trace-forward and trace-back inspection. See *APPENDIX D – VFD Requirements (21 CFR §558.6)* on how to reference these ancillary inspections in the distributor EIR.

See *APPENDIX D – VFD Requirements (21 CFR §558.6)* for specifics on how to conduct these establishment inspections.

(b) **Selection and review of Veterinarian and Client for Trace-forward/back (*PAC 71023 and 71S023*)**

Using the selected VFD from the distributor inspection, obtain the contact information for the veterinarian who issued the VFD as well as the client who received the VFD feed. Conduct a separate inspection (OP 12) for the ancillary trace-forward/back inspections and be sure to document the contact information for the originating VFD distributor (where the inspection started) in either the VFD Tool or inspectional protocol (IP) if available.

In situations when a veterinarian is also the distributor of the VFD feed, a trace-back inspection to the feed manufacturer may not be necessary. Similarly, if the VFD distributer is a feed retailer (i.e., did not manufacture the VFD feed), a trace-back to the VFD feed manufacturer may not be necessary. However, if a violation is identified in the finished product, then a follow-up to the VFD feed manufacturer may be warranted.

A trace-forward or trace-back inspection that will involve crossing Division jurisdiction should not be pursued for routine surveillance inspections unless significant deviations are observed which warrant follow-up. States should take a similar approach and not pursue routine surveillance inspections across State borders.

See *APPENDIX D – VFD Requirements (21 CFR §558.6)* for specifics on how to conduct these establishment inspections.

(4) BSE Inspection (21 CFR §§589.2000 and 2001, PAC 71009 and 71S011)

Unless otherwise directed, only conduct a BSE inspection if a facility is handling prohibited material. This subprogram of the comprehensive animal inspection will focus on determining what practices the facility has in place to ensure the prohibited materials they handle will not be incorporated into ruminant animal food.

If the facility is handling prohibited material, field inspection staff should focus on reviewing the facility's incoming ingredients to determine what prohibited materials they handle, the labeling and identification of ingredients and animal food from receipt through distribution (including caution statements), any potential points of cross-contamination in their facility, and where animal food may be diverted (e.g., out of specification pet food diverted to a livestock manufacturer).

See *APPENDIX E – BSE Requirements (21 CFR §§589.2000 and 2001)* for specifics on how to conduct these establishment inspections.

(5) DIRECTED ONLY: Sanitary Transportation (ST) Inspection (21 CFR part 1, subpart O, PAC 71018 and 71S018)

Unless otherwise directed, routine surveillance inspections under this CP will not automatically include the ST sub-program. Divisions will be notified of the need to perform routine surveillance ST inspections via the annual workplan and FSMA inventory. The ST sub-program should not be included as part of a routine surveillance animal food inspection unless specifically identified in the annual workplan and/or FSMA inventory.

For-cause ST inspections should be performed as part of a comprehensive animal food inspection at carriers or facilities subject to the ST transportation when they meet one of the factors identified in Part II.2.C.(4).(c). *DIRECTED ONLY: Sanitary Transportation*.

As a reminder, the sanitary transportation requirements only apply at facilities that are performing transportation operations and not subject to an exemption or waiver. Generally, this means ST requirements will only apply at facilities that are: (1) distributing exposed (e.g., bulk) animal food; or (2) distributing food that requires a temperature control for safety (regardless of whether bulk or packaged). It is important to remember that there are several activities that are outside of the definition of transportation operations, as well as waivers and exemptions to the ST requirements. The ST requirements do not apply to facilities that are farms, retail food establishments, or by-products of human food facilities (unless further manufactured/processed).

ST inspections conducted under this subprogram should assess the facility's compliance with 21 CFR part 1, subpart O. Sanitary transportation inspections may only be performed by field

inspection staff who have successfully completed FD9001W Sanitary Transportation Training of Human and Animal Food Rule.

When using the IP, field inspection staff will be asked to identify each operation that a facility plays in the transportation of food(s) when determining how the sanitary transportation regulation applies. A single facility may conduct multiple transportation operations for the specific product inspected and may act as the shipper, loader, receiver, and carrier, or any combination thereof.

Inspections under ST should focus on ensuring that vehicles and equipment used for transportation operations meet the requirements and that the facility has in place sufficient conditions and controls for their transportation operations as necessary to prevent the food from becoming unsafe during transportation operations. Requirements related to training and recordkeeping may also apply depending on the facility's activities.

See *APPENDIX F – Sanitary Transportation Requirements (21 CFR part 1, subpart O)*for specifics on how to conduct these establishment inspections and for more information on the exemptions and waivers.

(6) Adulteration and Misbranding Provisions for Facilities not Subject to Specific Food Safety Regulations (21 U.S.C. §§342 and 343, PAC 71030)

If a facility is not required to register as a food facility and is not subject to any of the other subprograms of a comprehensive animal food inspection, contact Division management and CVM at CVMAnimalFoodPrograms@fda.hhs.gov to determine if it is appropriate to conduct an inspection and/or to define the scope of an inspection. For example, this type of inspection would be performed at:

- pet food manufacturers that sell directly to consumers and therefore meet the definition of a retail food establishment (i.e., not required to register as a food facility or meet the 21 CFR part 507 requirements); and
- facilities that are exempt and/or under enforcement discretion from the requirements in 21 CFR part 507, such as facilities solely engaged in the holding of raw agricultural commodities.

Inspectional approach will depend on the facility, their operations, and the reason for the inspection (i.e. class I recall follow-up, OAI follow-up, etc.), which must be discussed with Division management and CVM prior to conducting the inspection. If the activities observed during the inspection are different than what was discussed prior to the inspection on the call, contact Division management and CVM for further direction prior to the inspection closeout.

Facilities that are not subject to the specific regulations, listed in this CP, are still prohibited from violating the FD&C Act, including adulterating or misbranding animal food, or distributing adulterated or misbranded animal food as described under section 402 and 403 of the FD&C Act (21 U.S.C. §§342 and 343). As a result, field staff should evaluate the facility's activities to determine whether they are in compliance with the FD&C Act. Generally, during an inspection where specific animal food safety regulations do not apply, field staff should:

- Determine the food safety issue and the root cause of that issue at the facility
- Consider what adulteration provision(s) might fit the conditions observed
- Collect necessary and available evidence to document the adulteration

- Document any observations under the adulteration provisions of the FD&C Act

Examples of animal food situations where FD&C Act adulteration observations may apply include:

- Poisonous or deleterious substances (FD&C Act 402(a)(1)/21 U.S.C §342(a)(1))
  - Analytical results demonstrate that a poisonous or deleterious substance is present in the animal food. For example, analytical results document the presence of pathogenic microorganisms, mycotoxins, or chemical hazards that are present at unsafe levels, such as copper or non-protein nitrogen toxicity.
- Filthy, putrid substances or unfit for food (FD&C Act 402(a)(3)/21 U.S.C. §342(a)(3))
  - Observations that document that the animal food consists in whole or in part of any filthy, putrid, or decomposed substance.
  - Observations that document an animal food is unfit for food. For example, the animal food included a substance that was not fit for animal food, such as waste oil by-product of drug manufacturing that was designated for industrial use only. In addition, observations that the composition of the food rendered it unfit for animal food, such as mineral licks that has an incorrect consistency resulting in overconsumption of a nutrient.
- Insanitary conditions (FD&C Act 402(a)(4)/21 U.S.C. §342(a)(4))
  - Observations the facility failed to follow industry practices (e.g., sanitation practices, process controls, recordkeeping, etc.) that result in insanitary conditions and/or adulteration of animal food

If field inspection staff observes potential issues related to labels or labeling contact CVM at CVMAnimalFoodPrograms@fda.hhs.gov. Examples of animal food situations where FD&C Act misbranding observations may apply include:

- If the label does not bear the common or usual name of the food, or the common or usual name of each ingredient for a multi-ingredient food (FD&C Act 403(i)/21 U.S.C. §343(i))
  - Documentation and/or observations demonstrating that the animal food is not what is indicated on the label. For example, the label does not list an ingredient that is included in the animal food or does not use a common or usual name for the animal food or one of the ingredients.
- If a required statement, such as a caution statement, is not included (FD&C Act 403(f)/21 U.S.C. §343(f)
  - Documentation and/or observations that the animal food requires a caution statement and the caution statement is not included. For example, ammonium formate is an approved food additive and the approval requires certain caution information to be on the label.
- If the label or labeling includes claims that indicate the product is intended for uses to diagnose, cure, treat, mitigate or prevent, disease, or it is intended to affect the structure or function of the body in a manner other than food (consumed for taste, aroma, or nutritional value), this results in the product being an unapproved new animal drug and thus adulterated (FD&C Act 501(a)(5)/21 U.S.C §351).

For a more complete list of common animal food adulteration and misbranding cites and corresponding prohibited acts see Part V.2. *Charges.* In addition, see the Animal Food

Adulteration Citation Spreadsheet in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

Contact CVM at CVMAnimalFoodPrograms@fda.hhs.gov if the Division feels sampling is warranted. Furthermore, if deviations are observed, or violative sample results are obtained, contact CVM to hold a pre-closeout meeting and discuss any intended observations prior to issuing a Form FDA 483. See Part II.2.H.(1). *Notification of CVM – Violative Conditions.*

B. Investigations

Domestic or foreign investigations (OP 13 or OP 15) may be performed at facilities covered by this program. See IOM Subchapter 8.10 *General Investigation Reporting* for instructions covering how to conduct and report an investigation.

If a domestic or foreign facility assigned for inspection is no longer operational, does not manufacture products that fall under FDA jurisdiction, or cannot be inspected for any other reason, an investigation may be created by utilizing the washout conversion function in eNSpect. Administrative information should be updated in Firm Management Services (FMS) as appropriate. The eNSpect job aid will be helpful in converting the OP 12 to an OP 13.

Follow the procedures noted in the IOM Subchapter 5-14.3.13 *Out-of-Business Firm* to confirm the facility operational status for facilities suspected to be out of business (OOB). In addition, for Licensed Medicated Feed Mills and VFD distributors if OOB is confirmed also notify CVM see Part II.2.H.(5). *Medicated Feed Mill Licensing, Drug Establishment Registration and VFD Notification*.

C. Sample Collections

Surveillance sample collections are not planned under this compliance program. However, surveillance samples under other compliance programs (e.g., Feed Contaminants Compliance Program) or active sampling assignments (e.g., product or environmental sampling) may be collected during inspections covered by this compliance program, so long as the facility and/or food meets the criteria for those compliance programs or assignments. See Part II.2.F. *Program Interactions.*

If egregious conditions are observed during an inspection, consult with CVM before collecting any samples. If there are questions or concerns regarding when to sample during a potential OAI inspection, email CVM at CVMAnimalFoodPrograms@fda.hhs.gov or call the rTAN telephone number at 301-796-0001. **NOTE: Include "Animal Food For-Cause Sampling" in the subject line of the email**.

D. Documentary Sample Collections

The collection of evidence to demonstrate and document the elements of proof (Jurisdiction, Interstate, Violation, and Responsibility (JIVR)) is necessary for advisory and judicial action.

- For advisory action (e.g., untitled letters, warning letters, or regulatory meetings), JIVR should be collected and included as part of the EIR, but does not need to be submitted as a documentary sample.
- For judicial or administrative actions (e.g., injunction, seizure, warrant, prosecution, mandatory recall, or food facility registration suspension), JIVR should be included with the EIR and a documentary sample of interstate commerce records should be collected for at least one animal food product representative of an observation.

For additional details, see IOM Subchapter 4.1.4.2 *Documentary Samples*.

E. Import Activities

The following resources may be useful when field inspection staff receive or have questions related to import activities.

- Questions or issues involving general import operations should be addressed to ORA's Division of Import Operations at (301) 796-0356 or FDAImportsInquiry@fda.hhs.gov.
- Questions or issues involving OASIS or PREDICT screening should be addressed to ORA/DSS/Import Systems Branch at oraoismdssimpcomplsysbr@fda.hhs.gov.
- Questions or issues involving science policy, analysis, preparation, or analytical methodology, should be addressed to ORA/Office of Regulatory Science at (301) 796-6600 or oraorsprivatelabimportalerts@fda.hhs.gov.
- Resources for private laboratory testing are available at: https://www.fda.gov/science-research/field-science-and-laboratories/private-laboratory-testing.
- Issues regarding policy, sample collection, or general questions related to the importation of animal food, should be addressed to CVM/Division of Compliance at CVMImportRequests@fda.hhs.gov.

F. Other

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2. Reporting

Establishment inspection reports must be completed in eNSpect per IOM subchapter 5.11.1 *Establishment Inspection Report (EIR)*. Additionally, the following must be completed:

- Animal Food Risk-Data Form IP must be completed for each animal food inspection under reporting PAC 71R894/71S894;
- eNSpect IP or state reporting equivalent for each subprogram must be completed when available;
- If an IP is not available for VFD subprogram inspections, the VFD tool must be completed for each inspection; and
    - Use the current version of the VFD tool – the most current fillable PDF version of the VFD Inspectional Tool can be found in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).
    - Only use a fillable PDF version of the VFD Inspection Tool so that the data can be easily extracted. Save each completed Tool by using Adobe Acrobat's File>Save As… function. Do NOT scan handwritten paper copies or use the 'Print to PDF' function. Completed Tools, including those which are filled out by state counterparts under contract, should be reported by the close of business on the last Thursday of each quarter to the 'ORA HQ FOOD FEED PROGRAM REPORTING' email box: ORAHQFOODFEEDPROGRAMREPORTING@fda.hhs.gov.
- If an IP is not available for licensed medicated feed mill subprogram inspections, the elements of the Form 2481 must be reviewed during the inspection. Any resulting relevant information and observations must be captured in the EIR write-up, but the Form 2481 does not have to be completed and attached (i.e., it can be used as a job aid, but is not necessary for reporting).

- If an IP is not available for BSE inspections, the elements of the Form FDA 3719 – Report of Inspection for Compliance with 21 CFR §589.2000 and §589.2001, must be reviewed during the inspection. The Form 3719 should be submitted with the EIR.

Investigational reports must be prepared per IOM Subchapter 8.10 *General Investigation Reporting*.

Voluntary corrections should be encouraged during the inspection, and corrective actions taken by the facility shall be verified and documented in the corrective action reporting (CAR) system. Field inspection staff are encouraged to take the web-based CAR training. All corrective actions taken by a facility in response to inspectional observations must be documented in the CAR system, accessible via eNSpect and Compliance Management Services (CMS) database. Use eNSpect to report corrective actions observed during the inspection (including any taken since the prior inspection) and those received after the inspection but before the inspection report is finalized. The Division should use CMS to report and assess any corrective actions received after the report has been finalized in eNSpect.

In instances where FDA IT systems are not available for States, they should follow the instructions in their SOW or talk to their FDA Program Division Director or designee.

Information on how to respond to the Form FDA 483 *Inspectional Observations* should be provided to the facility's management. For foreign inspections, Form FDA 483 responses should be sent to FDA483responseinternational@fda.hhs.gov. Field inspection staff must inform the facility that the adequacy of their response to the Form FDA 483 may impact FDA's determination of the need for follow-up action. FDA expects the facility to respond to the Form FDA 483 within 15 business days from the date of issuance.

PART IV – ANALYTICAL

For analytical information, visit the Field Science and Laboratories website. This website includes links to ORA's Laboratory Manual, a listing of Food and Feed Laboratory Operations (including links to their laboratory program capabilities), and Laboratory Information Bulletins. Use the online lab servicing table for sample submission, unless otherwise directed by an assignment or ORA management.

1. Analyzing Laboratories

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2. Analyses to be Conducted

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3. Methodology

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4. Reporting

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PART V - REGULATORY/ADMINISTRATIVE STRATEGY

1. Findings

The goal of this regulatory strategy is to obtain high rates of industry compliance with all the subprograms applicable at a facility by prompt voluntary correction of deficiencies; however, as appropriate, compliance action will be taken when significant problems present a threat to public health.

Consideration for compliance action depends on several factors including the facility's compliance history, the significance and egregiousness of inspectional observations (i.e., the impact on public health), the totality of the facts and circumstances involved, and the adequacy and timeliness of the facility's corrective actions. Divisions should also consider their State agencies' willingness and ability to gain prompt voluntary correction of deficiencies or pursue State enforcement action. See Part II.2.G.(2).(a). *Animal Feed Regulatory Control Officials.*

Voluntary corrections are often the most effective and expedient means to protect public health and obtain compliance. Divisions should take steps to encourage voluntary corrections prior to considering advisory, administrative, or legal action. When voluntary corrections are not forthcoming, the Agency should pursue regulatory action to address significant observations. See FMD-86 Establishment Inspection Report Conclusions and Decisions for further guidance.

CVM requires that Division management contact the Center prior to the initiation of any for-cause inspections and prior to close-out for any inspections that are likely to result in an OAI classification so a pre-closeout meeting can be held. See Part II.2.H.(1). *Notification of CVM – Violative Conditions*.

A Citation Ranking Spreadsheet for each subprogram can be found in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

A. Regulatory Significance

(1) Critical

Deviations that are categorized as "critical" are the most serious deviations from the regulation. Specifically, the facility has a breakdown of animal food safety systems that results in a reasonable probability of causing serious adverse health consequences or death to humans or animals (SAHCODHA). Classification of observations as "critical" are expected to be limited to situations that are likely to pose an imminent public health threat. **Contact Division Management and CVM for concurrence in determining whether critical deviations exist. If critical deviations are suspected or identified, immediately contact CVM.** See Part II.2.H.(1). *Notification of CVM – Violative Conditions*.

(2) Major

Deviations that are categorized as "major" are of significant public health concern. Specifically, the facility has a deviation that results in unsatisfactory conditions that present a food safety risk and are likely to result in a system breakdown. These major observations are significant and should be documented on a Form FDA 483.

(3) Minor

Deviations that are categorized as "minor" are not of significant public health concern. Specifically, the facility has a deviation that results in unsatisfactory conditions that if not addressed may lead to a risk to food safety but is not likely to cause a system breakdown. These minor observations are typically discussion items.

B. Classification

Inspection classifications are based on the public health significance and the facility's response and include "No Action Indicated (NAI)," "Voluntary Action Indicated (VAI)," and "Official Action Indicated (OAI)." For additional information, see FMD-86 Establishment Inspection Report Conclusions and Decisions. For inspections classified as OAI, the Division should submit any recommendation for enforcement follow-up via CMS. If CVM feels an inspection classified as NAI or VAI should be classified as OAI, a request will be made to the Division to provide the full narrative EIR and exhibits through CMS for review. If CVM recommends an OAI reclassification, a meeting will be scheduled between the Division, ORA/OHAFO, and CVM/DC.

The following are examples of situations that may warrant inspectional classifications and/or compliance actions. **NOTE:** This list is not intended to be all-inclusive and more examples specific to subprograms may be contained in the relevant subprogram appendix. **All compliance actions require CVM review and concurrence (i.e., direct reference is not provided).**

(1) No Action Indicated (NAI):

- No significant adverse conditions observed.
- Only minor conditions observed that does not impact public or animal health or animal food safety.

(2) Voluntary Action Indicated (VAI)

- Significant adverse conditions that may or may not have been observed to directly affect animal food products and/or animal food contact surfaces.
- Significant adverse conditions are observed, and the facility provides an adequate response or corrective action plan within established timeframes (e.g., during the inspection or 15 working days after the issuance of a Form FDA 483).

(3) Official Action Indicated (OAI)

- Significant and wide-spread adverse conditions that are observed to directly affect animal products and/or animal food contact surfaces; or are very likely to lead to the adulteration of animal food products.
- Systemic breakdown in any subprogram of this compliance program that is likely to result in a SAHCODHA hazard(s).
- Analytical results from FDA or State official samples indicating animal food is adulterated (and the facility did not independently identify and correct the issue prior to distributing the animal food).
- Significant adverse conditions are observed, and the facility does not provide an adequate response or corrective action plan that demonstrates effectiveness and consistent

implementation within established timeframes (e.g., no adequate corrective actions taken during inspection or reported after 15 working days).

C. Factors to Consider

The following factors should be considered when assessing deviations and considering compliance actions:

- What is the potential public health impact to animal and human health?
  - Systemic breakdowns that result in animal food hazards that can harm, not only the animals consuming the food, but can also be harmful to human health (e.g., hazards like aflatoxin that can be present in milk or eggs, or pathogens that can infect humans when a pet food is handled in the home).
  - Some animal food/hazard pairs can have a greater public health impact depending on the situation. For example, a system failure that could result in a vitamin deficiency or toxicity in a pre-mix facility that makes a variety of vitamin and mineral mixes as ingredients for other customers manufacturing animal food may have a larger public health impact.
  - Some animal food ingredients that are necessary for one species can be toxic to other species at a mixed-species manufacturing facility (e.g., animal drugs such as monensin in horse feed, or minerals such as copper in sheep feed).
- Can the observation be corrected during the inspection?
  - It may be possible to verify and document correction of "minor" deviations; however, this is less likely for significant observations as those generally require more time and resources to adequately address.
- Is the deficiency indicative of an isolated problem or system failure?
  - An isolated issue (e.g., one missing record that is not connected to a food safety issue) may be "minor," whereas, a repeat problem or pattern of deviations (e.g., numerous missing records, a general lack of records, or a missing record associated with a food safety issue) may be considered "major".
- Are appropriate practices or controls in place to prevent animal food contamination or adulteration?
  - A facility that is missing records or a component of their food safety plan may be implementing adequate controls for significant hazards in practice.
- Is the facility or animal food associated with a recent outbreak or recall?
  - If so, observations likely associated with the root cause of the outbreak or recall may rise to the level of "critical." See *Table 8: Compliance Activity Summary* for more information.
- Is the finding a first-time observation or repeat over multiple inspections?
  - Repeat observations may become "major" if they are indicative of a general lack of control and inability to make lasting corrections.

