

# Overview of FDA's Animal Feed Safety System

July 2016

**Purpose and Scope:** The U. S. Food and Drug Administration (FDA) is the primary Federal regulatory agency responsible for ensuring the safety of animal feed. The FDA manages this responsibility under its Animal Feed Safety System (AFSS).

The AFSS covers the entire continuum of agency animal feed regulatory activities, including:

- pre-approving additives for use in feed;
- establishing limits on feed hazards;
- providing education and training;
- conducting research;
- performing inspections and investigations;
- taking enforcement actions for removing unsafe feed from the marketplace and for failure of firms to be in compliance with Agency regulations; and
- establishing partnerships with other government agencies with responsibility for feed safety.

The AFSS includes regulations and guidance pertaining to the...

- manufacture
- labeling
- storage
- distribution and
- use

...of **all** feed at **all** stages of production and use, whether at commercial or non-commercial feed manufacturing establishments, farms where animals are raised, or homes where pet animals are kept.

Management of the AFSS is directed by the Center for Veterinary Medicine (CVM or Center) within FDA.

This document provides an overview of all the elements that make up the AFSS and presents the status of major ongoing animal feed safety projects, which are important components of AFSS.

## Background

FDA has regulated animal feed for more than 100 years. Previously, FDA's regulatory approach was to develop a solution after a problem had been identified. More recently, though, FDA's approach is based on prevention – preventing the manufacture, distribution, and use of unsafe animal feed.

FDA first began its regulation of animal feed for safety in 1906, when Congress passed the Pure Food and Drug Act. In 1938, Congress passed the Federal Food, Drug, and Cosmetic Act (FDCA), which incorporated and expanded on the provisions of the 1906 Act and became the basic Federal statute giving FDA the authority to regulate food, including food for animals, and drugs for humans and animals. The Food Safety Modernization Act (FSMA), which was signed into law in January 2011, created the most significant change to the regulation of animal and human food safety since the 1938 law, and it strongly emphasizes prevention.

Animal feed ingredients and mixed feeds produced and used in the United States have a strong safety record. Government attention has been focused typically on known safety issues such as unsafe tissue residues resulting from feeding of medicated feeds, Bovine Spongiform Encephalopathy (BSE), *Salmonella*, and unsafe food additives. But, because the efforts didn't address feed safety in a comprehensive manner, issues affecting safety of animal feed still happened.

For example, in 1997 the U.S. Department of Agriculture (USDA) reported finding high levels of dioxins in poultry, which FDA traced to dioxins present in ball clay, an anti-caking agent used in animal feed. Then in 2002, a foreign government discovered high levels of dioxins in a mineral product for animal feed that the country had imported from the United States. It turned out that the dioxins were a result of a mineral manufacturing process that involved high temperatures and a combination of other ingredients.

In another example, the public became alarmed in 2007 when imported feed ingredients that were deliberately (and secretly) contaminated with melamine and related compounds to make the ingredients appear to have a higher protein value. The contaminated ingredients were used in pet food that sickened and caused the death of some dogs and cats throughout the United States.

Other animal food problems that have become issues in international markets are BSE, Chronic Wasting Disease, and microbial contamination.

The AFSS was developed to provide for a comprehensive feed safety program to help identify feed hazards – like those cited above – and their potential sources, thus enabling feed establishments and FDA to prevent the occurrence of unacceptable feed risks.

The production and distribution of feed ingredients and mixed feed, and the marketing of human food (e.g., meat, milk, and eggs) derived from animals that consume these feed materials, have become global businesses. World markets and the customers they serve react negatively when questions arise about the safety of a feed commodity introduced into domestic or international markets.

Implementation of a preventive, risk-based system composed of required (through regulation) and voluntary components, designed to ensure the continued production of safe feed, will help maintain user confidence in the safety of U.S. animal feed and animal-derived human food.

FDA is not the only government entity overseeing the safety of animal feed. At the Federal level the Environmental Protection Agency (EPA) approves feed-through pesticides, and USDA approves biologics (vaccines) that are added to animal feed. The EPA also establishes tolerances for pesticides on raw agricultural commodities and feed ingredients.

### **State Partners**

The States have a significant role assisting the FDA, formally and informally, in ensuring compliance with Federal regulations designed to protect animal and human health. Also, the State programs help to ensure feeds are nutritionally adequate for the intended species. Along with feed safety programs, States have other programs to minimize economic losses for feed purchasers, such as programs ensuring that feed products meet label guarantees for nutritional components.

States work cooperatively by helping the Association of American Feed Control Officials (AAFCO) reach its goal of providing a means of putting uniform and equitable rules in place on manufacturing, distributing, labeling, and selling animal feeds. AAFCO membership includes State feed offices, FDA, USDA, the Canadian Food Inspection Agency, Puerto Rico, and Costa Rica.

One of AAFCO's major objectives since its inception in 1909 is to establish uniform regulations applying to animal feed through the development of model regulations and policies. Another major AAFCO objective is to provide a forum whereby the feed industry, academia, the public, consumers, and government can identify, discuss, and resolve animal feed safety issues.

Yearly, AAFCO publishes an updated version of its *Official Publication*, which contains proceedings from meetings, definitions of feed terms, official names and definitions for feed ingredients, and model regulations for States. AAFCO also now publishes an on-line version of the *Official Publication*, and updates it more frequently than the printed version.

### **Focus on Food Safety**

The U.S. has sharpened its focus on food safety in recent years, spurred on by outbreaks of illness associated with human food (spinach, tomatoes, cantaloupe, peanut butter, and cucumbers) and animal food (contamination of pet food by melamine and related chemicals), but aided by new authority provided by Congress.

The focus of this Overview is food for animals. Here are three significant initiatives for FDA's animal food safety work:

- The inauguration of FDA's AFSS in 2003, at which the AFSS Team introduced what it planned to do under AFSS and presented the AFSS goals, and invited public participation and input;

- The Food and Drug Administration Amendments Act of 2007 (FDAAA); and
- The Food Safety Modernization Act (FSMA), which made prevention a significant part of the U.S. feed safety effort.

AFSS: The initiative extends to all FDA’s activities in all areas of animal food safety and incorporates regulations and policies that apply to manufacturing, labeling, storage, distribution, and use of animal food.

FDAAA: Title X of the Act has several provisions that apply to animal food safety that were in response to the dog and cat illness and deaths in the United States from pet food imported from China that contained melamine, cyanuric acid, and related compounds. FDAAA required FDA to establish an early warning system about unsafe pet food. The early warning system has been implemented (see Component D in this document). Two other requirements – establishing improved labeling for pet food and setting standards for pet food ingredients – remain in development.

FSMA: The Act extensively changes the way FDA addresses human and animal food safety by placing a greater emphasis on prevention of food safety problems. FSMA gives FDA the legislative mandate to require comprehensive, science-based preventive controls across the food supply, including preventive controls for animal feed.

FSMA institutes a required frequency for FDA inspections and provides FDA with new enforcement authorities – such as mandatory recall authority, food safety records access, suspension of registration, and administrative detention – designed to achieve higher rates of compliance.

FSMA also provides FDA authority to ensure that imported products meet U.S. standards and are safe for U.S. consumers. Under FSMA, importers have an explicit responsibility to verify that their foreign suppliers have adequate preventive controls to ensure the safety of the food they produce and ship into the United States. New programs, such as the Voluntary Qualified Importer Program and Accreditation of Third-Party Auditors, are part of the FSMA imports provisions and were both published in the Federal Register on November 27, 2015.

To establish FSMA’s preventive control provisions for animal feed, FDA published a regulation in the September 17, 2015, Federal Register establishing the requirements for current good manufacturing practice, hazard analysis, and risk-based preventive controls for food for animals. (While FSMA utilizes the term “animal food” when referring to animal feed, we are utilizing the term “animal feed” for the most part in this document, because the term animal feed is most commonly used and understood in the animal feed industry.)

FSMA requires all domestic and foreign human food and animal feed facilities that are required to register under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Act) section of the FDCA to also implement current good manufacturing practices for manufacturing, processing, packing, and holding

animal feed. In addition, any facility covered by FSMA is required to conduct an analysis of likely hazards it could face (i.e., known or reasonably foreseeable animal food hazards), and implement risk-based preventive controls to address those hazards (<https://www.federalregister.gov/articles/2015/09/17/2015-21921/current-good-manufacturing-practice-hazard-analysis-and-risk-based-preventive-controls-for-food-for>).

Several types of firms would be exempted from the proposed rule. For more information on the exemptions, go to the FSMA portion of the FDA Website ([www.fda.gov/fsma](http://www.fda.gov/fsma)).

FDA has given the industry time to prepare for implementation of the FSMA rules. The amount of time varies, depending on the size of the business, with smaller business getting more time.