- **Charges**

A. Adulteration

Section 402 of the FD&C Act [21 U.S.C. 342] applies to food (e.g., animal food), and Section 501 of the FD&C Act [21 U.S.C. 351] applies to drugs (e.g., medicated feed or medicated articles). Common adulteration charges that may be applicable to this compliance program include:

Table 5: Common Adulteration Charges Applicable to Subprograms

FD&C Act Section	Language	Notes and Examples
402(a)(1)	If it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health.	This citation is typically used when there is evidence the animal food contains a harmful substance. For example, there are analytical results that establish the presence of a poisonous or deleterious substance and the presence, or a harmful level of a substance.
402(a)(2)(A)	If it bears or contains any added poisonous or added deleterious substance (other than a substance that is a pesticide chemical residue in or on a raw agricultural commodity or processed food, a food additive, a color additive, or a new animal drug) that is unsafe within the meaning of section 406 of the FD&C Act [Tolerances for poisonous or deleterious substances];	This citation is typically used when there is evidence an animal food intended for consumption by ruminants contains the presence of prohibited material.
402(a)(2)(C)(i)	If it is or if it bears or contains (i) any food additive that is unsafe within the meaning of section 409 of the FD&C Act [Unsafe food additives]	This citation is typically used when an unapproved food additive has been added to the animal food or when an approved food additive is not being used in conformance with the food additive approval. For example, there are analytical results that an ingredient approved for use in an animal food exceeds the level of the approval. This citation is also used when a facility has failed to meet the BSE requirements in 21 CFR §§589.2000(c)-(f) or 589.2001(c)(1) (see 21 CFR §§ 589.2000(g) and 589.2001(d)(2)).

FD&C Act Section	Language	Notes and Examples
402(a)(2)(C)(ii)	If it is or if it bears or contains (ii) a new animal drug (or conversion product thereof) that is unsafe within the meaning of section 512 of the FD&C Act [Unsafe new animal drugs and animal feed containing such drugs]	This citation is typically used when a non-medicated animal food is contaminated by a medicated article or medicated feed (e.g., unsafe contamination from drug carryover into a non-medicated feed), including when the failure to follow 21 CFR part 225 has caused a non-medicated animal food to be adulterated. (See 21 CFR §225.1(b)(1)). When used for 21 CFR part 225 violations, include a reference to 21 CFR §225.1(b)(1) – See section 402(a)(2)(C)(ii) of the FD&C Act [21 U.S.C. 342(a)(2)(C)(ii)] and 21 CFR 225.1(b)(1). When a medicated feed is adulterated because of improper use of a drug, typically section 501(a)(6) of the FD&C Act is used instead. (See 21 CFR §225.1(b)(1)).
402(a)(3)	If it consists in whole or in part any filthy, putrid, or decomposed substance, or if it is otherwise unfit for food.	This citation is typically used in animal food in situations where an animal food or animal food ingredient is not appropriate to be used as animal food. It also specifically applies when BSE requirements in 21 CFR §589.2001(c)(1) have not been met (see 21 CFR §589.2001(d)(2)).
402(a)(4)	If it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health.	This citation is typically used when an animal food may become adulterated because of insanitary practices at the facility. This may apply when a facility has not followed the requirements in a regulation intended to prevent insanitary conditions (e.g., 21 CFR part 507, or 21 CFR §§589.2000 and 2001). It may also apply in situations where a regulation does not apply, but there is evidence that insanitary conditions exist.
402(i)	If it is transported or offered for transport by a shipper, carrier by motor vehicle or rail vehicle, receiver, or any other person engaged in transportation of food under conditions that are not in compliance with the regulations promulgated under section 416 of the FD&C Act.	This citation is used when Sanitary Transportation requirements in 21 CFR part 1, subpart O were not followed.

FD&C Act Section	Language	Notes and Examples
501(a)(2)(B)	If it is a drug and 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 this 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; ... For purposes of paragraph (a)(2)(B), the term "current good manufacturing practice" includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products.(FD&C Act section 501(j)	Typically applies when medicated article or medicated feed does not meet the applicable CGMP requirements for safety/efficacy (21 CFR parts 225 or 226) and the focus of the requirement is to achieve safety/efficacy. When using for 21 CFR part 225 violations, include a reference to 21 CFR §225.1(b)(1) – See section 501(a)(2)(B) of the FD&C Act [21 U.S.C. 351(a)(2)(B)] and 21 CFR 225.1(b)(1). Per CPG 680.500 use when there was unsafe contamination from drug carryover, or the potential for unsafe contamination from carryover of drugs. Do not use when the failure to follow 21 CFR part 225 CGMPs has caused a non-medicated feed to be adulterated. Use section 401(a)(2)(C)(ii) of the FD&C Act instead (See §225.1(b)(1)).
501(a)(5)	If it is a new animal drug which is unsafe within the meaning of section 512 of the FD&C Act [Unsafe New Animal Drug];	This citation is typically used if the new animal drug is deemed unsafe because it is not approved, conditionally approved, or indexed, or it is not used in conformance with the approval, conditional approval, or index listing. When using this citation, also explain and cite the reason the new animal drug is considered unsafe under section 512 of the FD&C Act. An example may be the use of a VFD drug (e.g., medicated article) not in conformance with the VFD requirements. If the new animal drug has already been used in or on animal feed, the preference is to use the citation in section 501(a)(6) of the FD&C Act, which is more specific to that situation.

FD&C Act Section	Language	Notes and Examples
501(a)(6)	If it is an animal feed bearing or containing a new animal drug, and such animal feed is unsafe within the meaning of section 512 of the FD&C Act [Unsafe New Animal Drug];	This citation is typically used when an animal food contains a new animal drug that is deemed unsafe because it is not approved, conditionally approved, or indexed, or it is not used in conformance with the approval, conditional approval, or index listing. When using this citation, also include and cite the reason the animal food containing the new animal drug is considered unsafe under section 512 of the FD&C Act. Examples may include: (1) use of new animal drugs that are not approved for use in medicated feed; (2) use of new animal drugs in medicated feed for species/indication not approved (see CPG 615.115 for additional consideration); (3) use of new animal drugs in the medicated feed in combinations that are not approved; (4) use of new animal drugs in the medicated feed at levels that are not approved (5) use of a VFD feed (e.g. Type B or C medicated feed) not in conformance with the VFD requirements.
501(j)	If it is a drug and it has been manufactured, processed, packed, or held in any factory, warehouse, or establishment and the owner, operator, or agent of such factory, warehouse, or establishment delays, denies, or limits an inspection, or refuses to permit entry or inspection.	This citation is typically used when there is a refusal or limitation of a drug-related inspection.

B. Misbranding

Section 403 of the FD&C Act [21 U.S.C. 343] applies to food (e.g., animal food), Section 502 of the FD&C Act [21 U.S.C. 352] applies to drugs (e.g., medicated feed or medicated articles). Common misbranding charges that may be applicable to this compliance program include:

Table 6: Common Misbranding Charges Applicable to Subprograms

FD&C Act Section	Statutory Language	Notes and Examples
403(a)(1)	If its labeling is false or misleading in any particular…	If there is another misbranding citation that is applicable (e.g., the requirement that the label bears the established name, failure to include necessary caution statements) the preference is to use the more specific citation.
403(e)	If in package form unless it bears a label containing (1) the name and place of business of the manufacturer, packer, or distributor; and (2) an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count ….	This citation is typically used when a packaged animal food does not have a label, or the label does not include the manufacturer, packer, or distributor information or does not include the quantity or weight.
403(f)	If any word, statement, or other information required by or under authority of this Act to appear on the label or labeling is not prominently placed thereon with such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.	This citation is used when there is a failure to include, or make prominent, required information. For example, failure to follow BSE requirements related to labeling (see 21 CFR §§589.2000(g)(2) and 589.2001(d)(3)).
403(i)	Unless its label bears (1) the common or usual name of the food, if any there be, and (2) in case it is fabricated from two or more ingredients, the common or usual name of each such ingredient …	This citation is typically used when an animal food label does not include the common or usual name of the food or its ingredients.
502(a)(1)	If its labeling is false or misleading in any particular ….	If there is another misbranding citation that is applicable (e.g., the requirement that the label bears the established name, or failure to include necessary caution statements), then the preference is to use the more specific citation. For example, when the drug name or amount is incorrect, section 502(e)(1)(A) of the FD&C Act may be more appropriate.

FD&C Act Section	Statutory Language	Notes and Examples
502(b)	If in package form unless it bears a label containing (1) the name and place of business of the manufacturer, packer, or distributor; and (2) an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count: Provided, That under clause (2) of this paragraph reasonable variations shall be permitted, and exemptions as to small packages shall be established, by regulations prescribed by the Secretary.	Applies when the name, address, or weight is not included on the label for medicated feed. If there is a similar issue with the labels for medicated and non-medicated animal food, section 403(e) of the FD&C Act may be more appropriate to cover the issue across both types of animal food.
502(c)	If any word, statement, or other information required by or under authority of this Act to appear on the label or labeling is not prominently placed thereon with such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.	Typically applies when the label or labeling does not contain information required by the approval, conditional approval, or index listing (e.g., does not conform to the representative Blue Bird label). Also, typically applies if the medicated feed is a VFD feed that does not contain the caution statement required by 21 CFR §558.6(a)(6).
502(e)(1)(A)	If it is a drug, unless its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula)— (i) the established name (as defined in subparagraph (3)) of the drug, if there is such a name; (ii) the established name and quantity or, if determined to be appropriate by the Secretary, the proportion of each active ingredient, …; and …..	Section 502(e)(1)(A)(i) applies if the medicated feed label/labeling does not include the established (common) name of the drug. Section 502(e)(1)(A)(ii) applies if the medicated feed label/labeling does not include the quantity of the drug, or if the quantity is not listed correctly.

FD&C Act Section	Statutory Language	Notes and Examples
502(f)(1)	Unless its labeling bears adequate directions for use;	Typically applies when the labeling, distribution, or use of a VFD drug does not conform with the VFD requirements or statute. See section 504 of the FD&C Act, which says: "When labeled, distributed, held, and used in accordance with this section, a veterinary feed directive drug and any animal feed bearing or containing a veterinary feed directive drug shall be exempt from section 502(f) …."
502(o)	If it was manufactured, prepared, propagated, compounded, or processed in an establishment not duly registered under section 510, if it is a drug and was imported or offered for import by a commercial importer of drugs not duly registered under section 810(s) if it was not included in a list required by section 510(j)360(j), if a notice or other information respecting it was not provided as required by such section or section 510(k), or if it does not bear such symbols from the uniform system for identification of devices prescribed under section 510(e) of this title as the Secretary by regulation requires.	Typically applies when medicated feed requires a feed mill license and drug establishment registration and the facility it was manufactured in has not registered as a drug facility. Contact CVM prior to using this citation.

C. Prohibited Acts

Section 301 of the FD&C Act [21 U.S.C. 331] includes the prohibited acts. Common prohibited act charges for acts performed with respect to adulterated and misbranded animal food or drugs can be found in Section 301, subsections (a)-(d), and (g)-(k). Additional specific prohibited acts that may be applicable to this compliance program include:

Table 7: Specific Prohibited Acts Applicable to Subprograms

FD&C Act Section	Statutory Language	Notes and Examples
301(e)	The refusal to permit access to or copying of any record as required by section 412, 414, 417(j), 416, 504, 564, 703, 704(a), 760, or 761 of the FD&C Act; or the failure to establish or maintain any record, or make any report, required under section 412, 414(b), 417, 416, 504, 505(i) or (k), 512(a)(4)(C), 512(j), (l) or (m), 572(i), 515(f), 519, 564, 760, 761, 387i, or 920 of the FD&C Act or the refusal to permit access to or verification or copying of any such required record; or the violation of any recordkeeping requirement under section 2223 [1] of this title (except when such violation is committed by a farm).	Applies when there has been a refusal to review or copy required records (first check that the record is required under one of the listed statutory requirements). Generally, includes required records under the PCAF and ST regulations.
301(f)	The refusal to permit entry or inspection as authorized by section 704 of the FD&C Act.	Use when there has been an inspection refusal.
301(p)	The failure to register in accordance with section 510 or 905 of the FD&C Act, the failure to provide any information required by section 510(j), 510(k), 905(i), or 905(j) of this title, or the failure to provide a notice required by section 510(j)(2) or 905(i)(3) of this title.	Use when a facility has not registered as a drug facility, as required (i.e., licensed medicated feed mill).
301(dd)	The failure to register in accordance with section 415 of the FD&C Act.	Use when a facility has not registered as a food facility, as required.
301(hh)	The failure by a shipper, carrier by motor vehicle or rail vehicle, receiver, or any other person engaged in the transportation of food to comply with the sanitary transportation practices prescribed by the Secretary under section 416 of the FD&C Act.	Use when the sanitary transportation requirements in 21 CFR part 1, subpart O, have not been met.
301(mm)	The failure to submit a report or provide a notification required under section 417(d) of the FD&C Act.	Use when the facility has failed to file a reportable food registry notice, as required.
301(nn)	(nn) The falsification of a report or notification required under section 417(d) of the FD&C Act.	Use when the facility falsified a reportable food registry notice.
301(uu)	(uu) The operation of a facility that manufactures, processes, packs, or holds food for sale in the United States if the owner, operator, or agent in charge of such facility is not in compliance with section 418 of the FD&C Act.	Use when the facility is not in compliance with the hazard analysis and risk-based preventive control requirements in 21 CFR part 507, subparts C and E.

3. Actions

All reasonable steps should be taken to obtain voluntary compliance prior to initiating regulatory action. All possible administrative and legal regulatory actions should be discussed with State regulatory counterparts. Divisions should take into consideration State agencies' ability and willingness to gain prompt voluntary correction of deficiencies or pursue state enforcement action. See Part V.1. *Findings* and *Table 8: Compliance Activity Summary* of this compliance program to determine appropriate actions based on findings. If the facility's response is inadequate to protect public health, all available administrative and legal tools should be considered, such as a regulatory meeting, untitled letter, warning letter, administrative detention, registration suspension, mandatory recall, seizure, injunction, or prosecution. If the Division feels that administrative or legal action is warranted, management should initiate a preliminary assessment call with CVM's Division of Compliance. See the Regulatory Procedures Manual (RPM) for more information.

A. Advisory Actions for Public Health Hazards

Advisory Actions are defined as actions that do not include the judicial system, which may include actions such as untitled letters, warning letters, or regulatory meetings. (See IOM Subchapter 4.4.3 *Policy*, RPM Chapter 4: *Advisory Actions*, and RPM Chapter 10: *Other Procedures*). See the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States) for inspectional resources for a framework for writing advisory actions based on comprehensive animal food inspections.

(1) Regulatory Meeting

A Regulatory Meeting is a meeting requested by FDA management at its discretion, to inform responsible individuals or facilities about how one or more products, practices, processes, or other activities are considered to be in violation of the law. Regulatory Meetings can be an effective enforcement tool to obtain prompt voluntary compliance and have been used successfully in a variety of different situations, including: (1) in conjunction with another advisory action (e.g., untitled or warning letter), (2) as a follow-up to other advisory actions, or (3) to communicate violations that would not warrant another type of advisory action. Regulatory meetings provide the benefit of a real time, two-way discussion of the violations and the appropriate corrective actions. (See RPM Section 10-3 *Regulatory Meetings*).

(2) Untitled Letter

Untitled letters are used for violations that may not meet the threshold of regulatory significance for a warning letter and request correction of the violations. (See RPM Section 4-2 *Untitled Letters)*.

CVM requests that the Division post all Untitled Letters under this comprehensive animal food compliance program online to: (1) inform the public about violative practices and conditions that may pose a risk to health; and (2) deter future violations and allow similarly situated regulated entities to determine what activities and practices FDA finds violative and use the information to increase voluntary compliance with the law. For more information see: https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/issuance-untitled-letters.

(3) Warning Letter

Warning letters provide a facility the opportunity to take voluntary and prompt corrective action before FDA initiates an enforcement action for violations of regulatory significance (e.g., may lead to enforcement action if not promptly and adequately corrected). Warning Letters are issued to achieve voluntary compliance and to establish prior notice. Warning Letters are prior notice and issued with the expectation that most individuals and facilities will voluntarily come into compliance with the FD&C Act. (See RPM Section 4-1: *Warning Letters*).

B. Administrative and Judicial Actions for Imminent Public Health Hazards (All Facilities)

The following are administrative and judicial actions that can be taken, regardless of whether a facility is required to register as a food facility.

(1) FDA-Requested Recall

Although unusual in the absence of demonstrating specific product contamination, an FDA-requested recall could be considered in urgent situations and based on a Class I health hazard evaluation. (See RPM Chapter 7: *Recall Procedures*).

(2) Administrative Detention

If a determination is made that there is reason to believe that an article of food is adulterated or misbranded, administrative detention under section 304 of the FD&C Act [21 U.S.C. §334] may be considered to prevent the movement of such food while the FDA prepares for additional administrative or legal action (e.g., seizure, injunction, mandatory recall, etc.). (See RPM Chapter 5-3: *Administrative Detention of Foods)*

(3) Seizure/Injunction

When the facility's response is inadequate to protect public health and/or the facility refuses to conduct a voluntary recall, a seizure and/or injunction should be considered. (See RPM Chapter 6-1 and 6-2: *Seizures and Injunctions).*

(4) Criminal Prosecution

All criminal referrals, whether initiated by ORA, the Center, or another FDA Headquarters component, must be sent to the Office of Criminal Investigations (OCI) for initial review in accordance with Chapter 6 in the RPM. If OCI declines the referral, the Center or ORA may pursue the matter through the preparation of a Summary and Recommendation in accordance with subsection 6-5-5 et seq. (See RPM Chapter 6-5: *Prosecution).*

C. Administrative Actions for Imminent Public Health Hazards Specific to Facilities Required to Register as a Food Facility

The following are administrative actions that only apply to facilities that are required to register as food facilities.

(1) Mandatory Recall Order

If a determination is made that there is reasonable probability that an article of food is adulterated under section 402 of the FD&C Act, will cause a SAHCODHA and the facility refuses to take

voluntary corrective actions, including recall, after FDA request, mandatory recall under section 423 of the FD&C Act [21 U.S.C. §350l] may be warranted. See RPM Chapter 7: *Attachment J – Mandatory Recall Authority for Foods* and https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-and-fda-staff-questions-and-answers-regarding-mandatory-food-recalls.

(2) Suspension of Food Facility Registration

If a facility registered under section 415(a) of the FD&C Act manufactures, processes, packs, receives, or holds food that has a reasonable probability of causing SAHCODHA; and that facility created, caused or was otherwise responsible for that reasonable probability of SAHCODHA; or knew of, or had reason to know of, the reasonable probability of SAHCODHA, and packed, received, or held such food, suspension of food facility registration may be considered. If warranted, the State agency should be engaged to determine if State enforcement actions, such as embargo or permit revocation, can be utilized to stop the movement of product or production while FDA is considering enforcement actions. See CPG Sec. 100.250, *Food Facility Registration – Human and Animal Food.*

(3) Withdrawal of Qualified Facility Exemption (21 CFR part 507, subpart D)

If a facility registered under section 415(a) of the FD&C Act meets the definition of a qualified facility in 21 CFR §507.3 and has filed an attestation that they are such, FDA may withdraw their exemption from 21 CFR part 507, subparts C and E under certain circumstances. These are outlined in 21 CFR §507.60 and include:

- An active investigation of a foodborne illness outbreak that is directly linked to the qualified facility; or
- After a determination that it is necessary to protect the public health and prevent or mitigate a foodborne illness outbreak based on conditions or conduct associated with the qualified facility that are material to the safety of the animal food.

There are specific steps that must be taken in order to withdraw the qualified facility exemption, as outlined in 21 CFR part 507, subpart D.

D. Compliance Activities

CVM has not authorized Direct Reference Authority for any of the subprograms contained in this comprehensive animal food compliance program. All possible FDA compliance actions (e.g., advisory, administrative, or judicial) must receive concurrence from CVM. When warranted and allowable under FOIA, the Division should also notify State regulatory counterparts of any compliance actions within their jurisdiction to rely on, coordinate with, and leverage one another's work, data, and actions to meet the public health goal of a safe national food supply. See Part II.2.H.(1). *Notification of CVM – Violative Conditions*.

See *Table 8: Compliance Activity Summary* for a summary of potential compliance activities associated with assessing and classification outcomes. This summary is a starting point and should not be the sole basis for evaluating the significance of noncompliance. Findings should be assessed on a case-by-case basis and should consider the totality of the inspectional findings.

Table 8: Compliance Activity Summary

Significance	Example Deficiencies	Classification	Follow-up
Critical **Breakdown of animal food safety systems that results in a reasonable probability of <u>causing serious adverse health consequences or death to humans or animals (SAHCODHA)</u>.** **Limited to situations that are likely to pose an imminent public health threat.**	**21 CFR part 507:** Significant food system failure (e.g., no food safety plan, lack of food safety plan element, or lack of other practices to prevent contamination or adulteration) that results in or is likely to result in SAHCODHA and/or adulterated food, such as: • Pathogens in a ready-to-eat pet food or a pet food ingredient that will be applied post-thermal processing (e.g., palatant). • Vitamin or mineral deficiencies or toxicities (e.g., vitamin D or selenium toxicity) • Mycotoxin contamination **21 CFR part 225:** Significant system failure (e.g., lack of drug controls such as inventory, sequencing, flushing, daily reconciliation, etc.) that results in SAHCODHA and/or adulterated food, such as: • Super/sub-potency of drug level (e.g., amprolium in a chicken feed at toxic levels) • Contamination of non-target animal food with animal drug (e.g., monensin in horse feed) **21 CFR §558.6:** Extralabel Use (ELU) of a VFD feed that could result in SAHCODHA. **21 CFR §§589.2000 and 2001:** Significant system failure that results in recurring instances of prohibited material in ruminant feed or recurring failure to remove Cattle Materials Prohibited in Animal Feed (CMPAF) from raw material destined for rendering that is likely to result in SAHCODHA. **21 CFR part 1, subpart O:** Failure in practices that results or could result in contamination of animal food, or temperature failure when temperature control is required for food safety.	**OAI**	**For All:** Issue Form FDA 483 **<u>Domestic</u>** Urge immediate voluntary shutdown and submission of corrective action plan, urge voluntary recall if warranted. **Consider the following actions:** <u>All Domestic Facilities:</u> Warning Letter, FDA-requested Recall, Administrative Detention, Seizure, Injunction (Preliminary or Permanent), Criminal Prosecution <u>Registered Food Facility ONLY:</u> Mandatory Recall, Suspension of Food Facility Registration **<u>Foreign</u>** Urge immediate voluntary shutdown and submission of corrective action plan. **Consider the following actions:** Warning Letter, Detention/Refusal, Import Alert, Modifying PREDICT score, following up with FSVP and VQIP importers, contacting foreign government authorities to recommend follow up as appropriate.