### **Risk-Based Inspection Programs**

Although facility inspection is an important element of an effective regulatory program, FDA does not have the resources to inspect each feed ingredient and mixed feed manufacturer or distributor frequently, especially considering the size of the industry and the amount of feed that is produced and then fed just a few days later. Instead, a risk-based approach is used to identify which feed products, processes, and establishments present significant risk to the health of animals and the safety of food from animals.

FDA established priorities for inspections under the BSE program, starting in FY 2009, by using a mathematically modeled, risk-based approach. This approach was originally developed in FY 2008 for inspection of FDA-licensed medicated feed mills for compliance with the medicated feed current Good Manufacturing Practice (cGMP) regulation (21 Code of Federal Regulations [CFR] 225) and other Agency regulations. CVM is currently in the process of implementing a risk-based approach for feed-related inspections, which will allow the Center to prioritize inspections for a given fiscal year or other time frame and will permit the Center to identify specific establishments or types of establishments to be inspected.

A risk-based, preventive animal feed safety program requires feed manufacturers and distributors to take into consideration hazards that could cause animal feed to be unsafe, and to develop and implement plans to minimize or prevent hazards from becoming significant animal health risks. By taking those steps, feed manufacturers should improve their ability to identify and minimize or eliminate hazards associated with animal feed before those hazards result in decreased animal productivity, adverse animal health consequences, and potential risks to human health. Also, animal feed manufacturers who understand their own business and technical processes well enough to establish effective control points for naturally occurring or accidental feed hazards are likely to be more capable of detecting and controlling deliberately introduced feed hazards.

FDA and State resources available for use in enforcement programs are limited, but can be more effectively utilized by focusing research, inspections, and feed sampling-and-analysis programs on those situations representing the greatest risks to animal health and

the public well-being. Also, we believe a more effective overall risk-based prevention-oriented feed safety program will lead to fewer feed emergencies for government agencies to address.

## **Operating Principles of the AFSS**

These operating principles are the basis for the AFSS:

1. Federal and State regulatory agencies provide the rules, guidance, and oversight to assist industry in producing and distributing safe feed ingredients and mixed feed;
2. Feed and animal production industries are responsible for the production, distribution, and use of safe feed;
3. Rules and guidance provide flexibility in the approaches individual producers of feed can use to meet acceptable safety criteria;
4. Federal and State regulatory agencies cooperate on all aspects of feed regulation;
5. Federal and State feed regulatory agencies conduct inspections of feed-manufacturing establishments, review product labels, sample and analyze feed for feed hazards and for compliance with label guarantees, and take appropriate actions to address violations;
6. FDA uses risk-based decision-making to help determine which feed hazards should receive an inspection, enforcement, and research focus, and the best methods for addressing the hazards;
7. FDA directs its regulatory resources to those feed hazards that are a risk to animal and public health;
8. Feed defense measures as they relate to preventing and responding to intentional acts of feed contamination are part of the AFSS;
9. Training is critical for ensuring that industry and regulatory agencies have the most up-to-date knowledge about FDA rules and guidance, and that enforcement by FDA and States is consistent and conducted in an appropriate manner;
10. Feed intended for non-food-producing animals, such as pets, is included along with feed for food-producing animals; and
11. Feed establishments covered by the AFSS include all facilities, equipment, and conveyances involved in the production, packaging, storage, and distribution of individual feed ingredients and mixed feed, and the feeding of animals.

## **Major Components of the AFSS and Key Definitions**

Seven operating components (labeled A through G) make up the AFSS. These components cover the processes used by FDA to ensure that:

- Ingredients used in animal feed are safe (components A and B);
- The methods used to make, store, and distribute animal feed result in safe products (component C);

- The Agency acquires timely information about unsafe animal feed and, when appropriate, makes such information publicly available (component D);
- The levels of regulatory oversight are commensurate with risk to human and animal health (component E);
- Training, education, and outreach activities keep our partners and stakeholders well informed and ensure that FDA and State feed regulatory personnel are adequately trained (component F); and
- An active and aggressive research program is employed to generate data to aid in addressing animal feed safety issues (component G).

More information on each component follows, including the identification of work in progress to strengthen the ability of the Agency to ensure that its regulatory program is effective and efficient and to help the industry ensure that its animal feed products are safe. The identified work in progress does not reflect all the steps the Agency is taking to improve its feed safety program; however, the identified work does present the more important actions.