Significance	Example Deficiencies	Classification	Follow-up
Major **Deviation that presents a significant public health concern.** **Specifically, a deviation that results in unsatisfactory conditions that <u>present a food safety risk and are likely to result in a system breakdown.</u>**	**21 CFR part 507:** Significant conditions that are likely to present a food safety risk, or system breakdown, such as: • Failure to follow CGMPs that could result in animal food contamination • Failure to consistently implement prerequisite programs, preventive controls, monitoring or verification activities **21 CFR part 225:** Significant conditions that are likely to present a food safety risk, or system breakdown, such as: • For licensed medicated feed mills: o Failure to perform periodic assays on medicated feeds requiring a medicated feed mill license o Failure to perform required daily reconciliation • For medicated feed mills NOT requiring a license o Failure to investigate an assay of drug components not meeting permissible drug levels **21 CFR §558.6:** Extralabel use of a VFD drug (see CPG 615.115 for low regulatory priority for minor species). **21 CFR §§589.2000&2001:** Failure to enact practices to prevent contamination of feed with prohibited materials or failure to properly label feeds containing prohibited materials. **21 CFR part 1, subpart O:** Failure in practices that results or could result in contamination of animal food, or temperature failure when temperature control is required for food safety but would not pose a SAHCODHA risk to animals consuming it.	**OAI** **or** **VAI – if unlikely to present an immediate food safety or public health risk**	**For All OAI:** Issue Form FDA 483 **<u>Domestic OAI</u>** **Consider the following actions for OAI:** <u>All Domestic Facilities</u>: Regulatory Meeting, Untitled Letter, Warning Letter, FDA-requested Recall, Administrative Detention, Seizure, Injunction (Permanent), Criminal Prosecution **<u>Foreign OAI</u>** **Consider the following actions for OAI:** Warning Letter, Detention/Refusal, Import Alert, Modifying PREDICT score, following up with FSVP and VQIP importers, contacting foreign government authorities to recommend follow up as appropriate. **<u>Domestic and Foreign VAI</u>** **Consider the following actions for VAI:** Issue Form FDA 483 and consider advisory action (e.g., regulatory meeting, Warning Letter, Untitled Letter) if there are uncorrected, repeat items that may lead to food safety or public health risk.

Significance	Example Deficiencies	Classification	Follow-up
Minor **Minor deviations that are not a significant public health concern. Deviation results in unsatisfactory conditions that if not addressed may lead to a risk to food safety risk, but is not likely to cause a system breakdown.**	**For all subprograms:** • Failure to document training (but personnel appear to appropriately carry out duties). • Minor recordkeeping deviations that are not systemic and do not lead to an immediate food safety issue. Inadequate CGMPs that relate to quality or filth (not food safety).	**NAI** **Or** **VAI – if repeat, or other conditions exist that raise public health significance**	**For NAI:** Generally, minor observations are not significant to public health. Facilities should be urged to correct observations during the inspection. Corrections should be verified and documented. Do not print on Form FDA 483. **For VAI:** Issue Form FDA 483

E. Additional Information

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4. Follow-Up

A. Regulatory Follow-Up

To verify the implementation of corrective actions, divisions should conduct domestic follow-up inspections for facilities observed to have significant deficiencies within **six (6) months** or promptly after the agreed upon date of completion of the promised corrections following the issuance of any advisory actions with an OAI classification (See FMD-86 and RPM Chapter 4). **If there are critical deviations related to an animal or human public health concern, then consider whether a shorter time frame for a follow-up inspection is warranted.**

Prior to initiating the re-inspection, the Division **must** hold a pre-inspection (enforcement strategy discussion) call with CVM DC, ORA OHAFO program contacts (e.g., National Experts) when appropriate, and, if possible, State agencies, to discuss potential follow-up actions if the facility continues to have significant violations. If the follow-up inspection reveals that the facility continues to have conditions that are likely to lead to the adulteration of animal food products or animal and/or human health concerns, the Division should consider additional compliance action based on these repeat observations. See Part II.2.H.(1). *Notification of CVM – Violative Conditions* for when to contact CVM during the inspection.

If an inspection is initially classified OAI but reclassified VAI and the facility has not taken adequate corrective action, the Division should consider reinspection of the facility within 1 year when warranted (e.g., firm response to 483 is inadequate). Facilities with an inspection classification of NAI and VAI should be re-inspected at the routine surveillance priority and frequency identified in Part II.2.D. *Comprehensive Inspection Frequency*.

B. Violative Samples

Division management must contact CVM when notified of violative sample results through the CVM email as provided in Part II.2.H.(1). *Notification of CVM – Violative Conditions*. If CVM and ORA agree that for-cause samples should be collected and analyzed, and those samples indicate a violation of the FD&C Act and applicable regulations encompassed in this compliance program, the Division must contact CVM to discuss whether a recall or compliance action is appropriate.

If State analytical results are to be used as evidence in a compliance action recommendation (i.e., there are no FDA analytical results to support the compliance action and/or charge), then the Division in which the manufacturer resides, and the State who obtained the sample, should be prepared to discuss the sample collection in detail to determine whether the evidence can support compliance action. Divisions should consider the following in determining whether the evidence is suitable for inclusion in a case submission: the manner in which the sample was obtained, sample integrity, chain of custody, method of shipping, State sampling procedures, and other relevant information to how the sample was collected and maintained prior to submission to the laboratory.

The Division recommending the compliance action must prepare a memorandum documenting the Division's review of the chain of custody as performed by the State (e.g., obtain evidence and affidavits from State individuals). The memorandum must be uploaded into CMS and must describe the manner in

which the sample was obtained, held, and transported prior to submission to the laboratory in order to ensure that the methods and procedures used to collect the sample will support a FDA compliance action. Supporting documents should include but are not limited to; Form FDA 463a (affidavit), labeling, photos, sampling procedures, State collection reports, supporting evidence obtained during the course of the sample collection, etc. Additional details may be found in the RPM 4-3*: Use of State Evidence for FDA Warning Letters and Untitled Letters*. Divisions are encouraged to contact CVM if questions arise. See Part II.2.H.(1). *Notification of CVM – Violative Conditions.*

PART VI REFERENCES, ATTACHMENTS, AND PROGRAM CONTACTS

1. General References

Major guidance and reference materials pertaining to this compliance program are listed below. Additional information and inspectional resources may be found in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

Subprogram specific references are in the relevant Appendixes.

General comprehensive animal food compliance program references:

- Investigations Operations Manual (IOM)
- Regulatory Procedures Manual (RPM)
- ORA Field Management Directives
    - FMD-70 Observation and Corrective Action Report (OCAR) – Corrective Action Report (CAR), New Expanded Functionality
    - FMD-86 Establishment Inspection Report Conclusions and Decisions
    - FMD-147 Procedure for Release of Analytical Results Pursuant to Section 704(d) and Situations When Dealer is Voluntarily Holding Product
- Manual of Compliance Policy Guides (CPGs)
- ORA Production Applications
- ORA OHAFO Dashboard
- CVM Guidance by Number
- Reportable Food Registry for Industry

2. Attachments

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3. Program Contacts

A. CVM

Purpose	Name	Organization	Contact
General Comprehensive Animal Food Compliance Program Guidance	Isaac Carney	CVM/OSC/DC/Animal Food Programs Team	EMAIL: Isaac.Carney@fda.hhs.gov PHONE: 802-309-7415
Regulatory Technical Assistance Network	rTAN Coordinator	CVM/OSC/DC/Animal Food Programs Team	EMAIL: CVMAnimalFoodPrograms@fda.hhs.gov PHONE: 301-796-0001

Purpose	Name	Organization	Contact
All Animal Food Inspection and Compliance Inquiries All Food Facility Registration Inquiries		CVM/OSC/DC/Human and Animal Food Investigations Team	
Medicated Feed Mill Licensing, Drug Establishment Registration, and VFD Distributor Notification Inquiries	Program and Business Management Team	CVM/OSC/DAF/ Program and Business Management Team	EMAIL: MedicatedFeedsTeamMail@fda.hhs.gov FAX: 240-453-6882

B. ORA

Role/Purpose	Name	Organization	Contact
ORA CVM National Experts	Josh Schafer Joe Haynes	ORA/OHAFOW ORA/OHAFOW	570-704-7175 313-393-8258
ORA Project Coordinator	Lourdes Andujar	ORA/OHAFOW	787-729-9010
Foreign Inspection Guidance	Leslie A. (Cartmill) Jackanicz	ORA/OHAFO/OHAFOE/DFHAFOE	813-915-7991
State Programs	Brenita Walker	ORA/OPOP/OP	972-804-4980

PART VII - CENTER RESPONSIBILITIES

The Center for Veterinary Medicine Office of Surveillance and Compliance will provide subject matter expertise in the maintenance and evaluation of the compliance program. The Office of Surveillance and Compliance will determine program priorities, relevant evaluation reviews, and recommend program changes. The Office of Surveillance and Compliance will lead the effort to initiate compliance program evaluations.

The Division of Animal Feeds will lead the effort in gathering and assessing data related to the medicated feed mill licensing and the VFD distributor notification programs. The Division of Animal Feeds will utilize the knowledge of subject matter experts in conjunction with outcomes of the data assessment process to make science-based program recommendations. Evaluations will be conducted on a periodic basis and outline the office's current objectives, general and specific program evaluation questions, list recommendations for process improvement, and highlight data patterns and trends for better targeting and allocation of resources.

The Division of Compliance will utilize information obtained by the program evaluations to promote consistency and continuity of inspectional approach and inspectional outcomes across all OHAFO Divisions and with our State and local regulatory partners conducting work on the Agency's behalf. In addition, the Division of Compliance will continue to provide "real time" ORA inspectional assistance when encountering violative inspections, violative sample collections, for-cause follow-up, and assistance with policy guidance when warranted and as outlined in this compliance program.

APPENDIX A – Registration, Licensing and Notification Requirements

This appendix is intended to complement and be used in conjunction with the information located in Part I-VII; review those sections as well prior to performing work under this compliance program.

1. Inspectional Approach

Prior to the inspection, field inspection staff must verify whether a facility has a food facility registration, medicated feed mill license and drug establishment registration, and/or is on the VFD distributor notification list. During the inspection, verify that the facility has the correct registration, licensure, and/or notification status based on the activities they are performing. This appendix is intended to help determine whether the facility has the correct status based on their activities.

A. Food Facility Registration (21 CFR part 1, subpart H)

Domestic or foreign facilities that manufacture, process, pack, or hold food for human or animal consumption in the United States are required to register with FDA as a food facility under Section 415 of the FD&C Act (21 U.S.C. 350d), unless an exemption applies. As a reminder, the exemptions in 21 CFR §1.226 have specific definitions associated with them in 21 CFR §1.227.

There are a number of questions and answers in the Questions and Answers Regarding Food Facility Registration (Seventh Edition): Guidance for Industry specific to animal food and the exemptions. In particular, the following references may be helpful in locating animal food topics in the GFI:

- Farms – growing and selling hay (B.1.15), growing and selling grain (B.1.18), milling and selling animal food (B.1.21), sending carcasses to a rendering plant (B.1.22), agricultural feed cooperative business model (B.1.24);
- Retail Food establishments - animal food retail food establishments (B.2.16), off-farm feed mills (B.2.17), farm supply-store (B.2.18), manufacturing and selling at retail (B.2.19)
- Restaurants –pet shelters, kennels and veterinary facilities (B.3.2);
- Non-profits –food banks with animal food (B.4.4)
- USDA establishments –USDA facilities producing pet food (B.6.3);
- General facility and animal food – university research facility selling live animals for food use (C.1.7), animal food warehouse supplying retail stores (C.1.19), feed mill (C.1.10), animal food distributor (C.1.11), animal food broker (C.1.13), pet rawhide chews (C.2.4), food for research (C.2.11), stockyard or livestock market (C.3.8), human food by-products (C.4.2), animal food by-products category information (F.3.4)

In addition, CVM has been tracking specific questions frequently received from field inspection staff about food facility registration, including:

- Is a USDA facility that is also producing pet food under USDA's voluntary pet food certification exempt from food facility registration?
    - No. The exemption in 21 CFR 1.226(g) states that FDA food facility registration does not apply to "[f]acilities that are regulated exclusively, throughout the entire facility, by the U.S. Department of Agriculture under the Federal Meat Inspection Act (21 U.S.C. 601 et seq.), the Poultry Products Inspection Act (21 U.S.C. 451 et seq.), or the Egg Products Inspection Act (21 U.S.C. 1031 et seq.)." The authority for the USDA voluntary pet food certification program comes from the Agricultural Marketing Act (7 U.S.C. 1621 et seq.), which is not part of the Federal Meat Inspection Act, the Poultry

Products Inspection Act, or the Egg Products Inspection Act. As a result, this exemption does not apply because the facility is not regulated exclusively under the Federal Meat Inspection Act, the Poultry Products Inspection Act, or the Egg Products Inspection Act. Therefore, they would need to register the pet food operation.

- Does a business that manufactures product for both animal food and other non-food uses (e.g., salt and mineral mining, biofuel production with dried-distillers grains (DDGs), etc.) have to register?
  - Yes. The facility is manufacturing, processing, packing, or holding food for consumption in the United States so they would have to register as a food facility unless another exemption applies.
- Does a retail feed store or farm feed store have to register?
  - A retail feed store (sometimes referred to as a farm feed store) is a facility that sells a variety of farm supplies, including animal food. A farm feed store may sell animal food to both farms (e.g., livestock and/or poultry food) and to end consumers (e.g., pet food). Many farm feed stores have a majority of their animal food sales to farms, which are considered businesses. Thus, many of these farm feed stores (depending on the individual store's percentage of sales to end consumers vs businesses, including farms) do not meet the retail food establishment definition and are not exempt from food facility registration. Therefore, these farm feed stores would be subject to food facility registration and 21 CFR part 507. However, they are a low regulatory priority for routine surveillance inspection (see Part II.2.C.(2). *Low Regulatory Priority*).

For facilities with questions about how to obtain a Unique Facility Identifier (DUNS number), food facility registration, and/or qualified facility attestation, the following resource may be provided: Animal Food Facility Registration and Qualified Facility Attestation Frequently Asked Questions.

B. Medicated Feed Mill License and Drug Establishment Registration

All medicated feed mills that are manufacturing a medicated feed that requires an approved medicated feed mill license must also register as a drug facility.

(1) Medicated Feed Mill License

An approved medicated feed mill license, Form FDA 3448, is **required** for facilities that manufacture:

- medicated feed using Category II, Type A medicated articles (21 CFR § 558.4(a));
- all free-choice medicated feeds that contain a Category II drug (21 CFR § 510.455(f)(1));
- free-choice medicated feeds that contain a Category I drug and use a proprietary formula and/or specifications (21 CFR § 510.455(f)(2));
- all liquid medicated feeds that contain a Category II drug (21 CFR § 558.5(g)(1)); and
- liquid medicated feeds that contain a Category I drug and use a proprietary formula and/or specifications (21 CFR § 558.5(g)(2)).

When drugs from both categories are in combination, the Category II requirements will apply to the combination drug product (21 CFR § 558.4(e)) and a mill would require a license for manufacturing that combination from a Type A medicated article.

When there is a change to the facility's name, address or responsible person, they should:

- update their unique facility identifier (UFI) information (e.g., with Dunn & Bradstreet) prior to updating registration
- submit a supplement to their medicated feed mill license
- update their drug establishment registration
- update their food facility registration

When there is a change in ownership, the facility should:

- withdraw or transfer their medicated feed mill license to the new owner
- update their drug establishment registration
- update their food facility registration

Contact CVM when there is a question about whether a facility has or needs to have an approved medicated feed mill license. See Part II.2.H.(5). *Medicated Feed Mill Licensing, Drug Establishment Registration and VFD Notification*.

Licensed medicated feed mills are inspected according to the medicated feed CGMPs found in 21 CFR part, section 225.10 to 225.115. Before a license is approved, a pre-approval inspection is required to establish that a medicated feed facility has demonstrated their methods and controls for manufacturing medicated feed will preserve the identity, strength, quality, and purity of the new animal drug and that the manufacturing of the medicated feed meets the CGMP requirements and conditions of the drug approval. See Appendix C - 1.B. *Pre-approval Inspections*.

(2) Drug Establishment Registration

Manufacturing facilities that hold an approved medicated feed mill license are required, under 21 CFR part 207 (207.13(g)), to electronically register as a drug establishment with the FDA. Non-licensed medicated feed facilities are not required to register as a drug establishment.

If a facility is required to register as a drug establishment, but has not done so:

- Provide the facility with information about how to register as a drug establishment, Medicated Feed - Resources for Registering. Remind them that drug establishment registration is required to be renewed annually between October 1 and December 31.
- Provide the facility with information on where to find the Medicated Feed Mill License application (Form FDA 3448). The application is available as a fillable PDF but will need to be submitted in hard copy with an original signature to CVM (FDA/CVM, Division of Animal Feeds, HFV-220, 12225 Wilkins Avenue, Rockville, MD 20852).

Contact CVM when there is a question about whether a facility has or needs to have a drug establishment registration see Part II.2.H.(5). *Medicated Feed Mill Licensing, Drug Establishment Registration and VFD Notification*.

(3) Drug Establishment Registration Cancellation and Medicated Feed Mill License Voluntary Withdrawal

If requested by the facility, inform them to electronically withdraw (De-Registration) their drug establishment registration.

For a facility that wants to withdraw its medicated feed mill license without prejudice, have the facility contact the Medicated Feeds Team, see Part II.2.H.(5). *Medicated Feed Mill Licensing, Drug Establishment Registration and VFD Notification*.

A link to the "Registration Application (portal)" can be found on the FDA website under "Resources for Registering" at: https://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/default.htm.

C. Veterinary Feed Directive Distributor Notification and Removal

Distributors of VFD feed must submit a one-time notification to FDA of their intent to distribute VFD feed (21 CFR 558.6(c)(5)). To verify whether a distributor has submitted their notification, the VFD distributor list is located on Animal Drugs@FDA under the "Medicated Feeds" section.

There are two lists – one sorted by distributor name and one sorted by state.

Any new VFD distributor notifications, or changes in ownership, business name, or business address to an existing VFD distributor notification must be sent to:

Food and Drug Administration, Center for Veterinary Medicine, Division of Animal Feeds (HFV-220)
12225 Wilkins Avenue,
Rockville, MD 20852
FAX: 240-453-6882
EMAIL (attached): MedicatedFeedsTeamMail@fda.hhs.gov

If a VFD distributor wants to be removed from CVM's Veterinary Feed Directive Distributor Notification List, they should be encouraged to contact CVM and request removal see Part II.2.H.(5). *Medicated Feed Mill Licensing, Drug Establishment Registration and VFD Notification.*

2. Compliance and Regulatory Information

A. Food Facility Registration

Certain regulatory requirements and administrative actions are tied specifically to facilities that are required to register. Historically, animal food facility inspections and work planning inventories have been driven by the medicated feed mill CGMP and BSE regulations, not food facility registration. As a result, some animal food businesses may have voluntarily registered as a food facility, even if they were exempt from registration. Other animal food businesses may not have registered, even though they are required to, based on their activities.

When considering a compliance activity based on either (1) requirements that are tied to food facility registration (e.g., PCAF regulation), or (2) compliance actions that are tied to food facility registration (e.g., mandatory recall or food facility registration suspension), **first independently verify that the facility's activities would require them to register as a food facility**.

If a food facility voluntarily registered, but is exempt from registration, an inspection of the facility may still be performed based on any subprograms (e.g., medicated feed CGMPs, BSE, etc.) that are not tied to food facility registration. If the facility is not subject to any other subprograms, but there is a potential food safety issue, contact CVM to determine the best course of action under the FD&C Act requirements. See Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support*. For more

information see Part I.8. *Summary of Adulteration and Misbranding Provisions for Facilities not Subject to Specific Animal Food Safety Regulations (21 U.S.C. §§342 and 343).*

B. Medicated Feed Mill Licensure and Drug Establishment Registration

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C. VFD Distributor Notification

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3. Resources

- FDA Registration of Food Facilities and Other Submissions
- Questions and Answers Regarding Food Facility Registration (Seventh Edition): Guidance for Industry
- FDA Medicated Feeds
- FDA Drug Establishments Current Registration Site
- FDA Veterinary Feed Directive
- Guidance for Industry #120: Veterinary Feed Directive Regulation Questions and Answers
- Listing of VFD Distributor Notifications - see Animal Drugs @ FDA, under the Medicated Feeds section, for current listings. Lists are available in PDF and Excel formats. Updates to the lists are made as notifications are processed.
- Inspectional Resources: Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

4. Legal History

A. Food Facility Registration

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (the Bioterrorism Act) directs FDA, as the food regulatory agency of the Department of Health and Human Services (HHS), to take steps to protect the public from a threatened or actual terrorist attack on the U.S. food supply and other food-related emergencies.

To carry out certain provisions of the Bioterrorism Act, FDA established regulations requiring that:

- Food facilities register with FDA, and
- FDA be given advance notice on shipments of imported food.