A feed hazard is defined as any biological, chemical (including radiological), or physical agent in feed with the potential to cause illness or injury to animals or humans. One regulatory challenge is defining terms to take into account the fact that the presence of certain agents in feed does not always pose a likely risk to animal or human health. It is when controls are not adequate at feed establishments that these same agents may cause the feed to be a much greater risk to animal or human health. For example, corn containing aflatoxins at levels below 20 parts per billion (ppb) is not likely to cause an adverse health consequence for animals (except for trout) given feed made with this corn or for people consuming the food derived from these animals. However, if environmental or other pertinent conditions are not controlled while the corn is in storage at the feed establishment and aflatoxin levels in corn rise above 20 ppb, then the feed establishment's use of this corn to make feed for lactating dairy cattle causes a much greater risk to health for people consuming milk products from these animals. The goal of AFSS is to eliminate or control a feed hazard so that it does not become a significant risk of causing illness or injury to animals or humans.

In this document, the definition of animal feed includes feed ingredients and mixed feed intended for animals.

### **Component A – Ingredients and the Approval Process**

The primary purpose of animal feed is to provide nutrients. But some ingredients and additives are incorporated into feed for other purposes; for example, to add color to the animal feed or the human food derived from the animal, to ensure stability for nutrients, to provide flavor, and to prevent mold growth. Drugs may also be incorporated into feed for disease prevention and treatment. The FDCA provides FDA the authority to regulate

ingredients and additives used in feed.\* Depending on its intended purpose, an ingredient or additive could be classified as a food additive, a new animal drug, or a color additive. Regulations that mandate and specify data requirements and the application or petition format required to be submitted for Agency review and approval for food additives, new animal drugs, and color additives are contained in Title 21 of the CFR. These regulations also provide timeframes for Agency decisions on these applications and petitions.

FDA also controls some ingredients and additives by using procedures not presently covered by regulations. One example is the voluntary consultation process for plants modified through biotechnology. It is used to review data on the plants before the company introduces the modified plants into the marketplace.

A second example is the Generally Recognized as Safe (GRAS) Program for substances used in animal feed. The program was announced in the June 4, 2010, *Federal Register* (75 FR 31800-31803) initially as a pilot program (<http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/GenerallyRecognizedSafeGRASNotifications/ucm192219.htm>). Under the program, after evaluating a notice submitted by a notifier, the FDA will inform the notifier that the Agency either has currently no questions about the notifier's determination that the substance is GRAS for its intended use, or that the FDA has identified issues that call into question the GRAS status of the use of the ingredient. FDA is in the process of finalizing the pilot program.

A third example is the recognition by FDA of the names of feed ingredients defined in the AAFCO *Official Publication* as the common or usual name of the ingredients (see Compliance Policy Guide [CPG] 665.100, at <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074687.htm>).

All FDA-approved food additives and color additives for use in animal feed are listed in 21 CFR 573 and 21 CFR 73, respectively. FDA lists substances it considers GRAS at 21 CFR 582 and 21 CFR 584. However, the Agency notes that it is impracticable to list all GRAS substances. AAFCO publishes a book, the *Official Publication*, which provides a description of feed ingredients and additives. The printed version of the *Official Publication* is updated on an annual basis to incorporate substance description additions, modifications, or deletions, based on reviews completed by AAFCO members. In addition, AAFCO publishes an on-line version of the *Official Publication*.

A few years ago, FDA developed a Memorandum of Understanding (MOU) with AAFCO explaining the roles of each organization in AAFCO's process for adding or modifying feed ingredient definitions in the *Official Publication*. The MOU is available at <http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm115778.htm>.

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\* Some articles added to feed fall under the purview of other Federal agencies. Feed-through pesticides are regulated by the Environmental Protection Agency, and vaccines added to feed are the responsibility of the U.S. Department of Agriculture.

A complete list of the formal and informal processes used by FDA to review the safety of feed ingredients and additives and information about the location of ingredient/additive listings, are provided in Appendix I.

Antimicrobial drugs were largely approved as over-the-counter drugs until 1996 and used either in feed or water. However, by the mid-1990s, science had improved to provide more information about the potential for the development of resistance from the use of antimicrobial drugs. Since 1996, as provided in Animal Drug Availability Act, antimicrobial drugs approved for feed use were also approved as Veterinary Feed Directive (VFD) drugs.

VFD drugs approved for use in animal feed can be used only under the supervision of a veterinarian. The VFD regulation, which became effective in 2001, established requirements related to the distribution and use of VFD drugs and animal feeds that contain VFD drugs.