These regulations became effective on December 12, 2003.

There are some challenges with determining which animal food facilities must register that are unique to animal food facilities. At the time the food facility registration regulations were enacted, animal food facilities were primarily inspected under the medicated feed CGMP and BSE regulations – which both apply regardless of whether a facility is required to register as a food facility. Also, several of the definitions in food facility registration regulation, while inclusive of animal food facilities, are written in a way that is more intuitive for human food facilities and the human food regulatory structure. For example, the retail food establishment definition and exemption in food facility registration tracks very closely with how human food facilities are regulated by local authorities under the model retail food code.

Animal food facilities do not have a similar regulatory structure for retail establishments. In addition, some retail stores may not meet the definition of a retail food establishment because the majority of their customers are businesses, such as farms. As a result, some animal food businesses have traditionally registered as a food facility when they were unsure whether they met an exemption.

Since the enactment of food facility registration, several sets of requirements have been tied to food facility registration. Primarily these are the requirements for the reportable food registry under FDAAA in 2007 and a number of requirements under FSMA in 2011.

The FDA Food Safety Modernization Act (FSMA), enacted on January 4, 2011, amended section 415 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), in part, to require that facilities engaged in manufacturing, processing, packing, or holding food for consumption in the United States submit additional registration information to FDA, including an assurance that FDA will be permitted to inspect the facility at the times and in the manner permitted by the FD&C Act. Section 415 of the FD&C Act, as amended by FSMA, also requires food facilities required to register with FDA to renew such registrations every other year and provides FDA with authority to suspend the registration of a food facility and require a mandatory recall in certain circumstances. Many of the other requirements in FSMA, such as hazard analysis and risk-based preventive control requirements are tied to food facility registration. Note that for animal food, CGMP requirements are also tied to food facility registration, which is different than human food where CGMP requirements apply regardless of whether the facility is required to register.

B. Medicated Feed Mill Licensing and Drug Establishment Registration

The passage of the Animal Drug Availability Act (ADAA) in October of 1996, abolished medicated feed applications (Form FDA 1900) and established medicated feed mill licenses, (Form FDA 3448). The ADAA amended the FD&C Act to require a single medicated feed mill facility license to manufacture feeds that were previously covered by multiple Medicated Feed Applications (MFAs). New regulations, contained in 21 CFR Part 515, governing medicated feed mill licenses were published on November 19, 1999.

Any new animal drug approved for use in animal feed is placed in one of two categories, Category I or II. Facilities using Category II Type A Medicated Articles to make medicated feeds are required to register with FDA and hold an approved medicated feed mill license.

On May 28, 2003 (68 FR 31645), in the Federal Register, CVM proposed changes to the regulations for liquid medicated feed and free-choice medicated feed. The purpose of the proposed changes in the regulations for liquid medicated feed was to clarify what data are required to demonstrate chemical and physical stability of a drug in liquid feed, how such data may be submitted for use in the new animal drug approval process, and which liquid medicated feeds may be manufactured in a feed manufacturing facility that has not obtained a medicated feed mill license from FDA. The purpose of the proposed changes in the regulations for free-choice medicated feed was to ensure that they are consistent with the requirements for liquid medicated feed, and that provisions for free-choice medicated feed and liquid medicated feed comply with the terms of the Animal Drug Availability Act (ADAA) of 1996.

The final rule published on May 27, 2004 (69 FR 30194) with an effective date of June 28, 2004. The final rules adopted the proposed rules without change. For both the liquid and free-choice medicated feed final rules, FDA concluded that an approved medicated feed mill license is required for facilities that manufacture feeds using Category II drug(s) or manufacture those products using Category I drug(s) that must follow proprietary formulas or specifications.

C. VFD Distributor Notification

Before 1996, there were only two options for dispensing new animal drugs: (1) over-the-counter (OTC), and (2) prescription. In 1996, Congress enacted the Animal Drug Availability Act (ADAA) to facilitate the approval and marketing of new animal drugs and medicated feeds. As part of the ADAA, Congress recognized that certain new animal drugs intended for use in animal feed should only be administered under a veterinarian's order and professional supervision. Therefore, the ADAA created a new category of products called veterinary feed directive (VFD) drugs. As part of this amendment, Congress placed requirements on persons distributing VFD feed to notify FDA of their name and business address prior to the first time they engage in distribution of VFD feed (see Section 504(a)(3)(C) of the FD&C Act (21 U.S.C. 354(a)(3)(C)). In June 2015, FDA published a final rule that revised the VFD regulations in 21 CFR 558.6 and introduced clarifying changes to the definitions in 21 CFR 558.3 (80 FR 31708, June 3, 2015) to, in part, implement these statutory requirements.

APPENDIX B – PCAF Requirements (21 CFR part 507)

This appendix is intended to complement and be used in conjunction with the information located in Part I-VII; review those sections as well prior to performing work under this compliance program.

1. Inspectional

Inspections conducted under the comprehensive animal food compliance program should evaluate the facility's adherence, as applicable, to the requirements.

Your inspection should cover the requirements in 21 CFR subparts A and F, as well as the applicable requirements under the appropriate PAC, as follows:

- PAC 71014/71S014: CGMPs in part 507, subpart B
- PAC 71015/71S015: CGMPs in part 507, subpart B and PCs in part 507, subparts C and E
- PAC 71016/71S016: CGMPs in part 507, subpart B and Requirements for a Qualified Facility in 21 CFR §507.7
- PAC 71017/71S017: CGMPS in part 507, subpart B and Modified Requirements for Facilities Solely Engaged in the Storage of Unexposed Packaged Animal Food Requiring Time/Temperature Control for Food Safety (e.g., refrigerated warehouses) in 21 CFR §507.51

For more information about how to determine what requirements a facility should be inspected under and corresponding PAC, see Part III.1.A. *Inspections*.

A. Scope of Inspection

The scope of the inspection will depend, in part, on the purpose for your visit, previous inspectional findings, as well as the other applicable regulations as dictated by the facility's activities. Field inspection staff should select, at minimum, two types of animal food to follow during the comprehensive inspection. Field inspection staff must consider the following when selecting animal food to review during a comprehensive inspection, animal food that:

- may pose a higher public health risk and/or have not been previously reviewed, including:
  - animal food for which the facility has identified one or more hazards requiring a preventive control;
  - animal food associated with known or reasonably foreseeable hazards that may result in SAHCODHA;
  - animal food associated with more complex manufacturing processes at the facility which may be prone to manufacturing errors or the introduction of hazards during manufacturing; and/or
  - animal food that a facility has determined does not need a preventive control because of the use of prerequisite programs.
- would also be appropriate to review under other regulations that apply to the facility (e.g., BSE, part 225, or VFD requirements).

As always, the scope of the inspection may change based on the findings and totality of the inspection.

B. Inspection Approach

At the beginning of the inspection, perform an initial interview and walk-through of the facility and grounds to better understand the facility operations, product flow, employee flow, overall practices, and to

identify key personnel responsible for conducting different activities at the facility. During the initial interview and walk-through, the focus should be on reviewing the CGMP requirements and gaining more understanding of the facility's operations.

After the initial interview and walk-through, focus on the animal food products identified to review the facility's operations, procedures, and practices in more detail. During this part of the inspection, focus on the facility's procedures, food safety plan (if applicable), and implementation of their processes, procedures, and food safety plan. Interview key personnel performing the activities to ensure they are performed consistently and in accordance with the facility's procedures.

(1) CGMP Requirements in 21 CFR part 507, subpart B

The CGMPs serve as baseline food safety and sanitation standards for the manufacturing, processing, packing, and holding of animal food. The CGMPs are flexible in nature because they apply to a wide variety of animal food facility types that serve a wide variety of animal species. This flexibility is signaled by terms such as "if applicable," "adequate," or "as appropriate and necessary." What is applicable, adequate, appropriate, or necessary for one animal food facility may be very different than for another animal food facility, or for a human food facility.

For facilities that are subject to the hazard analysis and risk-based preventive controls requirements in 21 CFR part 507, subparts C and E, the CGMPs serve as the foundation of the facility's food safety plan. Some facilities may rely on their adherence to CGMPs as part of their determination as to whether a known or reasonably foreseeable hazard is likely to occur in their facility. For these facilities, it is important to review the CGMPs and the role they play in the facility's overall food safety system, but your inspectional focus may center more on the food safety plan and its implementation.

For facilities that are not subject to the hazard analysis and risk-based preventive controls requirements in 21 CFR part 507, subpart C or E, but are subject to modified requirements (e.g., qualified facilities and warehouses), the CGMPs may play a more significant role in the facility's overall food safety system. As a result, in these types of facilities your inspection may focus more heavily on reviewing the CGMP requirements.

Some facilities subject to the CGMPs in part 507, subpart B will also be subject to the medicated feed mill CGMPs in part 225 (see 21 CFR §507.1(c)). These two sets of CGMP requirements contain some overlap, particularly with respect to personnel, grounds, buildings, equipment and pest control requirements. The 21 CFR part 507 CGMP requirements are often more specific in these areas; however, the 21 CFR part 507 CGMP requirements do not specifically address the use of animal drugs in the manufacturing of medicated feed. When performing a comprehensive inspection, focus on the 21 CFR part 507 CGMP requirements when reviewing the areas where the CGMPs overlap, and focus on the 21 CFR part 225 medicated feed mill CGMP requirements when reviewing the use of drugs and the subsequent manufacture of medicated feed at the facility.

All facilities subject to part 507 are subject to the training requirements in 21 CFR §507.4. During the inspection, ask the facility about their training programs and requirements. If there are concerns, review the facility's training documentation, but the focus of written observations related to training should be limited to situations where an employee's lack of training can be directly correlated to a food safety failure. The only training documentation that is required for

each employee is the training in the principles of animal food hygiene and food safety. (21 CFR §507.4(c)).

As a reminder, there are no required records for the implementation of the CGMPs in 21 CFR part 507, subpart B. Some facilities may have written procedures and/or keep implementation records, but these records are not required and would not be subject to the recordkeeping requirements in subpart F unless these procedures and records are also being used as part of the facility's food safety plan (e.g., also used as a prerequisite program or preventive control). Facilities should be able to demonstrate that they are able to consistently and effectively implement their CGMP practices to meet the requirements since records are not required in 21 CFR part 507, Subpart F to document these practices.

(a) Plants, Buildings, Grounds, Water, and Pest Control

CGMPs: 21 CFR §507.17 Plants and Grounds, 21 CFR §507.20 Water Supply and Plumbing, and 21 CFR §507.19(d)/(e) Sanitation: toxic materials and pest exclusion.

The plant, buildings, grounds, and pest control requirements focus on ensuring that pests, and the physical space the animal food is produced in does not lead to the contamination of animal food. As a result, during the inspection focus on:

- Reviewing buildings and structures to ensure they do not serve as a source of contamination of animal food and prevent the ingress of pests.
    - Focus on the suitability of the plant or buildings for the animal food, adequate space for cleaning and maintenance, and overall design, construction and maintenance of the buildings. Look for potential routes of contamination that result from the construction of the facility, such as condensation or leaks that could contaminate animal food.
    - Remember in animal food facilities animal food may be stored outdoors. Ask the facility about ingredient turnover and practices to determine whether it is likely the animal food will become contaminated during outdoor storage.
- When water is used for the production of animal food, review and ensure the water supply used in the facility is safe and adequate for the activities being performed. As a reminder, some animal food facilities may not use water in their plants. Furthermore, what may be considered acceptable handwashing facilities in an animal food may differ from a human food facility – there may be some situations where handwashing with water is not necessary for the safe production of animal food and the use of waterless hand cleaners (including hand sanitizers) may be adequate.
- Reviewing grounds and areas around the plant with a focus on areas that could contaminate animal food (e.g., areas around outdoor bulk storage or loading/unloading areas) and a focus on areas that could serve as pest harborage.
- Asking questions about the facility's pest control practices and reviewing the grounds and buildings for evidence of recent pest activity to ensure pests and/or pesticides will not serve as a source of contamination for animal food. As a reminder, observations related to pest control should focus on whether there is an active infestation at the facility and how that infestation has or could contaminate the animal food. In addition, rodent bait may be acceptable within an animal food facility (unlike a human food facility) so long as the conditions in the facility would not result in the animal food being contaminated by the rodenticide.

(b) Equipment & Sanitation

CGMPs: 21 CFR §507.19 Equipment and 21 CFR §507.22 Sanitation

The equipment and sanitation requirements focus on ensuring that the animal food is appropriately manufactured and does not become contaminated. During the inspection, focus on:

- Reviewing the overall condition of equipment to ensure it does not serve as a source of contamination (e.g., made of suitable materials, no parts breaking off, leaks, animal food build-up, etc.)
- Reviewing the overall operation of equipment to ensure that it is working as intended (e.g., automatic features such as belts, pulleys, augers, conveyors, feeder bins, etc.). For example, if the facility is using automated systems to add ingredients, the system should work as intended to prevent the excess addition of nutrients that could result in a nutrient toxicity.
- Ensuring that instruments and measuring devices (e.g., thermometers, pH meters, etc.) are accurate and appropriate for their use.
- Asking about the facility's sanitation procedures and reviewing the sanitation practices for both food and non-food contact surfaces.
    - Not all animal food facilities will utilize wet-cleaning or sanitizing. For example, wet-cleaning and sanitizing may be unlikely in livestock facilities which may use flushing, sweeping, vacuuming, or other dry-cleaning methods.
    - Cleaning and sanitizing practices should be appropriate to the type of animal food being produced.
    - Cleaning and sanitizing agents should be appropriate for the application (e.g., food-contact, etc.) and used according to their labeled directions.

(c) Plant Operations, Animal Food Holding & Distribution

CGMPs: 21 CFR §507.25 Plant Operations, 21 CFR §507.27 Holding and Distribution

Plant operations and holding and distribution requirements focus on the processes and practices at the facility to ensure that animal food is safely manufactured and not contaminated from ingredient receipt to distribution. As a result, during the inspection focus on:

- Determining who is responsible for the facility's compliance with the requirements and who is responsible for supervising the overall cleanliness of the plant.
- Reviewing the facility's ingredient receiving and storage practices, including a review of how the facility examines raw materials and ingredients to ensure they are suitable and what they do if the ingredients are not suitable.
    - Ask the facility about their system for examining their ingredients to determine if they are suitable (e.g., right product, right concentration, no visual or olfactory defects, packaging is intact and no signs of contamination, etc.)
    - For facilities handling ingredients susceptible to mycotoxins or other natural toxins, ask how the facility is evaluating and using these ingredients.
    - For facilities handling ingredients that are refrigerated or frozen to minimize the potential for the growth of undesirable microorganisms, review the facility's practices for ensuring appropriate temperatures at receipt, and maintaining

appropriate temperatures after receipt, including during thawing processes to prevent the growth of undesirable microorganisms.

- Asking the facility about their system for ensuring that all animal food in the facility is accurately identified. As a reminder, the facility may use a variety of systems for identifying animal food including, but not limited to: placards, chalkboards, numbering systems, and other methods. Focus on determining if facility personnel can consistently and accurately identify ingredients using the system they have in place.
- Reviewing the facility's operations to ensure they are performed in a way that protects against the contamination of animal food and, if applicable, that controls are in place to minimize the growth of undesirable microorganisms or protect against contamination. Focus on how the facility's systems work together from ingredient receipt to distribution of finished animal food.
    - For example, management could direct employees to verify that equipment and automated systems are performing correctly to protect against contamination. To do so, employees might be required to routinely verify the accuracy of scales, or other measuring devices. In addition, they may be required to perform a visual check when the computer system says a bin is empty to ensure it is in fact empty before refilling. Ensure that the employees are consistent conducting these practices.
- Determining if the facility is using testing procedures, where necessary, to identify sanitation failures or possible animal food contamination.
- Reviewing the facility's practices for assessing animal food when the food has become adulterated or is returned from distribution (e.g., is it assessed, rejected, disposed of, or, as appropriate, treated or processed to eliminate the adulteration).
- Review the facility's distribution practices. For bulk animal food, focus on the facility's practices for ensuring that shipping containers are not going to contaminate the animal food.

(2) Hazard analysis and risk-based preventive controls requirements in 21 CFR part 507, subparts C and E

Facilities subject to the hazard analysis and risk-based preventive controls requirements in 21 CFR part 507, subparts C and E will have to develop a food safety plan that includes a hazard analysis, and, if applicable, preventive control(s) with associated management components.

During the review of the food safety plan, focus first on whether the decisions the facility made in their hazard analysis make sense for their animal food and facility, and then focus on whether the food safety system they have set up (e.g., prerequisite programs, preventive controls, management components, supply-chain applied preventive control, etc.) makes sense based on their conclusions in the hazard analysis. Also, review their implementation of their food safety plan by interviewing employees, observing practices, and reviewing a subset of implementation records.

The hazard analysis and food safety plan must be developed by a Preventive Controls Qualified Individual (PCQI), but that person does not have to be an employee of the facility. If the PCQI is not an employee of the facility, or is unavailable during your inspection, personnel at the facility should be able to answer questions about the food safety plan, including the hazard analysis. Regardless of who wrote the food safety plan, it is the facility's plan and they must have

sufficient working knowledge of the food safety plan, including the hazard analysis, to implement it.

(a) Hazard Analysis

The hazard analysis should be unique to the facility's animal food and facility. While there may be similarities between certain types of animal food facilities within the same corporate structure, there will also be differences that will affect the hazard analysis and food safety plan. As a result, the food safety plan, including the hazard analysis, should reflect the animal food and processes at that particular facility even if the company has developed a plan based on a corporate model. For example, the hazard analysis should not include ingredients or products that have never been made and that are not planned at a facility. Likewise, equipment and processes that are not specific to the facility's manufacturing activities should not be referenced in the food safety plan.

Unless otherwise directed, field inspection staff are not expected to conduct an independent written hazard analysis. However, field inspection staff should familiarize themselves with hazards that may be applicable based on the facility's animal food and processes using their inspectional tools. See the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States) for inspectional resources. During the review of the hazard analysis, first ask questions about how the facility, prepared the hazard analysis and what process they used to identify and evaluate their known or reasonably foreseeable hazards.

- If their hazard analysis process makes sense, review the hazard identification and evaluation for the selected animal foods. As a reminder, the facility only has to identify the known or reasonably foreseeable hazards associated with their animal food and facility; they do not have to document other hazards they considered but did not determine to be known or reasonably foreseeable.
- If there are concerns about the hazard analysis process, consider performing a broader review of the hazard analysis to determine if the facility identified applicable known or reasonably foreseeable hazards associated with their animal food and processes, and whether their conclusions of the hazard evaluation make sense (e.g., severity and probability of occurrence are supported by science and reflect the facility history or conditions).

Some animal food manufacturers are also subject to the requirements in 21 CFR part 113 for thermally processed low-acid foods packaged in hermetically sealed containers (LACF requirements). These facilities are exempt from considering microbiological hazards in their hazard analysis; however, they would still have to consider physical and chemical hazards.

Some facilities will rely on prerequisite programs to support how likely a hazard is to occur in the absence of a preventive control. Examples of prerequisite programs includes compliance with other FDA regulations that reduce the likelihood of a hazard (e.g., medicated feeds CGMPs, BSE regulations, or part 507 CGMPs), standard operating procedures (SOPs) (e.g., receiving procedures), or processes such as physical hazard screening or detection.

If a facility is using a prerequisite program in order to decrease the likelihood that a hazard is likely to occur in the absence of a preventive control, then your review should confirm:

- adequate documentation about the prerequisite program is included as part of the hazard analysis (e.g., SOPs, records demonstrating compliance with other regulations, etc.);

- the facility can demonstrate their prerequisite program is effective at reducing the likelihood that the hazard would occur; and
- the facility is consistently implementing the prerequisite program.

If the facility's prerequisite program is not sufficient to reduce the probability the hazard would occur, or if the facility is not consistently implementing the identified prerequisite program, then the conclusions in their hazard analysis are not supported.

If the facility is relying on compliance with another FDA regulation as the prerequisite program and they are out of compliance with that regulation, focus your observations on their compliance with that regulation rather than on the failure of the prerequisite program. For example, if a medicated feed facility is relying on compliance with 21 CFR 225 to prevent drug carryover and there is an issue with physical cleanout, sequencing, or flushing procedures, focus your observations on the failure to comply with 21 CFR 225 while noting in the "specifically" language that the facility is also using these procedures as a prerequisite program to prevent drug carryover.

In summary, the hazard analysis must be specific to the facility's activities and ultimately drives the facility's food safety program. During the review, make sure the facility has: (1) identified applicable the known or reasonably foreseeable hazards based on their animal food and processes; (2) made reasonable conclusions based on experience, illness data, scientific data, and other information in their hazard evaluation (i.e., whether a hazard requires a PC or not); and (3) if they are using prerequisite programs, demonstrated those programs are effective at reducing the probability a hazard will occur and are consistently implemented.

Some facilities may reasonably conclude that there are no hazards requiring a preventive control. If so, the facility's written food safety plan will not have PCs or associated management components. As a result, the only additional food safety plan requirement to review is the facility's history of reanalysis.

(b) Review of Preventive Controls and Validation

For each hazard requiring a preventive control, review the facility's preventive control, or set of preventive controls, for that hazard. The review should focus on whether the preventive controls will effectively control the hazard:

- PC location(s): Does the overall PC system make sense - will the PC or PCs control the hazard at or after each point in the process where the hazard may be introduced or re-introduced?
- PC validation: Does the PC significantly minimize or control the hazard – does the facility have sufficient scientific information for their validation to support that the PC will do its job?
    - As a reminder, sanitation controls and supply-chain-applied control do not require validation, but the facility should be following the manufacturers labels for the use of cleaning and sanitizing agents.
    - The facility can rely on available scientific information or generate their own information. Validation should reflect the facility's conditions. For example, if a facility is relying on a mixer study, then the facility should be using the same

type of equipment and using it per manufacturer's specifications as specified in the study.
    - Information may not be as readily available in animal food matrices as human food matrices. It is acceptable to rely on data generated in human food matrices so long as they are similar to the animal food matrix. Contact CVM's rTAN if there are questions about the suitability of validation data. See Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support.*
- PC procedures: Do the procedures have all the required information and do they match the validation information? For example, if the validation identifies time, temperature, and moisture as relevant to the control, does the PC procedure account for all three of these parameters?

(c) Review of Preventive Controls Management Components

The PC management components are intended to ensure that the facility's preventive controls are effective and consistently implemented. During the review, focus on: (1) whether the facility's PC management component system achieves these purposes and (2) if the facility is identifying and resolving food safety issues before introducing animal food into interstate commerce. While it's important to review the preventive control management component procedures, the primary inspectional focus should be to observe the facility's implementation of those procedures and review historical records to determine if the facility is managing the implementation of their preventive controls.

During the inspection, interview various personnel to determine if they understand their role in implementing the PC management component(s). Observe employee practices, or conduct a record review to determine if the actions they perform in that role are consistent with the written procedures. For example, if the written procedure says monitoring will be done hourly, but line personnel say it is monitored once per shift, there could be a PC parameter that the facility is failing to meet.

Also review a subset of management component records to determine how a facility identifies and handles a situation where a PC or management component has failed. Did the facility fail to identify situations that should have resulted in a corrective action (e.g., monitoring or verification of implementation and effectiveness failures)? Did the corrective actions: (1) fix the immediate food safety problem, (2) prevent the likelihood that the problem would reoccur, and (3) appropriately address the disposition of the affected food. If so, this is an indication that the facility's food safety plan is effective. If not, determine whether the problem is systemic and identify the scope of all potential product affected.

If the facility has a hazard requiring a preventive control, review the written recall plan. As a reminder, a recall plan is only required if the facility has identified a hazard requiring a preventive control. In addition, the recall plan requirements are specific to the facility, must contain procedures to take during a recall, and these procedures must be assigned to individuals. The procedures do not have to identify the circumstances under which a facility would initiate a recall and do not obligate a facility to conduct a recall (see 21 CFR part 7 for instructions regarding voluntary recalls).

Review the reanalysis history for the past three years or since the last inspection was conducted, whichever is shorter. Focus your review of the reanalysis history on determining whether the

facility has had any circumstances that require a reanalysis (e.g., new ingredients, new processes, unanticipated food safety issues, PC or food safety plan as a whole is ineffective, etc.). As a reminder, when a facility conducts a reanalysis because of a specific change or issue, they do not have to reanalyze the entire food safety plan. They would, however, have to reanalyze the applicable portions of the food safety plan that would be impacted by the change or incident. In addition, reanalysis of the food safety plan as a whole must be conducted at least once every three years. See section 5.8.6 *Reanalysis* of Draft Guidance for Industry #245: Hazard Analysis and Risk-Based Preventive Controls for Food for Animals.

Throughout the inspection, also review required records to ensure they meet the recordkeeping requirements as required in 21 CFR part 507, subpart F, and ensure that the food safety plan has been signed by the owner, operator, or agent in charge. For your reference, the PCAF Recordkeeping Requirements Summary is available in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

(d) Review of Supply-Chain Program

The supply-chain-applied control, also referred to as the supply-chain program, is a type of preventive control where the control must be applied at a supplier prior to receipt by the receiving facility. There are a number of activities that may look like a supply-chain program, **but are not**, such as:

- Facilities may have supplier or ingredient receiving procedures as part of their normal business practices, but do not review those under the supply-chain program requirements.
- Facilities may also have preventive controls at receiving where the facility is performing an action to control the hazard, but do not review those under the supply-chain program requirements because their supplier is not controlling the hazard.
- Facilities may have normal business practices that include procedures for ingredient receiving that requires the supplier to provide a Certificate of Analysis or other documentation. Review these practices under the CGMP requirements or as part of the hazard analysis if they are identified as a prerequisite program.

Only review a supply-chain program if the facility has identified, in their food safety plan, that they have a hazard requiring a preventive control that they are controlling with a supply-chain-applied control. Facilities may use similar terminology to describe all of these practices. As a result, be very clear in your discussions about whether a hazard is being controlled by the supplier as part of a supply-chain program.

As a reminder, there are definitions for the roles of supplier and receiving facility in a supply-chain program. Key points from these definitions include:

- The receiving facility (the facility being inspected) must be a manufacturer/processor and subject to the PC requirements.
- The supplier is not necessarily the person that directly provided an ingredient to the receiving facility. The supplier is the last person that performed an activity on the ingredient beyond some minimal processing like labeling.

If the facility has identified a hazard requiring a preventive control AND has determined in their food safety plan that they will control that hazard with a supply-chain program, then review the supply-chain program according to the requirements in 21 CFR part 507, subpart E. The focus of

the review should be on ensuring that the receiving facility has approved their suppliers, has identified appropriate supplier verification activities, and is implementing those supplier verification activities to ensure that the hazard was indeed controlled prior to receipt of the ingredient. As a reminder, the receiving facility may rely on a third-party to identify and perform supplier verification activities, but the receiving facility must agree with those activities and review the documentation. A third-party cannot approve suppliers for the receiving facility.

Because the receiving facility must approve the individual suppliers in order to meet the supply-chain requirements, it may not be practical to use a supply-chain applied control for raw agricultural commodities. In some situations, it may be easier for a facility to control the hazard themselves. As a result, it is not likely that many animal food facilities will implement a supply-chain program to control a hazard. Some examples of where a supply-chain program may be used to control a hazard are: (1) controlling a nutrient deficiency or toxicity in an ingredient purchased from a pre-mix manufacturer; or (2) controlling a pathogen hazard in an ingredient that is applied post kill step (e.g., spray on fats and palatants in pet food manufacturing).

NOTE: A supply-chain program is not required for food that is supplied for research or evaluation use, provided that certain conditions are met, e.g., the food is not sold or distributed to the public and the food is labeled with the statement "Food for research or evaluation use." Additionally, if a manufacturer/processor is an importer, they are not required to conduct supplier verification activities for the imported product if they are in compliance with 21 CFR 1, subpart L *Foreign Supplier Verification Programs for Importers of Food for Humans and Animals* (FSVP) for the covered animal food. Further guidance covering the interaction between FSVP and Preventive Controls (PC) supply-chain programs can be found here.

(e) Review of use of Customer Provisions

Some facilities may identify a hazard requiring a preventive control, but may instead rely on a customer (another manufacturer) to control the hazard. As an example, a manufacturer of raw, meat-based proteins may utilize the customer provisions and rely on their customer, a manufacturer of extruded, dry dog food, to control the hazard of pathogens. **As a reminder, customer provisions cannot be used to pass a hazard on to the end user – there must be another manufacturer/processor later in the supply-chain who will control the hazard.**

When reviewing the facility's use of customer provisions, focus the review on the facility's disclosure that the hazard has not been controlled in "documents of the trade" that will be sent to their customer. Some key things to keep in mind about the disclosure statement and documents of the trade:

- The facility must specifically identify the hazard so that the key food safety personnel receiving the animal food knows what needs to be controlled. The only exception to this is microbiological pathogens, which can be identified using a general description for the hazard, instead of listing each of the specific pathogens. While the regulation specifies the disclosure should say "Not processed to control [x] hazard," from an inspectional standpoint focus on whether the language the facility uses conveys the key food safety information that would be needed by the customer's personnel to identify what hazard(s) have not been controlled.
- Documents of the trade is a very broad term that can include a variety of documents that accompany the animal food. During the review it is important to ensure that: (1) the

document accompanies the animal food, (2) the document is shipment specific, and (3) the document is the type of document food safety personnel are likely to receive and read (e.g., they are likely to receive and read a bill of lading, but not a contractual agreement).

NOTE: There are written assurance requirements in the regulation, but these are not currently being enforced while they are being revised. (See Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs: Guidance for Industry).

(3) Modified Requirements for Facilities Solely Engaged in the Storage of Unexposed Packaged Animal Food Requiring Time/Temperature Control for Food Safety (21 CFR §507.51)

Refrigerated warehouses are the facilities most likely to be inspected under these requirements. As a reminder, these facilities are subject to CGMP requirements, subpart B. which should also be evaluated during the course of the inspection. These facilities are exempt from 21 CFR part 507, subparts C and E. As a result, they may not have a hazard analysis. Instead, they will be following the modified requirements for time and temperature control in 21 CFR § 507.51. Focus this part of the inspection on ensuring that the facility is: (1) monitoring the temperature and/or time; (2) taking corrective action if there is a loss in temperature; and (3) performing the required verification activities (calibration/accuracy checks and reviewing monitoring, corrective action, and calibration records).

(4) Qualified Facility Requirements

Review the facility's compliance with CGMPs. Qualified facilities will submit an attestation with their food facility registration. When preparing for an inspection, review the attestation information to determine whether the facility attested to: (1) identifying potential hazards and subsequently controlling the hazards (including monitoring the controls), or (2) comply with non-Federal food safety laws (e.g., local or state regulations). There are different requirements associated with each attestation type, as such focus the review on the requirements associated with the attestation type the facility selected.

If the facility has attested that they have identified their potential hazards and are controlling them, ask what procedures they have implemented and review their processes and any supporting documentation that demonstrates the hazard is being controlled. Note that qualified facilities are exempt from most recordkeeping requirements. As a result, focus on observing the process and interviewing various employees to determine if they are effectively and consistently controlling the hazard.

If the facility has attested that they are in compliance with non-Federal food safety laws (e.g., local or state regulations), ensure that their business address information is available as appropriate (e.g., on label for packaged animal food, or at point of purchase for bulk animal food) and review any supporting documentation the facility relies on to show that they are subject to and in compliance with local or state animal food safety regulations (e.g., active license, registration, recent inspection report, etc.).

When an animal food facility has not filed an attestation, conduct a full PCAF inspection even if they meet the definition of a qualified facility. If the firm meets the definition of a qualified facility, provide them the information on how to submit an attestation. If there are circumstances

that exist where a full CGMP/PC inspection under PAC 71015/71S015 may not be warranted, contact your Division management prior to proceeding.

2. Compliance and Regulatory Information

A. **Examples of Inspectional Classifications**

Below are examples of violations of the PCAF regulation and suggested classifications that may be warranted depending on the totality of the comprehensive inspection, facility's history, and corrective action/response to observed deviations:

- No Action Indicated (NAI):
  - No significant adverse conditions observed.
  - Only minor conditions observed that do not impact public or animal health or animal food safety (e.g., training records missing).
- Voluntary Action Indicated (VAI)
  - Written procedures do not include all required elements (but food safety implementation is not affected).
  - Hazard Analysis failed to assess a known or reasonably foreseeable hazard, but the facility is inadvertently controlling the hazard.
  - Errors in record keeping requirements that do not impact public or animal health or animal food safety.
  - Significant CGMP conditions (e.g., contaminants) that may or may not have been observed to directly affect food contact surfaces and/or food products.
- Official Action Indicated (OAI)
  - Failed to develop a Food Safety Plan and facility has uncontrolled hazards.
  - Failed to identify and evaluate all known or reasonably foreseeable hazards and facility has uncontrolled hazards that could result in a food safety issue.
  - Failed to control a hazard requiring a preventive control.
  - Failed to implement a prerequisite program that was relied upon, in the hazard analysis, to reduce the probability a hazard would occur.
  - Failed to perform required corrective actions when PC or verification activity deviations occur (e.g., calibration, testing, or missed monitoring noticed during record review) and food safety is or is likely to be affected.
  - Egregious and wide-spread CGMP conditions that are observed to directly affect food contact surfaces and/or food products; or are very likely to lead to the adulteration of food products.
  - Egregious CGMP conditions are observed and the facility does not provide an adequate response or corrective action plan within established timeframes (e.g., 15 working days).
  - Undesirable microorganisms are found by a qualified facility's testing program indicating a presence of pathogenic bacteria, e.g., *Salmonella spp*., within a pet food facility with no or inadequate corrective actions taken.

B. Reanalysis after food safety event

CVM has received multiple questions about whether a facility needs to reanalyze because of a food safety event. There are a number of factors that require reanalysis to occur. The following are some examples of food safety events that likely require reanalysis:

- The facility had a recall or similar food safety event that resulted from either an unanticipated food safety problem (e.g., did not consider in their hazard analysis or food safety plan) or
- The facility had a recall or similar food safety event that resulted from the facility's preventive control or food safety plan as a whole (including prerequisite program implementation) being ineffective.

While there are no concrete timelines that reanalysis should reoccur during a food safety event, it is important to remind facilities that if their food safety plan has either: (1) not considered all known or reasonably foreseeable hazards, or (2) is ineffective, then it is possible that other similarly situated animal food (e.g., made from the same ingredients or with the same process that caused the food safety event) may be adulterated. See section 5.8.6 *Reanalysis* of Draft Guidance for Industry #245: Hazard Analysis and Risk-Based Preventive Controls for Food for Animals.

3. Resources

- 21 CFR part 507 Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals
- Preventive Controls for Animal Food fact sheet
- Guidance for Industry #235: Current Good Manufacturing Practice Requirements for Food for Animals
- Draft Guidance for Industry #239: Human Food By-Products For Use As Animal Food
- Draft Guidance for Industry #245: Hazard Analysis and Risk-Based Preventive Controls for Food for Animals
- Guidance for Industry: Determination of Status as a Qualified Facility
- FSMA Compliance Dates for Animal Foods
- Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs: Guidance for Industry
- Foreign Supplier Verification Programs
- Inspectional Resources: Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

4. Legal History

On January 4, 2011, the FDA Food Safety Modernization Act (FSMA) was signed into law (Pub. L. 111-353). This law enables FDA to better protect public health by helping to ensure the safety and security of the animal food supply by focusing on prevention of food safety problems rather than reacting to problems after they occur. As part of the implementation of FSMA, FDA established risk-based preventive control requirements for the production of animal food by food facilities required to register under section 415 of the FD&C Act (see section 418 of the FD&C Act). At the same time, FDA established Current Good Manufacturing Practice requirements (CGMPs) for the manufacturing, processing, packing, and holding of animal food under section 402(a)(3) and (4) of the FD&C Act and sections 311, 361, and 368 of the Public Health Service Act.

In October 2013, FDA proposed to establish baseline standards in the form of CGMPs that would apply to most facilities manufacturing, processing, packing, or holding animal food. These CGMPs were proposed to provide baseline food safety standards that would complement the proposed requirements for hazard analysis and risk-based preventive controls for food for animals authorized by FSMA (78 FR

64736). In September 2014, FDA issued a supplemental notice of proposed rulemaking based on extensive stakeholder input on the proposed rule, which revised key provisions of the proposed rule, including the CGMP provisions (79 FR 58475). In September 2015, FDA issued a final rule for facilities that are required to register with FDA because they manufacture, process, pack, or hold animal food for consumption in the U.S. that established: (1) CGMP regulations in 21 CFR part 507, subpart B; and (2) hazard analysis and risk-based preventive controls regulations in 21 CFR part 507, subpart C and E. Associated training and recordkeeping requirements are located in 21 CFR part 507, subparts A and F. There are also provisions for withdrawing a qualified facility exemption located in 21 CFR part 507, subpart D.

APPENDIX C – Medicated CGMP Requirements (21 CFR part 225)

This appendix is intended to complement and be used in conjunction with the information located in Part I-VII; review those sections as well prior to performing work under this compliance program.

1. Inspectional

Inspections conducted under the comprehensive animal food compliance program should evaluate the facility's adherence, as applicable, to the Medicated Feed Mill CGMP requirements for:

- licensed medicated feed mills (21 CFR §§225.10 - 225.115) under PAC 71004/71S004, or
- non-licensed medicated feed mills (21 CFR §§225.120 - 225.202) under PAC 71012/71S012.

For more information about how to determine what requirements a facility should be inspected under and the corresponding PAC, see Part III.1.A. *Inspections*.

A. Scope of inspection

The scope of the inspection will in part depend on the purpose for the visit, previous inspectional findings, as well as the other regulations applicable during the comprehensive inspection. In preparing for the inspection, determine if the facility holds a medicated feed mill license. A facility's medicated feed mill license status may be found on the Animal Drugs @FDA webpage. Select at least one or two medicated feeds to review during the comprehensive inspection. When selecting medicated feeds to review during a comprehensive inspection, please consider the following factors:

- for licensed medicated feed mill inspections, if available, select at least one Category II, Type A medicated article (or other medicated feed requiring a license), to follow from receipt through distribution;
- select medicated feeds that pose a higher public health risk because they:
    - could present a health risk if a batch were over-formulated or unsafe contamination from drug carryover were to occur (e.g., ionophores such as monensin or lasalocid), or
    - are the product of a complex manufacturing process which may be more sensitive to manufacturing errors (e.g., liquid or free choice feeds); and
- select medicated feeds that would also be appropriate to review under other regulations that apply to the facility (e.g., PCAF (part 507) or VFD (21 CFR §558.6) requirements).

B. Pre-approval Inspections

The goal of a pre-approval inspection is to determine if a facility can comply with the licensed feed mill CGMPs. New medicated feed mill license applicants may be newly constructed or acquired facilities, or active medicated feed facilities that wish to secure a license. When a facility applies for a license, CVM will request the Division conduct a pre-approval inspection.

Field inspection staff performing these inspections determine whether the facility has the necessary knowledge of CGMP requirements, adequate equipment, drug receipt and inventory controls, formula and production instructions/records, and sampling and assay plans to demonstrate their ability to comply with the CGMP requirements for licensed feed mills (21 CFR §§225.10 - 225.115). Although a facility does not have to currently be compliant with these CGMPs, they should be able to demonstrate their knowledge of and ability to comply with the more stringent requirements of the licensed feed mill CGMP

regulations. Some examples of a facility demonstrating their knowledge and ability to comply during the FDA inspection include:

- discussing with field inspection staff, in detail, the procedures that will be created and implemented;
- having licensed feed mill procedures created and ready to be implemented; or
- having licensed feed mill procedures already created and implemented in daily operations.

At the time of a pre-approval inspection, the feed mill is only legally required to comply with the CGMP regulations that apply to non-licensed facilities (21 CFR §§225.120 - 225.202). If field inspection staff observe significant deviations from the CGMPs applicable to non-licensed facilities, those observations should be documented on a Form FDA 483. Significant deviations observed from the CGMPs that apply only to licensed facilities should not be documented on a Form FDA 483 during a pre-approval inspection. They should, however, be documented in the EIR. If the observation is also a deviation of the CGMPs that apply to a non-licensed facility, then document that on a Form FDA 483.

The Division should inform CVM of their recommendation to approve the license for inspections classified as NAI or for inspections classified as VAI (i.e., the issue did not directly affect medicated feed or animal food safety or efficacy and the facility provided adequate corrective actions).

When the facility cannot demonstrate that they can manufacture medicated feed in accordance with the licensed medicated feed CGMP requirements, the Division should recommend to the Center that the license should not be approved (see Part II.2.H.(5). *Medicated Feed Mill Licensing, Drug Establishment Registration and VFD Notification*). The Center will review the recommendation and coordinate notifying the facility. The Division should advise the facility that a decision is pending and schedule a pre-meeting with CVM to discuss the inspection. If the Division is recommending a license should not be approved, then an informal meeting should be held with the facility and CVM to discuss the observations and facility's response. After communication with the facility, the Division and CVM will determine if the CGMPs corrections are sufficient to warrant approval of the license and CVM will notify the facility.

Additionally, if major and critical deviations from the non-licensed CGMP regulations are observed during a pre-approval inspection, the Agency may consider follow-up compliance action. Facilities with significant CGMP deviations (21 CFR §§225.120 – 225.202) may be classified as OAI (see Part V.1.B. *Classification*).

C. Inspection Approach

At the beginning of the inspection, perform an initial interview and walk-through of the facility and grounds to better understand the facility operations, product flow, overall facility practices, and to identify key personnel responsible for conducting different activities at the facility. During the initial interview and walk-through, your focus should be on reviewing the building, equipment, pest control and general housekeeping practices, as well as gaining more understanding of the facility's operations.

After the initial interview and walk-through, focus on reviewing the facility's operations and practices with respect to the use of the drug components and safe manufacturing of medicated feed in more detail. The focus of reviewing the 21 CFR part 225 requirements during a comprehensive animal food inspection should be on whether or not the facility is handling and using drug components in a way that results in a safe and effective medicated feed and that does not result in unsafe contamination from carryover or cross-contamination of other animal food.

As always, depending on the inspectional findings, the scope of the inspection may expand to review more products and processes.

When inspecting a medicated feed mill that also is required to register as a food facility, review the facility's compliance with both the animal food CGMPs in 21 CFR part 507 and the medicated feed CGMPs in 21 CFR part 225. These two sets of CGMP requirements contain some overlap, particularly with respect to personnel, grounds, buildings, equipment and pest control requirements. The 21 CFR part 507 CGMP requirements often have more specific requirements in these areas; however, the 21 CFR part 507 CGMP requirements do not specifically address the use of animal drugs in the manufacturing of medicated feed. When performing a comprehensive inspection, focus on the 21 CFR part 507 CGMP requirements when reviewing overlapping CGMP requirements and focus on the 21 CFR part 225 medicated feed mill CGMP requirements when reviewing the use of drugs and the subsequent manufacture of medicated feed at the facility. The 21 CFR part 225 citation spreadsheet notes areas of overlap between the 21 CFR part 225 CGMP and the 21 CFR part 507 CGMPs. The spreadsheet can be located in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

For licensed medicated feed mills, use Form FDA 2481 as a job aid until an inspectional protocol (IP) becomes available (see Part III.2. *Reporting*). In addition, fully describe and document any deviations or observations per the IOM (e.g., EIR, CARS). For the purpose of this appendix, the terms Form FDA 2481 and IP can be used interchangeably.