FDA believes that antimicrobial drugs play an important role in helping to protect the health of animals. But to address the issue of the development of antimicrobial resistance, the use of certain antimicrobials should be controlled by veterinarians, who have the scientific and clinical training to know how to use antimicrobials judiciously. The way to give veterinarians a role in deciding when antimicrobial use is appropriate is by eliminating the over-the-counter marketing status of certain drugs and instead make them Rx or VFD use only, which is FDA's goal under Guidance #213. To implement Guidance #213, FDA realized that it needed to improve the VFD process.

Late in 2013, FDA proposed significant changes in rules applying to VFD drugs. The proposed changes were finalized in June 3, 2015, and went into effect October 1, 2015

### **Current Project Work:**

**Project A1.** As required by the FDAAA, FDA will be establishing feed ingredient standards and definitions through the comment and rulemaking process. FDA established a docket (FDA-2007-N-0442) in a Federal Register notice on January 7, 2008, for receiving comments from stakeholders on section 1002(a) of the FDAAA. In addition, a public meeting was held on May 13, 2008, in Gaithersburg, MD, at which the Agency received oral and written comments on the mandate from Congress to write regulations to ensure pet food safety. FDA is drafting a regulation to fulfill the mandate to establish standards and definitions.

**Project A2.** FDA is developing the final regulation for accepting GRAS notices for feed ingredients. The regulation would transform the current pilot program into an official regulatory program. By the end of April 2016, 20 GRAS notices have been filed since the pilot program started in 2010.

**Project A3.** CVM is taking steps to address concerns about the development of resistance in antimicrobial drugs important for human health stemming from the use of those drugs

in food-producing animals, including drugs used in animal feeds. Antimicrobial drugs used for human health are known as “medically important” antimicrobials. In April 2012, CVM finalized Guidance for Industry #209, *Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*, after receiving and reviewing public comments. It provides a policy framework regarding the appropriate or judicious use of medically important antimicrobial drugs in food-producing animals and is based on available scientific information. The regulatory framework presented in the guidance includes phasing-in measures to limit use of medically important antimicrobial drugs in food-producing animals to those considered necessary to protect animal health. In addition, the regulatory framework would limit the use of such drugs to cases in which there was veterinarian oversight.

In December 2013, CVM issued Guidance for Industry #213, which presented information to drug sponsors to help them voluntarily remove growth promotion and feed efficiency indications from the labels on antimicrobial drugs. FDA asked affected sponsors to notify the agency in writing within 3 months, or by March 12, 2014, of their intent to engage with FDA as defined in Guidance for Industry #213. All 26 of the affected sponsors have confirmed in writing their intent to engage with FDA as defined in Guidance #213. These sponsors hold 100 percent of the applications affected by Guidance #213.

The last step in this process is for the sponsors to submit supplemental NADAs asking that their drug’s regulations be revised to no longer include the growth promotion and feed efficiency claims.

### **Component B – Limits for Feed Hazards**

Feed contamination can result from exposure of finished feed, feed ingredients, and mixed feed to environmental, agricultural, industrial, or other sources of hazards, at any stage of the feed production continuum – from pre-harvest activities through feed manufacture, storage, and transportation, and continuing to on-farm feeding practices. The likelihood of a feed hazard reaching levels that lead to safety concerns depends on a multitude of factors. For example, feed hazards initially present in feed ingredients and mixed feed at levels below the level of concern can be inadvertently increased to toxic or deleterious levels by certain harvesting and manufacturing practices or storage or transportation conditions. For example, if corn is not stored appropriately, aflatoxin produced by fungi present on it can reach levels that are toxic to animals. Feed hazards could also be added deliberately to feed to cause serious adverse animal and human health and economic problems.

Under FSMA, manufacturers, distributors, and holders of animal feed that are required to register with the FDA as animal food facilities must implement preventive controls for any known or reasonably foreseeable hazard that they identify as part of their operation.

Meanwhile, the Agency uses several approaches to help eliminate or prevent risks from feed hazards in regulated feed products, such as establishing regulatory or guidance

maximum limits for feed hazards, implementing preventive controls, establishing tolerances through the food additive petition process, or relying on a case-by-case review by experts to determine whether specific contamination incidents are unsafe.

Tolerances are regulations and have the force of law; action levels are informal judgments about the levels at which consumers may be safely exposed to feed hazards; regulatory limits identify levels of feed hazards at which feed ingredients and mixed feed are considered to be adulterated; and guidance levels represent the Agency's current policy to industry. Once limits are created and understood, it becomes easier to control the risks from the feed hazards by product-based or process-based approaches, either initiated by industry or required by a Federal or State regulation.