For non-licensed medicated feed mills, fully describe and document any deviations or observations per the IOM (e.g., EIR, CARS). Do not use Form FDA 2481 for non-licensed feed mill inspections.

Generally, the same inspectional approach will be used at both licensed and non-licensed medicated feed mills. However, there are some differences between the licensed and non-licensed requirements. The following designations are used to note the differences between requirements that apply to:

- **(B)** – both licensed and non-licensed medicated feed mills,
- **(L)** – licensed medicated feed mills only, and
- **(NL)** – non-licensed feed mills only.

As a reminder, all required records must be kept by the facility for one year, unless they are also used as required records for compliance in 21 CFR part 507 which has a two-year record retention.

(1) Drug Component(s) and Batching

Licensed: 21 CFR §225.42 (Drug components), 21 CFR §225.58 (Laboratory controls)

Non-licensed: 21 CFR §225.142 (Components), 21 CFR §225.158 (Laboratory assays)

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, these medicated feeds must contain the labeled amounts of drugs. One of the primary purposes of the medicated feed CGMPs is to ensure that all medicated articles and medicated feeds are properly identified, stored, and handled in a manner to prevent mix-ups and contamination that may adversely affect the identity, strength, quality, or purity of the drug and medicated feed. As a result, review the facility's practices and documentation for:

- Drug Component Receipt, Storage and Use
  - **(B)** - Ensure facility is inspecting all incoming drug shipments to ensure packages are intact and properly identified, and if not, that the shipment is not accepted for use.
  - **(L)** - Licensed facilities must have documentation of their shipment inspection.
  - **(B)** - Verify drug components are stored in their original containers preserving critical identifying information such as: drug name, lot number, expiration date, etc.
  - **(B)** - Ensure the facility has adequate procedures for the identification, storage, and inventory control (receipt and use) of drug components to ensure identity, strength, quality, and purity of these drug components and to prevent mix-ups and contamination that may adversely affect finished animal feeds.
  - **(L)** - At a licensed mill, ensure the facility has established and maintained a record for each lot of drug component so that adequate investigations of product defects can be accomplished and satisfactorily resolved.
  - **(L)** - At a licensed mill, ensure the facility has established and maintains a daily inventory record for each drug. Review these inventory records for completeness and ensure an investigation was performed for any inventory discrepancies.
- Assay, Out-of-Specification results, Investigations, and Corrective Actions
  - **(L)** - Licensed mills are required to collect at least three representative samples of medicated feed containing each drug, or drug combination (for each drug requiring a license) at periodic intervals throughout the calendar year. Remember that if a medicated feed contains a combination of drugs, only one needs to be analyzed each time, provided the one tested is different from the one(s) most recently tested. Review the facility's assay results to confirm the results are within permissible ranges.
  - **(NL)** - Non-licensed mills are not required to take periodic assays but may assay their medicated feed or receive results from assays of their medicated feed (e.g., state feed sampling results). Ask the facility if they have received the results of any assays and confirm the results are within permissible ranges.
  - **(B)** - When an out-of-specification result is received, both licensed and non-licensed mills are required to perform an adequate investigation into the root cause and take corrective action. If the facility has had an out-of-specification result, review their investigation and corrective actions to ensure they (1) determined the cause of the out-of-specification results, (2) took steps to prevent reoccurrence and (3) properly handled affected product (e.g., placed it on hold, recalled it, reworked or disposed of it, etc.).
  - **(B)** - For all medicated feeds, the results of the investigation into an out-of-specification assay result must be maintained for one year.
  - **(L)** - For all medicated feed requiring a license, all out-of-limits assays along with the subsequent investigation and resolution should have been reported to CVM (HFV-226) as required by 21 CFR §§510.301 and 225.115.
  - **(B)** - If the out-of-limits assay also meets the definition of a reportable food and the facility is required to register as a food facility, the facility must also file an RFR.

(2) Master Record Files, Production Records, Complaint files, and Traceability

Licensed: 21 CFR §225.102 (Master record file and production records), 21 CFR §225.110 (Distribution records), 21 CFR §225.115 (Complaint files)

Non-licensed: 21 CFR §225.202 (Formula, production and distribution records)

There are a number of records that a medicated feed mill is required to keep in order to ensure the medicated feed they produce is safe and effective and, in the event it needs to be recalled, can be readily identified to allow for an effective recall. Review a subset of the following records:

- **(B)** - For all medicated feeds, the results of the investigation into an out-of-specification assay result must be maintained for one year.
- **(L)** - Only licensed feed mills are required to maintain a master record file, which contains the formulation (e.g., weights/amounts of all ingredients), theoretical yield, manufacturing procedures (e.g., mixing steps, times, other directions necessary to properly produce the feed), assay requirements, and labeling for batches or production runs.
    - Master record files were historically on paper and kept together in a central location. Now, it is more likely that facilities use a combination of paper and electronic records that are stored separately but together comprise the master record file.
- **(NL)** - Non-licensed feed mill's formulation records. As a reminder, all Type A medicated articles and Type B medicated feeds shall be used in accordance with their labeled mixing directions.
- **(B)** - Production records at both licensed and non-licensed feed mills. Check the production records against the master record file, or formulation with a focus on ensuring the medicated feed is appropriately manufactured to achieve the desired level of drug in the medicated feed.
- **(B)** - Ensure the facility has sufficient production and distribution records to facilitate a recall, if necessary, at both licensed and non-licensed feed mills.
- **(L)** - Licensed feed mill's required medicated feed complaint file. Review a subset of the complaints and focus your review on complaints that relate to medicated feed safety and effectiveness and ensure that the records are complete and that appropriate investigation/corrective actions were taken. Also review any other complaints related to food safety that the facility maintains.
- **(NL)** - Non-licensed facilities are not required to maintain a complaint file, but ask the facility about their process for handling and reviewing complaints they receive to determine if a medicated feed may have a safety or efficacy issue and review any documentation they may have.

(3) Drug Carryover/Physical Clean-out

Licensed: 21 CFR §225.65 (Equipment cleanout procedures)

Non-licensed: 21 CFR §225.165 (Equipment cleanout procedures)

During your inspection of both licensed or non-licensed feed mills, review the facility's practices to ensure drug carryover does not occur between batches of animal food (e.g., a drug component

used to manufacture a batch of medicated feed gets inadvertently included in the subsequent batch of a non-medicated animal food, a different medicated feed for which the drug is not approved, or a new batch of medicated feed that contains the same drug that can result in a higher drug level than what is stated on the labeling).

Equipment design and performance do not allow for an absolute avoidance of drug carryover from one batch to another. As a result, the focus is establishing adequate cleanout procedures to prevent unsafe contamination from carry-over of drugs into subsequent production of animal food.

The most commonly used cleanout practices are described below. Many medicated feed manufacturers use a combination of these methods to suit the requirements of their manufacturing system and production schedule to minimize drug carryover and prevent unsafe contamination.

- **Flushing** is a practice where a predetermined volume of a non-medicated animal food ingredient is used to help cleanout residual drugs from the manufacturing line following a batch or lot of medicated feed, to prevent unsafe contamination of a subsequent batch of animal food. The type and quantity of flush material and the frequency of flushing will vary depending on the facility, the types of medicated feed they are manufacturing, and the capacity of the equipment based on the manufacturer's specification (commonly 5-10% of the manufacturing equipment capacity is used). Corn, soybean meal, and peanut hulls are often used for this purpose due to their abrasiveness.
- **Physical cleanout** is a practice of cleaning out mixing and handling equipment used to manufacture medicated feed. This may be done by using dry-type cleaning (e.g., vacuuming, sweeping, or scraping equipment used to make dry food) or wet-type cleaning (e.g., washing equipment used to make liquid feed). Physical cleanout can often be effectively used on a single piece of equipment when physical cleanout of the entire system is not necessary for animal food safety. Physical cleanout is an important practice used to prevent unsafe drug carryover.
- **Sequencing** is a practice where a preplanned order of production, storage, and distribution of different animal foods is conducted. The sequence is designed to direct drug carryover into subsequent animal food which will not result in unsafe contamination. (see CPG 680.600, *Sequencing as a Means to Prevent Unsafe Drug Contamination in the Production, Storage, and Distribution of Feeds*). When the same equipment is used, the greatest potential for drug carryover is in the first batch of animal food manufactured following the manufacturing of a batch of medicated feed. Therefore, sequencing helps ensure that any drug carryover in the next batch of animal food made after a medicated feed does not result in unsafe contamination. For sequencing to be effective, sequencing practices should be carefully planned and executed. Whenever sequencing is interrupted or not followed through as planned, cleanout practices, such as flushing or physical cleanout should be considered.

Since every animal food manufacturing system is unique, the steps taken to establish adequate practices to minimize drug carryover may be different from other facilities. To review whether the facility's procedures will prevent unsafe contamination from drug carryover:

- **(B) -** Determine whether the facility's standard operating procedures appear adequate to prevent unsafe carry-over of drug residues and whether the facility follows the written procedures. As a reminder, some facilities may follow different SOPs depending on the

type of medicated feed. The following are some questions to think about to determine if the procedures appear adequate based on the method the facility is using:

- **Flushing** – What is the facility using as flush material? Is the facility flushing all necessary equipment in the system? How did the facility determine the quantity used? How does the facility know the flush is effective (e.g., drug carryover studies, analytical, etc.)? What does the facility do with flush material (e.g., becomes part of the animal food, discarded, given away, etc.)? If the flush material is used to manufacture a subsequent batch, will it affect the overall composition of the animal food?
- **Physical Cleanout** – What kind of cleanout procedures does the facility conduct (e.g., dry or wet, frequency, equipment cleaned, etc.)? Does the frequency of cleanout procedures differ (e.g., daily, weekly, monthly, as needed, etc.)? Are cleanout procedures implemented as outlined? What is the disposition of the cleanout material (e.g., discarded, given away, reworked, etc.)?
- **Sequencing** – Do the facility's sequence procedures make sense? Are they consistently implemented? Does the facility's production schedule conflict with the procedure? How does the facility handle production schedule changes (i.e., customer requests expedited manufacturing of bulk animal food)?

- **(B) -** Ensure that the practices are understood by all personnel involved in the production and scheduling of medicated feeds.
- **(B) -** Determine if the facility has a plan to reevaluate the practices periodically to prevent unsafe contamination from drug carryover.

If there are concerns about the adequacy of the facility's cleanout procedures, follow CPG 680.500, *Unsafe contamination of Animal Feed from Drug Carryover*.

(4) Packaging and Labeling

Licensed: 21 CFR §225.80 (Labeling)

Non-licensed: 21 CFR §225.180 (Labeling)

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. As a reminder, the FDA approved representative medicated feed labels (blue bird labels) can be accessed at: https://www.fda.gov/animal-veterinary/medicated-feeds/blue-bird-labels.

During the inspection, verify the facility's labeling (including placards and invoices when used in lieu of bag labels) are consistent with the drug approval, actual medicated feed formulation, and that labeling accompanies the distribution of bulk medicated feed.

- **(B) –** Verify against the drug approval: drug concentration, indications of use, adequate directions and warnings for the safe and effective use of medicated feeds, and proper withdrawal times. There are several FDA references to verify the labeling is consistent with the drug approval (e.g., 21 CFR part 558, NADAs or ANADAs on Animal Drugs @FDA , representative Blue Bird Labels, etc.).
- **(B) -** Also review the label or labeling to ensure that it matches the master record file and/or formulation records for the medicated feed.

- **(L) -** Licensed facilities are required to sign and date the proofread label and maintain the label on the premise for one year.
- **(B) -** If the facility sells/distributes their medicated feed in bulk, verify during the inspection that complete labeling accompanies each shipment of medicated feed (labeling can be included with the invoice, placard, delivery ticket, etc.).

(5) General Building & Equipment

Licensed: 21 CFR §225.20 (Buildings), 21 CFR §225.35 (Use of work areas, equipment and storage areas for other manufacturing and storage purposes)

Non-licensed: 21 CFR §§225.120 (Building and grounds), 21 CFR §225.130 (Equipment), 21 CFR §225.135 (Work and storage areas)

As a reminder, animal food facilities may be using the same building, grounds, employees, supervisors, management, equipment, and utensils to perform operations under 21 CFR part 507, subpart B, and part 21 CFR part 225. If this is the case, focus on the requirements in part 507.

Some facilities will not be subject to part 507. If so, review the building and equipment provisions under 225. Focus your review on ensuring that equipment is designed and operating properly so that ingredients (including drug ingredients) are incorporated at the inclusion rate identified in the formulation records and drug carryover or cross-contamination does not occur between batches. Also ensure the building and equipment maintenance, construction, and space do not contribute to the contamination of animal food with filth or allow pest infestation. To do so:

- **(B) -** Ensure equipment is suitable for its intended use and has the capability to produce a homogenous medicated feed at the target potency. Focus on equipment that weighs ingredients, adds ingredients, or mixes ingredients to ensure they are operating as intended to include ingredients in the appropriate amounts to the correct batch and obtain a homogenous mixture. For example, one way a facility could demonstrate their equipment can produce a homogeneous medicated feed by conducting a mixer study.
- **(B) -** Ask to review facility procedures, mixing studies, and calibration or accuracy check records. As a reminder, licensed medicated feed mills must annually test their scales and liquid metering devices; non-licensed mills must ensure they are accurate.
- **(B) -** Also check equipment for excessive product build-up or other conditions that indicate the equipment is not being maintained in a reasonably clean and orderly manner.
- **(B) -** Ensure buildings have appropriate space available to perform cleaning and maintenance operations. Review the buildings and grounds around the buildings for evidence of conditions that may lead to a pest infestation. Recognize that many medicated feed mills will have open doors, windows or not entirely enclosed buildings, pest management can be effective despite the opportunity for pests to access the building. Focus on whether the building and ground conditions are contributing to an infestation.
- **(B) -** If the facility is manufacturing or storing non-food products such as pesticides and industrial chemicals, ensure that these products are stored and/or handled so as not to be inadvertently mistaken for animal food or become a source of contamination for the animal food. For example, ensuring non-food products are stored in a separate area, or that a physical barrier is between the non-food products and animal food. As a reminder, in some isolated instances, a substance may be used both as animal food and for a non-

food purpose (e.g., as a soil nutrient or fertilizer). In these instances, the substance could be manufactured, processed, packed, or held in the same plant, on the same equipment so long as the relevant animal food regulations are followed for manufacturing the substance.

2. Compliance and Regulatory Information

A. Examples of Inspectional Classifications

Below are examples of violations of the Medicated Feeds CGMP regulation and suggested classifications they may warrant depending on the totality of the comprehensive inspection, facility's history, and corrective action/response to observed deviations:

- No Action Indicated (NAI)
  - No significant adverse conditions observed.
  - Only minor conditions observed that does not impact public or animal health or animal food safety.
- Voluntary Action Indicated (VAI)
  - Isolated incidences of elements lacking in master record file or production records; however, medicated feed safety or efficacy is unlikely to be impacted.
  - Scales are not checked for accuracy, but medicated feed safety or efficacy is unlikely to be impacted.
- Official Action Indicated (OAI)
  - Systemic failures to conduct adequate cleanout procedures which have or could result in unsafe contamination of finished product.
  - Scales or metering devices used to determine the amount of drug ingredient in the product are inaccurate or are operating in a manner that has caused or could be expected to cause incorrect or inconsistent drug levels in the medicated feed.
  - Lack of daily drug inventory records or failure to make a daily comparison between the actual amount of drug used and the theoretical amount of drug used or failure to take corrective action when significant discrepancies are detected.
  - A failure to perform corrective actions for out-of-specification medicated feed assays.
  - Failure to have master record file (licensed mill only) or production records, or if such records are lacking elements that can reasonably be expected to cause an adverse effect on the finished product.
  - Failure to properly label medicated feed and medicated feed safety or efficacy is likely to be impacted.

B. Manufacture of Medicated Feed Without the Required Feed Mill License

The manufacture of a medicated feed that requires a license without a medicated feed mill license results in the medicated feed being considered unsafe. (Section 512(a)(2)(B) of the Act). A drug or medicated feed that is considered unsafe is considered adulterated. (Section 501(a)(5) and 501(a)(6) of the Act).

If a feed mill does not have an approved medicated feed mill license but has a medicated article or feed requiring a license in its drug inventory or is manufacturing a medicated feed requiring an approved medicated feed mill license, then fully document the findings per the IOM as described in Part III.2. *Reporting* to cover the following:

- Receipt and use of a medicated article requiring a medicated feed mill license and/or distribution of a medicated feed (21 CFR § 558.4).
- Information of the shipper of the Category II Type A medicated article. The shipper of the Type A medicated article may have caused the drug to be deemed unsafe if the receiver and user do not have the required approved medicated feed mill license for such use (See 21 CFR §510.7 and section 512(a)(1) of the FD&C Act).

Contact your Division management and CVM to determine whether a follow-up investigation at the shipper is necessary to determine their practices of distributing drugs requiring an approved medicated feed mill license.

C. Unapproved Drugs Used in Medicated Feed

The manufacture of medicated feed without required approvals, with illegal combinations, or from unapproved sources of drugs are violations that may warrant advisory or enforcement action. Fully document the mixing and distribution of unapproved drugs or the manufacture and distribution of medicated feed containing unapproved combinations of new animal drugs. Extralabel use of drugs in or on animal feed is not permitted (See 21 CFR §530.11(b)). As a result, FDA's extralabel use policy in 21 CFR part 530 does not apply to medicated feeds. For information regarding extralabel use of medicated feed in minor species, see CPG 615.115, Extra-Label Use of Medicated Feed for Minor Species.

Contact CVM if either of the following conditions exist that could result in the initiation of a medicated feed mill license denial or revocation:

- A medicated feed mill license applicant manufactures unapproved medicated feed (see 21 CFR §515.21(a)(3)); or
- A licensed feed mill manufactures unapproved medicated feed and does not discontinue that manufacturing within a reasonable time (see 21 CFR §515.22 (c)(4)).

D. Enforcement Discretion for Extralabel Use of Medicated Feed for Minor Species

In December 2016, FDA revised Compliance Policy Guide (CPG) Sec. 615.115 Extralabel Use of Medicated Feeds for Minor Species to provide additional guidance on how to address the extralabel use of both OTC and VFD drugs in medicated feed for minor species. Under the CPG, when there are no approved treatment options available, the health of animals is threatened, and failure to treat affected animals would result in suffering or death, the extralabel use of medicated feeds may be considered for treatment of minor species if the conditions and procedures described in the CPG are followed. Minor species are all species of animals that are not major species (e.g., horses, dogs, cats, cattle, pigs, turkeys, and chickens).

In general, FDA will not initiate compliance action when the extralabel use of a medicated feed for a minor species is conducted in a manner consistent with the CPG. The CPG addresses the extralabel use of both OTC and VFD medicated feeds in minor species. Contact CVM prior to considering issuance of a Form FDA 483 for extralabel use of a VFD feed in a minor species. See Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support*.

E. Prescription Drugs

Be alert for possible sales of prescription animal drugs, particularly drugs administered in drinking water, and determine whether these drugs are dispensed through a person lawfully filling the order (e.g., veterinarian, licensed pharmacist, etc.) on the order (i.e., prescription) of a licensed veterinarian. Many of

the drugs administered in drinking water that were previously available over-the-counter transitioned to prescription status on January 1, 2017. In 2019, FDA released an additional draft guidance on bringing additional dosage forms of medically important antimicrobial drugs used for animals under veterinary oversight. For more information, see CVM's Judicious Use of Antimicrobials website.

3. Resources

- 21 CFR part 225, Current Good Manufacturing Practice for Medicated Feeds
- Animal Drug Availability Act of 1996
- Blue Bird Labels
- Animal Drugs @FDA List of medicated feed licensed mills
- Inspectional Resources: Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States)

4. Legal History

Section 501(a)(2)(B) of the FD&C 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. The CGMP requirements assure that such drugs meet the requirements of the Act as to safety and have the identify, strength, and meet the quality and purity characteristics, which it purports or is represented to possess. The Medicated Feed CGMPs in 21 CFR part 225 were promulgated to set these CGMP methods and standards (see 41 FR 52618, Nov. 30, 1976). The Medicated Feed CGMPs are divided into two sections, those that apply to a medicated feed mill manufacturing at least one medicated feed requiring a medicated feed license, and those that apply to medicated feed mills that do not manufacture medicated feed requiring a medicated feed license.

The following provides background to the terms used to describe drugs used in or on medicated feed, located in 21 CFR §558.3. Medicated feed is an animal food that contains a drug, in the form of a Type A medicated article, and animal food ingredients. Type A medicated articles can be mixed with animal food ingredients to produce a:

- Type B medicated feed, which contains a concentrated amount of the Type A medicated article along with other nutrients but is not to be fed directly to animals.
- Type C medicated feed, which contains an appropriate amount of the Type A medicated article to be fed directly to animals.

Any new animal drug approved for use in animal feed is placed in one of two categories, Category I or II. Category I drugs are drugs which require no withdrawal period at the lowest use level in each major species for which they are approved or are approved for use only in minor species. Category II drugs are drugs which require a withdrawal period at the lowest use level for at least one major species for which they are approved, or are regulated on a "no-residue" basis or with a zero tolerance because of carcinogenic concern regardless of whether a withdrawal period is required in any species.

Approval information for new animal drugs intended for use in animal feeds are located in 21 CFR part 558.

APPENDIX D – VFD Requirements (21 CFR §558.6)

This appendix is intended to complement and be used in conjunction with the information located in Part I-VII; review those sections as well prior to performing work under this compliance program.

1. Inspectional

The scope of the inspection will in part depend on the purpose for the visit, previous inspectional findings, as well as the other regulations applicable during the comprehensive inspection. Inspections conducted under the comprehensive animal food compliance program should evaluate the facility's adherence, as applicable, to the VFD regulations in 21 CFR §558.6 under PAC 71023 by:

- VFD feed manufacturers involved in the manufacturing and distribution of VFD feed,
- VFD distributors involved in the distribution of VFD feed,
- Veterinarians involved in the issuance of VFDs, and
- animal producers involved in the feeding of VFD feeds.

For more information about how to determine what requirements a facility should be inspected under and corresponding PAC, see Part III.1.A. *Inspections*. For a listing of new animal drugs used in or on medicated feed with a VFD marketing status, see Drugs with VFD Marketing Status.

A. Scope of Inspection

During the inspection, identify up to three VFDs to review. If possible, review VFDs issued for different drugs, authorized by different veterinarians, and/or distributed to different clients. If fewer than three VFDs are available, review those that are available. If applicable, select one of the three VFDs to perform a trace-forward and trace-back inspection.

A single VFD facility can be categorized as more than one operational type (i.e., have more than one role under the VFD regulation). For example, a veterinarian may also be a distributor. In these instances, fill out all pertinent sections of the VFD Inspection Tool.

When conducting inspections at VFD feed manufacturers, VFD feed facilities, and farms, adhere to biosecurity procedures (see Part III.1.A. *Inspections*).

B. Inspection Approach

Inspections of feed mills should determine compliance with the requirements for production and distribution of VFD feed found in 21 CFR 558.6. Associated inspections may extend to animal producers, non-licensed feed mills, and to veterinarians when following or tracing the use of VFD feed. A brief description of all associated inspections/investigations should be contained in the originating facility's EIR, summary section, in order to make apparent all related work accomplished.

The VFD Inspection Tool should be used until an inspectional protocol (IP) is available in order to report inspectional data about compliance with the VFD requirements. For the purpose of this appendix, the terms VFD Inspection Tool and IP can be used interchangeably. The VFD Inspection Tool is available in the Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States).

Each VFD distributor inspection and subsequent trace-forward/back inspection is a separate inspection (Op12). (e.g., separate inspection for each visit to the distributor, client, and veterinarian).

As with any drug used in medicated feed, attention should be given to ensure medicated feed is not manufactured or used in an extralabel manner and labeling has appropriate directions for use and includes all required caution statements. Questions concerning the VFD requirements are addressed in Draft GFI #120: Veterinary Feed Directive Regulation Questions and Answers.

Some facilities will have identified themselves as a distributor but have not yet distributed VFD feed (this would not be considered a washout but should be accurately captured in the EIR during the inspection). If the facility wishes to be removed from CVM's Veterinary Feed Directive Distributor Notification List, they should be encouraged to contact CVM and request removal, see Part II.2.H.(5). *Medicated Feed Mill Licensing, Drug Establishment Registration and VFD Notification*.

(1) Distributor Inspection

At the distributor, review their VFD records, with a focus on ensuring the facility is (1) maintaining VFDs or acknowledgment letters prior to shipping VFD feed and (2) manufacturing the VFD feed in accordance with the VFD and the approval (i.e., extralabel use of medicated feed is prohibited). Specifically, during the inspection:

- From the three VFDs selected to review, select one VFD feed and review the entire paper trail (e.g., the VFD or acknowledgment letter, the batch records, and distribution records) to evaluate conformance with the regulation.
- Review records for VFDs to determine compliance with the VFD distribution regulations.
- Compare either the VFD or the acknowledgement letter with the VFD feed production and distribution records to ensure that the VFD feed was distributed in accordance with either the VFD or the acknowledgment letter (i.e., the right feed was distributed to the right person under a valid VFD or acknowledgement letter).
- Verify the disposition of any overrun or leftover VFD feed to ensure safe disposal, appropriate rework, or distribution in accordance with a valid VFD.

(2) Trace-forward (Client) and Trace-back (Veterinarian) Inspection from the Distributor

When identified as a trace-forward/back inspection, field inspection staff should select one VFD at the distributor to be used for the trace-forward and trace-back inspection.

- Using the selected VFD, obtain the contact information for the veterinarian who issued the VFD as well as the client who received the VFD feed.
- Conduct the trace-forward and trace-back inspection and complete a VFD Inspection Tool for each inspection. Be sure to enter the contact information for the originating VFD distributor (where the inspection started).
- Do not conduct routine trace-forward or trace-back inspections across jurisdictional lines (e.g., Division or State borders) unless a significant problem is identified.
- In situations in which a veterinarian is also the distributor of the VFD feed, a trace-back inspection to the feed manufacturer may not be necessary. Similarly, if a feed retailer that does not manufacture is the distributor, a trace-back to the manufacturer may not be necessary. However, if a violation is identified in the finished product, then a follow-up to the manufacturer may be warranted.
- In the distributor EIR, briefly reference the trace-forward/trace-back inspection using their legal entity name so that they can easily be referenced for review. For example, "This inspection was associated with a trace-forward inspection at XYZ Farms and a

trace-back inspection at Dr. Smith's Veterinary Clinic." Do not include inspectional findings or other information that would require additional FOIA redaction.

(3) Drug Residue Inspections

During the course of a violative drug residue follow-up inspection (PAC 71006), viable VFD inspections as identified by the Divisions (i.e., farms that are currently utilizing VFD feeds) are to be conducted with the reporting PAC 71023.

Situations as to when a pre-announced inspection can occur are outlined in the IOM. Field inspection staff should discuss whether to pre-announce an inspection with management and CVM prior to doing so. See Part III.1.A. *Inspections.*

(a) Inspection at the Client

- If, during the inspection of a violative drug residue, it is determined that the client received a VFD feed, a VFD inspection should be conducted regardless of whether or not the VFD feed caused the drug residue.
- Clients should be notified that in addition to determining the cause of the drug residue, the Agency is also attempting to conduct a comprehensive evaluation of all animal drugs used at the facility, including the use of VFD feeds.
- Review up to three VFDs at the client. If fewer than three VFDs are available, field inspection staff should review those that are available. Select one of the three VFDs to perform a trace-back with the veterinarian.
- Focus the review on ensuring that the client is only feeding VFD feed in accordance with a valid VFD.

(b) Inspection at the Veterinarian

- Conduct a trace-back inspection at the veterinarian who issued the VFD(s) as identified during the client inspection. If multiple veterinarians were observed to issue VFDs to the client, choose the veterinarian who would most likely be visited during the course of the drug residue inspection. Also, be sure to document the contact information for the originating VFD client (where the inspection started).
- Veterinarians should be notified that in addition to determining the cause of the drug residue, the Agency is also attempting to determine compliance with the VFD regulations.
- When violative conditions related to VFD requirements are observed during the client inspections:
    - review those VFDs during the inspection of the veterinarian along with any other VFDs chosen at the veterinarian;
    - fully discuss all violative conditions observed related to VFDs written by that veterinarian, regardless of whether they were reviewed during the client or veterinarian inspection; and
    - determine what other VFDs and clients may be impacted by similar violative practices. If the veterinarian is part of a multi-veterinarian practice, review similar VFDs written by other veterinarians to see if the violation is a clinic-wide practice.

- The inspection at the veterinarian should be documented as a separate inspection from the client inspection. Any inspectional findings related to the VFD regulations should be documented as part of the veterinarian's EIR related to the violative drug residue.
- Additional trace-forward/back inspections are not expected as a result of the veterinarian inspection unless violative conditions are observed that would warrant additional follow-up (i.e., VFD feed suspected of causing drug residue, threat to human or animal health, etc.).
- In cases where the veterinarian who issued the VFD is different from the veterinarian identified for subsequent follow-up to the violative drug residue inspection, contact CVM. See Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support.*
- Generally, do not conduct VFD inspections at ancillary follow-up operations (i.e., haulers, sale barns, etc.) that are performed under PAC 71006; however, if violative conditions associated with the VFD regulation are observed, contact CVM. See Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support.*

(4) Recordkeeping

The distributor and the client must retain a copy of the VFD for 2 years. In addition to other applicable recordkeeping requirements found in 21 CFR 558.6, if the distributor manufactures the animal food bearing or containing the VFD drug, the distributor must also keep VFD feed manufacturing records for 1 year in accordance with part 21 CFR part 225.

2. Compliance and Regulatory Information

A. Examples of Inspectional Classifications

Below are examples of violations of the VFD regulation and suggested classifications that may be warranted depending on the totality of the comprehensive inspection, facility's history, and corrective action/response to observed deviations:

- No Action Indicated (NAI)
  - No significant adverse conditions observed.
  - Only minor conditions observed that do not impact public or animal health or animal food safety.
- Voluntary Action Indicated (VAI)
  - Isolated situations (e.g., not systemic) where the use of a VFD drug has not been authorized by a veterinarian, but public health is not significantly impacted.
  - Distribution of a VFD feed without first notifying FDA of intent to distribute.
  - Distribution of a VFD feed that does not conform to a lawful VFD or does not conform to the approved labeling, but the issues are not systemic or egregious and are unlikely to have a significant impact on public health.
- Official Action Indicated (OAI)
  - When use of the VFD drug has not been authorized by a veterinarian resulting in a significant impact on public health.
  - Systemic issues with manufacturing VFD feed which is not in accordance with the VFD, or the VFD drug's approval, conditional approval, or index listing.
  - Systemic issues related to the distribution of VFD feed without first obtaining a VFD or an acknowledgment letter.

- Systemic issues, such as veterinarians issuing VFDs that do not conform with the VFD drug approval, or clients not using VFD feed in conformance with the VFD.
- Distribution of a VFD feed that does not conform to a lawful VFD or does not conform to the approved labeling, and the issues are egregious and likely to have a significant impact on public health.
- Authorization, distribution, or use of a VFD drug by a person knowingly in violation of the VFD requirements.

B. Determining Distributor/Client/Veterinarian Roles

(1) Distributor

A distributor is defined in 21 CFR 558.3 as "any person who distributes a medicated feed containing a VFD drug to another person. Such other person may be another distributor or the client-recipient of a VFD." A "person" can be an individual or business entity.

- If the same person is both (1) distributing VFD feed and (2) acting as the client in the context of the veterinarian-client-patient-relationship (VCPR) under which the VFD has been authorized, then the person is not distributing VFD feed to another person and is not a distributor.
- If different people are doing each activity, then the person distributing the VFD feed is distributing VFD feed to another person and is therefore a distributor within the context of the VFD regulation.

(2) Client

A client is defined as the owner, or other caretaker of the animal (21 CFR § 558.3). CVM has received questions from field staff about who the client is (for the purposes of the VFD) when the animals are raised in an integrated operation. An integrated operation is when a company owns the animals, supplies the VFD feed and veterinary care, but the animals are raised by a contract grower. The client listed on the VFD must have a copy of the VFD as required under the regulation. In some business models, the animals are raised in integrator-owned or operated facilities by company employees and so the integrator meets the definition of the client. In other business models, the animals are integrator-owned but raised by a contract grower and so both the integrator and the grower meet the definition of a client. As a result, in some cases the integrator is the client and in others the contract grower is the client.

Generally, if the client is the integrator, the grower should have a copy of the VFD or be able to assist the field inspection staff in obtaining a copy of the VFD. While the statute requires that any persons involved in the distribution or use of a VFD drug maintain a copy of the VFD, it is not necessary to verify the integrator has proactively provided a copy of the VFD to every grower. However, growers should be able to assist field inspection staff in obtaining a copy of the VFD from the integrator if the grower does not have a copy. In addition, growers should have received enough information from the client, veterinarian, and/or feed mill to be able to use the VFD feed according to its labeling and the VFD.

(3) Veterinarian

CVM has also received questions from field staff about the veterinarian licensing and applicable practice requirements. Generally, during the inspection it is not necessary to verify a

veterinarian's license status. Veterinarians may have questions about whether they have to follow the state or federal veterinarian-client-patient-relationship (VCPR) when issuing a VFD in their State. This information can be accessed at: https://www.fda.gov/animal-veterinary/development-approval-process/does-state-or-federal-vcpr-definition-apply-lawful-vfd-my-state. For additional questions about veterinarian licensing and practice requirements, contact CVM. See Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support.*

C. Acknowledgment Letters

In order to distribute VFD feed to another distributor, a distributor must have either a lawful VFD or an acknowledgement letter from the other distributor. An acknowledgement letter is a written guarantee between two distributors that VFD feed will not be further distributed without receiving another acknowledgement letter or VFD, but it does not take the place of a VFD (See 21 CFR 558.3(b)(11)). When a VFD is transferred between two locations of the same legal entity, that is not considered distributing to another person. Therefore, an acknowledgment letter would not be required for transfers within the same business entity.

D. Enforcement Discretion for Extralabel Use of Medicated Feed for Minor Species

Drugs that have VFD marketing status may only be used under the oversight of a veterinarian and in compliance with 21 CFR §558.6, whether they are used for major (e.g., swine, cattle) or minor (e.g., game bird, sheep, etc.) species.

In December 2016, FDA revised Compliance Policy Guide (CPG) Sec. 615.115 Extralabel Use of Medicated Feeds for Minor Species to provide additional guidance on how to address the extralabel use of both OTC and VFD drugs in medicated feed for minor species. Under the CPG, when there are no approved treatment options available, the health of animals is threatened, and failure to treat affected animals would result in suffering or death, the extralabel use of medicated feeds may be considered for treatment of minor species if the conditions and procedures described in the CPG are followed. Minor species are all species of animals that are not major species (horses, dogs, cats, cattle, pigs, turkeys, and chickens).

In general, FDA will not initiate compliance action when the extralabel use of a medicated feed for a minor species is conducted in a manner consistent with the CPG. The CPG addresses the extralabel use of both OTC and VFD medicated feeds in minor species. Contact CVM prior to considering issuance of a Form FDA 483 for extralabel use of a VFD feed in a minor species. See Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support*.

3. Resources

- Animal Drug Availability Act of 1996
- 21 CFR part 558.3, definitions applicable to new animal drugs for use in animal feeds
- 21 CFR part 558.6, Veterinary Feed Directive drugs
- 21 CFR part 225, Current Good Manufacturing Practice for Medicated Feeds
- CPG 615.115, Extra-Label Use of Medicated Feeds for Minor Species
- GFI #120 VFD Regulation Questions and Answers
- GFI #209 The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals

- GFI #213 New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209
- GFI #233 Veterinary Feed Directive Common Format Questions and Answers
- GFI #263 Recommendations for Sponsors of Medically Important Antimicrobial Drugs Approved for Use in Animals to Voluntarily Bring Under Veterinary Oversight All Products That Continue to be Available Over-the-Counter
- Animal Drugs @ FDA, current listings of Veterinary Feed Directive Distributor Notifications and Blue Bird Labels found under the Medicated Feeds section
- Veterinary Feed Directive (VFD)
- Drugs with Veterinary Feed Directive (VFD) Marketing Status
- Veterinary Feed Directive Producer Requirements
- Veterinary Feed Directive Requirements for Distributors (Who Manufacture VFD Feed)
- Veterinary Feed Directive Requirements for Distributors (Who Do Not Manufacture VFD Feed)
- Veterinary Feed Directive Requirements for Veterinarians
- American Association of Veterinary State Boards, to verify veterinary licensure and contact state board if compliance issues are identified
- Inspectional Resources: Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States)

4. Legal History

In 1996, Congress enacted the Animal Drug Availability Act (ADAA) (Pub. L. 104–250) to facilitate the approval and marketing of new animal drugs and medicated feeds. In passing the ADAA, Congress created a new regulatory category for certain animal drugs used in or on animal feed called veterinary feed directive (VFD) drugs. VFD drugs are new animal drugs intended for use in or on animal food which are limited to use under the professional supervision of a licensed veterinarian. The regulations for the authorization, distribution, and use of VFD feeds are in 21 CFR §558.6. Relevant definitions for these requirements are found in 21 CFR §558.3.

In 2013, to promote the judicious use of antimicrobials, FDA recommended that certain medically important antimicrobials in food-producing animals administered in or on animal food change from an over-the-counter marketing status, to a veterinary feed directive marketing status by January 1, 2017. The recommendation to change marketing status for certain medically important antimicrobials was published in Guidance for Industry #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals. The timeline for implementing this recommendation was published in Guidance for Industry #213: New Animal Drugs and Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209. Drug sponsors implemented this recommendation, which significantly increased the number of new animal drugs with VFD marketing status. In anticipation of this increase and in recognition of the need to improve the VFD program's efficiency, FDA's CVM finalized changes to the VFD rule on June 3, 2015 (80 FR 31708). These changes included defining the distributor, veterinarian, and client requirements for VFDs.

Like over-the-counter (OTC) drugs approved for use in animal feed, VFD drugs are also categorized as Category I or Category II drugs. VFD feeds are subject to the same licensure and medicated feed CGMP requirements as other medicated feeds.

APPENDIX E – BSE Requirements (21 CFR §§589.2000 and 2001)

This appendix is intended to complement and be used in conjunction with the information located in Part I-VII; review those sections as well prior to performing work under this compliance program.

1. Inspectional

The scope of the inspection will depend on the purpose for the visit, previous inspectional findings, as well as the other regulations applicable during the comprehensive inspection. Inspections conducted under the comprehensive animal food compliance program should evaluate the facility's adherence, as applicable, to the Bovine Spongiform Encephalopathy (BSE) requirements (21 CFR §§589.2000 and 589.2001) under PAC 71009/71S011.

This regulation applies to individuals manufacturing, handling, or feeding prohibited materials, such as: renderers, protein blenders, commercial animal feed manufacturers, distributors (including retailers), transporters of animal feed and feed ingredients, on-farm animal feed mixers, and ruminant feeders.

In most cases, BSE inspections will be conducted at facilities that handle prohibited material; remembering that prohibited material is any protein derived from mammalian animals (e.g., meat and bone meal, organs, offal, hair, collagen, etc.). Unless otherwise directed, routine surveillance BSE inspections will only be conducted at facilities that use prohibited materials to manufacture animal food. Field inspection staff will need to assess whether the facility is handling prohibited material to determine whether a BSE inspection is applicable.

For more information about how to determine what requirements a facility should be inspected under and corresponding PAC, see Part III.1.A. *Inspections*.

A. Scope of Inspection

The scope of the inspection will in part depend on the purpose of the inspection, as well as the other regulations applicable during the comprehensive inspection. Only review BSE requirements at a facility that handles prohibited material, unless it is a directed or for-cause inspection. Select at least one product that is or contains prohibited material and follow that product through the facility. If possible, select a product that would also be appropriate to review under other regulations that apply to the facility (e.g., 21 CFR part 507, 21 CFR part 225, or 21 CFR part 558.6).

B. Inspection Approach

Facilities inspected under the BSE regulation will fall into one of two categories: utilize/produce prohibited materials and do not utilize prohibited materials.

- **Utilize/Produce Prohibited Materials:** These facilities utilize/produce prohibited materials to manufacture an animal food that is not intended to be fed to ruminants. Common prohibited materials used include, but are not limited to: ruminant meat and bone meal, organs, and offal. The most common prohibited material is meat and bone meal originating from cattle. Another common source of prohibited material is non-rendered slaughter offal intended for pet food use.
- **Do Not Utilize Prohibited Material:** These facilities may use exempt protein ingredients that are not prohibited for use in ruminant feed (listed below) to manufacture animal food for ruminant and/or non-ruminant animals. The Center does not currently request routine

surveillance inspections at these facilities under this comprehensive animal food compliance program.

The following materials are not prohibited for use in ruminant feed under 21 CFR §589.2000 and a facility handling only these materials would be considered a facility that does not utilize prohibited material:

- Non-prohibited ingredients from cattle (e.g., tallow (cattle fat) containing 0.15% or less insoluble impurities; blood or plasma products, milk products, plate waste, amino acids, bone ash; bone phosphate; bone charcoal); and
- Non-mammalian sources of protein (e.g., fish, poultry, vegetable, non-protein nitrogen (NPN)).

Note: Many animal food manufacturers may not use prohibited materials to manufacture animal food (i.e., do not handle prohibited material), but they do have products of mammalian origin that are not intended to be used in the manufacture of animal food. For example, they might have pet food not intended for further manufacturing, and bone meal labeled for use as a fertilizer. These facilities are considered facilities that do not handle prohibited material.

At the beginning of the comprehensive animal food inspection, determine whether the facility uses prohibited materials. To determine if tallow contains 0.15% or less insoluble impurities, ask to review COAs or other documentation to determine if the tallow is a prohibited material. If the facility does not handle prohibited materials, then do not assess BSE as a sub-component of the comprehensive animal food inspection unless otherwise directed.

If the facility utilizes prohibited materials, perform an initial interview and walk-through of the facility and grounds to better understand the facility operations, product flow, overall facility practices, and to identify key personnel responsible for conducting different activities at the facility. During the initial interview and walk-through, focus on reviewing the facility's practices and procedures for handling prohibited materials. Focus next on the identified animal food products/ingredients containing prohibited material in order to review the facility's operations and practices related to handling prohibited material in more detail.

As always, depending on the inspectional findings, the scope of the inspection may expand to review more products and processes.

(1) BSE Requirements in 21 CFR §589.2000

The BSE requirements are used to ensure prohibited materials are excluded in animal food intended for ruminants. Remember that ruminants include: cattle, bison, sheep, goats, deer, elk, and antelopes. This regulation defines ruminants as animals that have a stomach with four chambers, and does not apply to camelids (e.g., camels, llamas, alpacas) which have a stomach with three chambers.

The entities most likely to utilize or produce prohibited materials are renderers, poultry and swine feed manufacturers, and pet food manufacturers. It is critical to determine during the inspection whether the facility is: (1) excluding prohibited materials from entering the facility if that is their intent, (2) identifying and segregating prohibited materials as appropriate if they do use them, and (3) adequately cleaning out equipment if shared equipment is being utilized to manufacture/process/store prohibited and non-prohibited material.

(a) Requirements for Renderers, Protein Blenders, Feed Manufacturers

BSE Requirements: 21 CFR §589.2000(c) and (d)

The BSE regulations are divided into the requirements for each type of industry: renderers, protein blenders, feed manufacturers, distributors, and ruminant feeders; however, the requirements are very similar so the same inspectional approach should be followed at each industry segment.