The Agency has established maximum limits for some of the more obvious feed hazards on an as-needed basis, but it has no process for systemically determining when there is a need for limits for other known or newly recognized feed hazards. Component B encompasses the steps by which FDA has assessed the need to establish regulatory or guidance limits in the past, and presents a prioritization system for determining the need for an assessment that is being developed based on the comparative levels of risk posed to animal or human health.

When the Agency decides that limits for feed hazards need to be established, the decision calls for the development of a rapid, inexpensive, and reliable feed ingredient and mixed feed analytical method(s) that then must be validated and made available for use by industry and government. FDA has developed an internal standard operating procedure (SOP) for ensuring that methods of detecting a feed hazard in feed ingredients or mixed feed are available for use by FDA and other government agencies and by the regulated industry. This SOP is available at <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/PoliciesProceduresManual/UCM046777.pdf>.

It places an emphasis on ensuring that such methods are capable of meeting the Agency's limits for feed hazards using established criteria. Appendix II contains the Agency's current procedures for establishing limits for feed hazards in feed and feed ingredients. The same appendix also contains references for the limits established by FDA, the U.S. Environmental Protection Agency, AAFCO, Codex Alimentarius Commission, the Food and Agricultural Organization, and the World Health Organization.

### **Current Project Work**

**Project B1.** Not all feed hazards carry the same risk for adverse consequences to animal or human health. The Agency needs a systematic process whereby it can distinguish among feed hazards based on the risks each hazard poses to animal or human health.

As indicated previously, whenever possible, the Agency relies on risk assessments when making decisions about feed safety. The use of risk concepts is not new for the Agency. We routinely estimate public health impact in deciding where to focus regulatory effort.

However, what will be new is the systematic application of a risk-ranking method that ranks all identified feed hazards in relation to each other. The risk-ranking method being developed by the Agency will try to account for the whole feed manufacturing continuum: from feed hazards present in incoming materials or feed ingredients (product-related risks); through the potential for modulation of these feed hazards – increase, decrease, or remain at the same level – by manufacturing processes (process-related risks); to how the feed ingredients and mixed feed are handled by feed manufacturers, transporters, and on-farm mixers (facility-related risks).

Public meetings were held on September 12, 2006, May 22, 2007, and May 14, 2008. At these meetings, CVM made presentations about risk, risk-ranking, potential feed hazards, and health consequence and exposure scoring for chemical and microbiological feed hazards.

A critical part of the risk-ranking method development is the population of the data cells with sufficient feed hazard data to ensure that the method will produce robust estimates. FDA recently concluded cooperative agreements with a dozen States under which the States collected feed hazard data and shared the data with the Agency. Further, data generated by FDA under its Feed Contamination Compliance Program are also being used, as are data collected through Health Hazard Evaluations associated with feed contamination occurrences.

Once the “model” is running, experts will be asked to conduct an evaluation to confirm the validity of the model’s assumptions and findings. CVM intends to have the risk model – covering a subset of chemical hazards, along with supporting documentation – reviewed to receive feedback on the practicality of the model and the clarity of the documentation.

### **Component C – Production, Storage, and Distribution of Safe Feed Ingredients and Mixed Feed**

Prevention is the cornerstone of any food safety control plan. For example, a plan could include the implementation of written procedures calling for testing incoming loads of feed ingredients that are known to be susceptible to the molds that produce aflatoxins, thus ensuring that aflatoxins are not present at unsafe levels. Established verification procedures in a feed safety system are used to confirm that products are safe and that they comply with regulatory requirements.

The FDCA provides FDA with the statutory authority to regulate the manufacture, packaging, storage, and use of animal drugs, including Type A medicated articles and Type B and C medicated feeds, to ensure conformity with the cGMP regulations. Regulations mandating and specifying medicated feed cGMP regulations are located in 21 CFR 225. The regulations for Type A medicated articles are located in 21 CFR 226. Complete citations of the regulations are listed in Appendix III.

Good manufacturing practices provide a systematic approach for ensuring feed safety through the identification and use of appropriate controls during the manufacture, packaging, storage, and distribution of feed ingredients and mixed feed, and the controls are useful beyond their utility for animal drugs. Our review of the U.S. feed safety system conducted prior to passage of FSMA found that the United States lacked certain baseline requirements for producing safe animal food, including Federal cGMP regulations.

The FSMA final rule calls for animal food and ingredient producers to comply with good manufacturing practices addressing manufacturing, processing, packing, and holding animal food. It also establishes hazard analysis and risk-based preventive controls for many animal food facilities. These measures will provide a greater assurance that animal food will not cause illness or injury to animals or to humans who handle animal food or consuming food derived from animals.