Renderer means any facility or individual that processes slaughter byproducts, animals unfit for human consumption, or meat scraps. This includes persons who collect such materials and subject them to minimal processing or distributes them to facilities other than renderers (as defined here) whose intended use for the products may include animal feed. This also includes those that blend animal protein products.

Rendering operations typically include: collecting slaughter by-products (offal, grease, tallow, bone, etc.) from large slaughter facilities or custom kill facilities; processing dead livestock from farmers/ranchers; collecting meat trimmings from grocery stores and/or restaurants, collecting grease from restaurants, etc.

It is important to note renderers typically receive and produce prohibited material. The primary product manufactured during rendering is meat and bone meal sold for animal food to non-ruminants (swine, poultry, pet food, mink, etc.).

Protein Blender means any facility or individual which obtains processed animal protein from more than one source or from more than one species, and subsequently mixes (blends) or redistributes an animal protein product.

Feed manufacturer includes manufacturers of complete and intermediate feeds intended for animals and includes on-farm in addition to off-farm feed manufacturing and mixing operations.

Distributor includes persons who distribute or transport feeds or feed ingredients intended for animals.

Note: The term “may contain” in the regulation or a guidance document is intended to speak to situations where animal food has become cross-contaminated because a facility required to conduct separation or cleanout practices did not adequately do so. The language “may contain” does not apply to products, like tallow that may contain insoluble impurities, or to virtually any other ingredients that could have possibly been contaminated at some point prior to receipt by the facility.

During the inspection:

- Review the facility’s incoming ingredients containing prohibited materials. It is important to verify that the caution statement, “Do not feed to cattle or other ruminants” appears on the labeling or records accompanying incoming shipments of prohibited materials. If the caution statement is required, but not present on the records, determine the source of the prohibited materials for potential follow-up and fully document your findings in the inspection report. If you feel subsequent follow-up is necessary, use the

rTAN in Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support*.

- Review how the facility has maintained records sufficient to track the materials throughout their receipt, processing, and distribution. During the inspection, request and review purchase orders, invoices, bills of lading or other records demonstrating the facility's receipt of the prohibited materials into their facility.
- If the facility handles or produces animal food containing a prohibited material, they must maintain processing records, batch records, or other documents demonstrating the use of the prohibited materials in the final product(s). If this is the case, select a sample of these records to review.
- Review a sample of the facility's distribution records to ensure the prohibited material was distributed with the caution statement, "Do not feed to cattle or other ruminants" on the labeling, or documents that accompany a bulk shipment of animal food. These animal food products are typically for non-ruminant animals including swine and poultry.
- There are some facilities that will be exempt from the caution statement labeling "Do not feed to cattle or other ruminants" and the recordkeeping requirements noted above. They include:
    - **Pet food labeling exemption:** It is important to note pet food products that are sold or are intended for sale at retail and feeds for nonruminant laboratory animals are exempt from labeling the pet food with the caution statement, "Do not feed to cattle or other ruminants".
    - If the pet food products or feeds for nonruminant laboratory animals are sold or are intended for sale as distressed or salvage items, then such products shall be labeled with the caution statement.
    - There are additional exemptions in 21 CFR §§589.2000(c)(2), (c)(3), and (d)(1-3). These exemptions are forward-looking, for example, in case a method to deactivate the BSE agent is developed. To date, none of these additional exemptions have been realized. If a facility is trying to use these exemptions, contact CVM, see Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support*.

(b) Requirements for Persons That Intend to Separate Mammalian and Nonmammalian Materials

BSE Requirements: 21 CFR §589.2000(e)

Most renderers of cattle manufacture prohibited material (meat and bone meal, for example) and non-prohibited material (such as tallow that is 0.15% or less insoluble purities, or poultry meal), and once these material fractions have been separated, they must remain separated. Although it is relatively uncommon in the rest of the feed industry, it is possible to encounter a protein blender, feed manufacturer, or someone else who manufactures, processes, blends and distributes both products that contain or may contain prohibited material and products that do not contain prohibited material.

During the inspection:

- Ensure the facility has labeled the products containing prohibited materials with the BSE cautionary statement, "Do not feed to cattle or other ruminants." Conversely, the BSE cautionary statement is not required on products that do not contain

prohibited materials. Situations have been encountered where a facility has labeled their product with the cautionary statement, but then advised their customers verbally that the product does not contain prohibited material. This is inappropriate and would result in the product being misbranded. If this situation is encountered, please contact CVM, see Part II.2.H.(3). *Regulator Technical Assistance Network (rTAN) and Inspectional Support*.

- For products that contain or may contain prohibited materials, the facility must maintain records sufficient to track the materials throughout their receipt, processing, and distribution as described above. Select a number of these records to review (outlined above).
- Review the facility's written procedures and implementation of those measures to avoid commingling or cross-contamination of prohibited materials from receipt until the time of shipment. The facility is required to provide these procedures upon request. There are a variety of methods the facility can employ:
  - Maintain separate equipment or facilities for the manufacture, processing, or blending of prohibited and non-prohibited materials
  - Use cleanout procedures or other means adequate to prevent carry-over of products that contain or may contain prohibited material into animal food that may be used for ruminants

(c) Requirements for Feeders of Ruminants

BSE Requirements: 21 CFR §589.2000(f)

BSE inspections at facilities feeding ruminant animals may occur during interactions with other programs, such as drug residue inspections. Examples include, but are not limited to: dairies, cattle feedlots, calf and lamb raising operations, and the general feeding of ruminants, such as cattle, bison, sheep, goats, deer, elk, and antelopes. It is essential these ruminant feeders do not allow ruminants to consume prohibited materials.

Ruminant feeders are required to maintain a copy of the label and invoice for every shipment of feed or ingredients they receive that contain any source of *animal protein*. Note the difference between animal protein and prohibited materials - there are numerous animal proteins that may be used in ruminant feeds. Review these documents to ensure the ruminant feeder is not receiving and feeding products containing prohibited materials.

(2) BSE Requirements in 21 CFR §589.2001

BSE Requirements: 21 CFR §589.2001

The purpose of these requirements is to prohibit the use of certain cattle origin materials in animal food to further reduce the risk of the spread of BSE within the United States. These cattle materials are collectively known as "Cattle Materials Prohibited in Animal Feed" (CMPAF). This regulation was promulgated to ensure no animal food shall be manufactured from, processed with, or otherwise contain, CMPAF.

CMPAF are bovine-derived materials that may not be used in any animal food, including pet food, as defined in 21 CFR §589.2001(b), and which includes:

- The brains and spinal cords of cattle 30 months of age and older;
- The entire carcass of cattle not inspected and passed for human consumption, unless;
    - shown to be less than 30 months of age, or
    - from which the brain and spinal cord were effectively removed.
- The entire carcass of BSE-positive cattle, including tallow;
- Tallow made from CMPAF that contains more than 0.15% insoluble impurities;
- Mechanically separated beef made from CMPAF

NOTE: Cattle not inspected and passed for human consumption usually means cattle that died on the farm. If these cattle are 30 months of age or older, the brain and spinal cord must be removed if the cattle are intended to be rendered for feed use.

These regulations have the most impact on slaughter and rendering facilities, which are the main producers of materials that enter the rendering stream. The regulations in 21 CFR §589.2000 specifically state renderers are expected to comply with 21 CFR §589.2001 (21 §589.2000(c)(4)). When inspecting a rendering facility, whether a stand-alone or associated with a slaughter facility, evaluate the renderer's compliance with 21 CFR §589.2001.

Most slaughter facilities will remove the brain and spinal cord of cattle 30 months of age and older during processing, sending that material straight to disposal (landfill may be the most common disposal). Smaller slaughter facilities will usually remove the brain and spinal cord for disposal – sending the CMPAF to a landfill and the rest of the carcass offal to an independent renderer. These small slaughter facilities will usually supply some type of certification to the renderer that CMPAF has been removed. Larger facilities may operate their own rendering plant or have a rendering facility associated with their operation.

When conducting an inspection at a rendering facility:

- Evaluate the facility's procedures and controls to ensure CMPAF is not introduced into animal feed. These procedures must ensure the carcass of cattle not inspected and passed for human consumption are not included in animal food if the brain and spinal cord of cattle age 30 months and older have not been effectively removed.
    - Rendering facilities may decide not to accept cattle 30 months of age or older. This would ensure the renderer is not producing an animal food containing CMPAF. If a renderer utilizes this control method, they must implement procedures designating how they are evaluating the age of the cow. Typically, cattle 30 months of age and older that do get rendered are from slaughter facilities that have removed the brain and spinal cord during processing.
    - Rendering facilities may decide to accept cattle 30 months of age or older; however, they must remove the brain and spinal cord from these animals – whether prior to collection, or at the rendering plant. If they accept cattle 30 months of age or older, they must implement procedures for how the brain and spinal cord from cattle 30 months of age and older are to be removed. It is critical that the CMPAF is segregated to avoid any cross contamination with cattle materials approved for use in animal food. This can be done by using separate equipment for CMPAF and non-CMPAF materials in the plant.
- At the few renderers that do handle CMPAF, review the facility's labeling of the CMPAF to ensure the CMPAF is labeled in a conspicuous manner with: "Do not feed to animals."

  - Renderers typically collect CMPAF from a day's production in a dedicated container. If this is the case, the container must be labeled "Do not feed to animals" to prevent the accidental use of this material in animal food.
  - Furthermore, the CMPAF must be marked with an agent that can be readily detected on visual inspection. This can include the addition of a denaturant (usually a food coloring dye, for example) applied to the CMPAF so it can be visually identified as CMPAF.
- Review a subset of the facility's records to track the CMPAF from receipt to disposal. Regardless of the methods used by the renderer to ensure CMPAF is not introduced into animal food, the renderer must establish and maintain records sufficient to track CMPAF from receipt to disposal.
- Some renderers receive cattle for processing from separate facilities. For example, from livestock producers or slaughter facilities. In these cases, verify the renderer is only accepting these animals for processing if:
  - The supplier demonstrates they have adequate procedures in place to segregate cattle 30 months of age or older; or
  - Certification or other documentation from the supplier that material supplied to the renderer does not include CMPAF. This documentation may include a description of how the supplier segregates cattle 30 months of age or older and/or documents how CMPAF has been removed from material supplied to the renderer. Also, verify that the renderer is periodically reviewing these certifications from their suppliers.
- Most renderers also produce tallow from cattle. Tallow is defined as the rendered fat of cattle obtained by pressing or by applying any other extraction process to tissues derived directly from discrete adipose tissue masses or to other carcass parts and tissues. Further, any rendered fat or oil that contains tallow is considered to be tallow, regardless of the amount of tallow it contains. If the renderer produces tallow, review the following record and labeling requirements:
  - Review a few records of analytical results to determine the amount of insoluble impurities in tallow being distributed. Tallow must contain 0.15% or less insoluble impurities to be used in ruminant feeds.
  - Tallow derived from raw materials that does not contain CMPAF may contain more than 0.15% insoluble impurities but must be labeled with the BSE caution statement, "Do not feed to cattle or other ruminants."
  - Tallow processed from raw materials that contained CMPAF, and with insoluble impurities greater than 0.15% cannot be used in any animal food and must be labeled "Do not feed to animals."

2. Compliance and Regulatory Information

A. Examples of Inspectional Classifications

Below are examples of violations of the BSE regulation and suggested classifications that may be warranted depending on the totality of the comprehensive inspection, facility's history, and corrective action/response to observed deviations:

- No Action Indicated (NAI)
  - No significant adverse conditions observed.

  - Only minor conditions observed that does not impact public or animal health or animal food safety.
- Voluntary Action Indicated (VAI)
  - Written procedures do not include all required information (but food safety implementation is not affected).
- Official Action Indicated (OAI)
  - Cattle known to have been fed with prohibited materials.
  - Failure to include required caution statement labeling.
  - Failure to maintain segregation of prohibited materials or perform adequate cleanout.

3. Resources

- Form FDA 3719 – Report of Inspection for Compliance with 21 CFR §589.2000 and §589.2001
- FDA Bovine Spongiform Encephalopathy website
- CVM GFI #67 Small Entities Compliance Guide for Renderers
- CVM GFI #68 Small Entities Compliance Guide for Protein Blenders, Feed Manufacturers, and Distributors
- CVM GFI #69 Small Entities Compliance Guide for Feeders of Ruminant Animals with On-Farm Feed Mixing Operations
- CVM GFI #70 Small Entities Compliance Guide for Feeders of Ruminant Animals Without On-Farm Feed Mixing Operations
- CVM GFI #76 Questions and Answers BSE Feed Regulations
- CVM GFI #158 Use of Material from Deer and Elk in Animal Feed
- CVM GFI #195 Small Entities Compliance Guide For Renderers—Substances Prohibited From Use In Animal Food Or Feed
- Feed Ban Enhancement: Implementation Questions and Answers
- Management of Certain Cattle Origin Material Pursuant to the Substances Prohibited from Use in Animal Food and Feed Final Rule (EPA)
- Inspectional Resources: Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States)

4. Legal History

In 1997, FDA published a final regulation, BSE/Ruminant Feed Regulations in 21 CFR Part §589.2000, that prohibits the use of most mammalian protein in the manufacture of animal feeds given to ruminant animals, such as cows, sheep, and goats. The regulation does not prohibit the use of mammalian protein as an ingredient in feed for non-ruminants, but requires process and control systems to ensure that such use does not cause contamination of ruminant feed during feed manufacturing or transport.

FDA strengthened the 1997 rule in 2008 with BSE/Substances Prohibited from Use in Animal Food or Feed 21 CFR Part §589.2001, by prohibiting the use of the highest risk cattle tissues in ALL animal feed. These high-risk cattle materials include the brains and spinal cords from cattle 30 months of age and older, and the entire carcass of cattle not inspected and passed for human consumption, unless the carcasses are shown to be from cattle less than 30 months of age, or the brains and spinal cords have been removed. By taking these highest-risk materials entirely out of the feed supply, the potential to cause infection via errors in manufacturing or feeding, or intentional misuse of these materials is reduced.

APPENDIX F – Sanitary Transportation Requirements (21 CFR part 1, subpart O)

This appendix is intended to complement and be used in conjunction with the information located in Part I-VII; review those sections as well prior to performing work under this compliance program. **NOTE: Sanitary Transportation inspections should only be conducted as directed.**

1. Inspectional

The Sanitary Transportation (ST) regulation establishes requirements for shippers, loaders, carriers by motor or rail vehicle, and receivers involved in transporting human and animal food to use sanitary practices to ensure the safety of that food. The purpose of these requirements is to prevent practices during transportation that create food safety risks, such as failure to properly refrigerate food, inadequate cleaning of vehicles between loads, and failure to properly protect food. This regulation applies to both human and animal food and contains sections including *General Provisions, Vehicles and Transportation Equipment, Transportation Operations, Training, Records, and Waivers*. The inspection should cover these requirements, as applicable, under PAC 71018.

Note that the ST sub-program will not be included at every facility that may be subject to the ST requirements and should only be conducted as directed. For details on when the ST sub-program should be included in a comprehensive animal food inspection, see Part II.2.C.(4).(c). *DIRECTED ONLY: Sanitary Transportation*.

For more information about how to determine what requirements a facility should be inspected under and corresponding PAC, see Part III.1.A. *Inspections*.

A. Vehicles and Transportation Equipment

- Vehicles and transportation equipment used in transportation operations must be so designed and of such material and workmanship as to be suitable and adequately cleanable for their intended use to prevent the food they transport from becoming unsafe, i.e., adulterated within the meaning of section 402(a)(1), (2), and (4) of the FD&C Act (21 U.S.C. §342(a)(1), (2), and (4)) during transportation operations.
- Vehicles and transportation equipment must be maintained in such a sanitary condition for their intended use as to prevent the food they transport from becoming unsafe during transportation operations.
- Vehicles and transportation equipment used in transportation operations for food requiring temperature control for safety must be designed, maintained, and equipped as necessary to provide adequate temperature control to prevent the food from becoming unsafe during transportation operations.
- Vehicles and transportation equipment must be stored in a manner that prevents it from harboring pests or becoming contaminated in any other manner that could result in food for which it will be used becoming unsafe during transportation operations.

B. Transportation Operations

Transportation operations, as defined in the ST regulation, must be conducted under conditions and controls necessary to prevent the food from becoming unsafe during transportation operations, including:

- Taking effective measures such as segregation, isolation, the use of packaging, or other protective measures to protect food from contamination by raw foods and nonfood items in the same load.

- Taking effective measures such as segregation, isolation, or other protective measures, such as hand washing, to protect food transported in bulk vehicles or food not completely enclosed by a container from contamination and cross-contact during transportation operations.
- Ensuring food that requires temperature control for safety is transported under adequate temperature control throughout their transportation operations.
- The type of food, e.g., animal food, pet food, human food, and its production stage, e.g., raw material, ingredient or finished food, must be considered in determining the necessary conditions and controls for the transportation operation. Additionally, there are specific requirements applicable to Shippers, Loaders, Receivers, and Carriers engaged in Transportation Operations.

C. Training

Carriers must provide and maintain documentation of adequate food safety training of personnel engaged in transportation operations when the carrier and shipper agree in writing that the carrier is responsible for sanitary conditions during transportation.

D. Records

The Sanitary Transportation regulation requires the following documents be maintained dependent on the operations of the inspected entity:

- Written procedures to ensure that vehicles and equipment used in its transportation operations are in appropriate sanitary condition for the transportation of the food, i.e., will prevent the food from becoming unsafe during the transportation operation.
- Written procedures to ensure food shipped in bulk does not become unsafe due to previous cargo.
- Written procedures to ensure that the food that requires temperature control for safety under the conditions of shipment is transported under adequate temperature control throughout their transportation operations.
- If included within the written procedures, records that demonstrate that shipper provide specifications and operating temperatures to carriers as required by 21 CFR §1.908(b)(1) and (2) as a regular part of their transportation operations.
- Any written agreements between the shipper and a carrier, **IF,** the carrier has agreed to take on any of the food safety responsibilities for transportation as permitted under 21 CFR§1.908(b)(3), (4), and (5).
- Carrier must develop and implement specifications (if applicable) regarding sanitation and temperature controls of the vehicles and provisions for bulk vehicles in accordance with 21 CFR §1.908(e)(6).
- Training records required by carriers in accordance with 21 CFR §1.910(b)
- Any other written agreements between one party and other entities subject to 21 CFR part 1, Subpart O, e.g., loaders, receivers, reassigning their responsibilities to a covered party.

2. Compliance and Regulatory Information

A. Examples of Inspectional Classification

Below are examples of violations of the ST regulation and suggested classifications they may warrant depending on the totality of the comprehensive inspection, facility's history, and corrective action/response to observed deviations:

- No Action Indicated (NAI):
  - No significant adverse conditions observed.
  - Only minor conditions observed that does not impact public or animal health or animal food safety (e.g., failure to keep training records).
- Voluntary Action Indicated (VAI)
  - Written procedures do not include all required information (but food safety implementation is not affected).
- Official Action Indicated (OAI)
  - Significant temperature deviations that may result in temperature abuse of foods requiring temperature control for safety.
  - Conditions that result in cross contamination of foods during transportation.
  - Failure to implement written procedures to ensure food is not rendered unsafe during transportation operations.

B. **Waivers**

21 CFR part 1, subpart O, *Sanitary Transportation of Human and Animal Food*, allows the Agency to waive the requirements of this regulation if it determines that the waiver will not result in the transportation of food under conditions that may render the food unsafe for humans or animals. The Agency published waivers on April 5, 2017; there are several waivers (including for milk and seafood). The most applicable waiver for animal food is:

- Food establishments holding valid permits issued by a relevant regulatory authority, such as a state, local, territorial, or tribal agency, when engaged as receivers, or as shippers and carriers in operations in which food is relinquished to customers after being transported from the establishment. Examples of such establishments include restaurants, supermarkets, and home grocery delivery operations. FDA acknowledges that controls for such transportation operations already exist under retail food protection programs enforced by state, territorial, tribal and local officials and with FDA oversight.

C. **Exemptions and Modified Requirements**

21 CFR part 1, subpart O, *Sanitary Transportation of Human and Animal Food*, provides several exclusions. They include:

- Shippers, loaders, receivers, or carriers engaged in food transportation operations that have less than $500,000 in average annual revenue.
- Transportation activities performed by a farm.
- Transportation of food that is transshipped through the United States to another country.
- Transportation of food that is imported for future export and that is neither consumed nor distributed in the United States.
- Transportation of human food byproducts for use as animal food without further processing.
- Transportation of food that is completely enclosed by a container except a food that requires temperature control for safety.
- Transportation of live food animals, except molluscan shellfish.
- Transportation of compressed food gases, and food contact substances as defined in section 409(h)(6) of the FD&C Act.

3. Resources

- FSMA Final Rule on Sanitary Transportation of Human and Animal Food – FDA Website
- Sanitary Transportation of Human and Animal Food Fact Sheet
- Sanitary Transportation of Human and Animal Food: What You Need to Know About the FDA Regulation: Guidance for Industry
- Guidance for Industry: Clarification on Food Establishment Waiver from Requirements of the Sanitary Transportation of Human and Animal Food Rule
- Training for Carriers covered by the Sanitary Transportation of Human and Animal Food Rule – FDA Website
- Inspectional Resources: Resource Library, CVM Animal Food Program Resources SharePoint Site (FDA) and FoodSHIELD Site (States)

4. Legal History

The FDA Food Safety Modernization Act of 2011 (FSMA) directed FDA as the food regulatory agency of the HHS to better protect public health by, among other things, adopting a modern, preventive, and risk-based approach to food safety regulation. On April 6, 2016, FDA published in the *Federal Register* a final rule, *Sanitary Transportation of Human and Animal Food* (Sanitary Transportation rule) (81 FR 20091), that establishes requirements for shippers, loaders, carriers by motor vehicle and rail vehicle, and receivers engaged in the transportation of food, including food for animals, to use sanitary transportation practices to ensure the safety of the food they transport. The final rule became effective on June 6, 2016.