### **Current Project Work**

**Project C1.** To ensure the animal food preventive controls rule is understood, the Agency is developing several “Guidance for Industry” documents. One guidance document would help the regulated industry conduct hazard analyses, and it offers a specific emphasis on hazard identification and evaluation, for determining appropriate preventive controls. A second guidance document will help the industry understand and comply with the cGMP requirements for animal feed. In addition, FDA is writing guidance about the use of human food by-products as animal feed, and a “Small Entity Compliance Guide” to explain the actions that small or very small business must take to comply with the animal feed preventive-controls rule.

Farms required to comply with the animal food preventive-control rule are those required to register with FDA as part of the Bioterrorism Act. Because most, in fact nearly all, farms that produce and store animal feed are not required to register with FDA under the Bioterrorism Act as food facilities, they will not be required to comply with the animal food preventive-controls rule. For these exempt farms, CVM has released a guidance document (Guidance of Industry #203, *Ensuring Safety of Animal Feed Maintained and Fed On-Farm*) that provides information animal producers can use to help them make sure that their animals’ health is not adversely affected by animal feed hazards and that human food derived from their animals does not compromise human health (see Project F1).

### **Component D – Reporting of Unsafe Feed**

The surveillance programs conducted by the FDA and State feed control offices generate data about unsafe feed. Surveillance by the feed industry, animal producers, practicing veterinarians, and the public can be an important source of additional information about feed that had been adulterated or misbranded.

The FDAAA directed the FDA to establish a “Reportable Food Registry,” through which instances of “reportable food,” including human food and animal feed, are reported to

FDA. Reports are sent to the Registry via an electronic portal. Reports of reportable foods are made by food and feed establishments that have registered with FDA as required by Section 415(a) of the FDCA, and by Federal, State, and local public health officials.

The Agency is charged to include in the Reportable Food Registry only those reports that describe cases in which the responsible party has determined the reportable food has a reasonable probability of causing serious health consequences or death to humans or animals. In the *Federal Register* of September 9, 2009, FDA's Center for Food Safety and Applied Nutrition and CVM announced the availability of a Reportable Food Registry guidance document that provides guidance to the industry about complying with the Reportable Food Registry requirements. Public workshops were held on July 25, 2009 (College Park, MD), August 5, 2009 (Chicago, IL), and August 25, 2009 (Oakland, CA), to explain the intent of the guidance in more detail. The Reportable Food Registry and guidance apply to all FDA-regulated categories of human foods (except dietary supplements and infant formula) and animal feeds.

In May 2010, FDA launched the Safety Reporting Portal, which allows responsible parties to report reportable foods directly to FDA's Reportable Food Registry. The Safety Reporting Portal is accessed from the FDA Website.

In addition providing a place to send Reportable Food Registry reports, the Safety Reporting Portal offers consumers and others an additional mechanism to report their pet food complaints to the FDA. Within days of opening the Safety Reporting Portal for pet food complaints, reports from veterinarians diagnosing thiamine deficiency in cats enabled FDA to facilitate a rapid recall by the manufacturer of a cat food that lacked adequate levels of thiamine.

The FDAAA also required that FDA establish a Pet Food Early Warning Surveillance System to detect adverse events associated with pet food. Consumer complaints are the primary source of surveillance data for the Pet Food Early Warning Surveillance System. Consumer complaint coordinators in each of FDA's District Offices collect complaints through telephone calls from consumers in their district.

Consumer complaints and Reportable Food Registry reports collected through the Safety Reporting Portal have proved that the Portal is a valuable new surveillance tool for the Pet Food Early Warning Surveillance System. The Portal has increased FDA's ability to identify animal feed problems earlier and respond more rapidly.

In March 2014, CVM added a portal for reporting problems with livestock feed. CVM enhanced its animal feed reporting systems by adding to the pet food safety portal and the reportable food registry a Website for the public to report problems related to livestock animal feed. The Livestock Food Reporting Portal accepts reports about foods made for species considered to be farmed animals, including but not limited to horses, cattle, swine, poultry, and fish. Anyone, including veterinarians and livestock producers, with concerns about the safety of an animal feed can file a report.

The Livestock Food Reporting portal is the latest addition to the Safety Reporting Portal, an online system designed to streamline the process of reporting product safety issues to the FDA and the National Institutes of Health. Animal feed manufacturers, distributors, retailers and public health officials at the Federal, State, and local level should continue to use the Reportable Food section of the Safety Reporting Portal. The Portal can be found here: <http://www.safetyreporting.hhs.gov/>.

Beginning in 2009, the Partnership for Food Protection started to develop a new program that will allow States and the Federal government to share information about contaminated pet food products. The Partnership for Food Protection is a program that brings together food safety professionals from Federal, State, and Local governments to coordinate work in food, feed, epidemiology, laboratory, animal health, environment, and public health to develop and implement an Integrated Food Safety System.

The Partnership was instrumental in the development of the CVM's Pet Event Tracking Network, or PETNet, which was officially launched on August 1, 2011. In PETNet, information is shared over a secure information network with State and Federal regulatory agencies with jurisdiction over pet food products. PETNet's goal is to disseminate information to regulators – typically State officials – who are in the best position to take quick action to protect the health of pets as soon as the information becomes available to FDA. (PETNet is for government use only. It is not accessible by the public.)

Two videos are available that explain how to report farm-animal feed and pet food safety problems to FDA. Both videos discuss the Reportable Food Register, the on-line portal that feed manufacturers, livestock and pet owners, and concerned citizens can use to report problems with animal food. One of the videos discusses the mandatory reporting requirements for certain feed manufacturers. The other discusses voluntary reporting of animal feed and pet food problems. Both videos are available through CVM's SafeFeed web page ([www.FDA.gov/safefeed](http://www.FDA.gov/safefeed)). (See Component E for more information about the SafeFeed web page.)

In late 2010, CVM's Office of Research initiated a project, the Veterinary Laboratory Investigation and Response Network (Vet-LIRN), to collaborate with veterinary diagnostic laboratories to exchange scientific information, build laboratory capacity for routine and emergency response, and train scientists. The overall goal is for participating laboratories to be ready, willing, and able to help CVM investigate potential problems with animal feed and animal drugs, providing a rapid response to reports of animal injury. By May 2016, the vet-LIRN Network has expanded from the 16 original member laboratories to 38 member laboratories.

During its first year, Vet-LIRN conducted five in-depth cases investigations and multiple case evaluations. Vet-LIRN now conducts between 30 and 50 in-depth investigations per year, as well as multiple case evaluations. Vet-LIRN has also been heavily involved in CVM's investigation of the illness in dogs associated with eating pet jerky treats. Since

2011, Vet-LIRN has conducted more than 1,000 tests on jerky pet treat samples and more than 850 tests on diagnostic samples from affected animals.

At the same time, the Vet-LIRN staff has managed the work of 11 laboratories doing research to harmonize a method for detecting *Salmonella* in pet fecal samples to evaluate the consequences of contaminated feed on background infection prevalence and to facilitate case investigations. Vet-LIRN also has funded 11 cooperative agreement projects designed to evaluate and validate chemical or microbial tests using animal diagnostic samples which are not typical food matrices (e.g., urine, blood, feces, saliva, liver, and kidney). In addition, the Vet-LIRN conducts approximately three network-wide chemical or microbial proficiency tests per year to demonstrate that the participating laboratories provide accurate and meaningful testing data to FDA.

Vet-LIRN laboratories are also participating in the presidential initiative to Combat Antibiotic Resistant Bacteria (CARB) in collaboration with USDA's laboratory network. Vet-LIRN has leveraged the resources of state-of-the-art veterinary diagnostic laboratories in a remarkably cost effective way to provide FDA with rapid information regarding potential animal feed related contamination events.

### **Current Project Work**

None at this time.

### **Component E – Regulatory Oversight**

The primary purpose of regulatory oversight is to determine an establishment's or a product's degree of compliance with applicable regulations. The term regulatory oversight should be considered in its broadest view, covering, for example, the review of labeling done at the regulator's site of business or on the firm's website, or an on-site inspection of the establishment's manufacturing facility. Surveillance inspections are conducted to determine whether an establishment is in compliance with the regulations and the operation is adequately controlled. Compliance inspections are conducted to evaluate an establishment's compliance with the provisions of the regulations and to document inspectional observations supporting possible enforcement action.

Because the majority of inspections of feed manufacturing and distribution establishments – which fall under the jurisdiction of FDA – are done by State agencies using Federal or State authority, FDA's strong working relationship with State counterparts will continue to be a significant component of the AFSS. A scientific risk-based approach will be used to improve the Agency's ability to prioritize and allocate inspection resources by targeting establishments, facilities, products, and processes posing significant risks to animal or human health.

A new approach the Agency is allowing is the use of third-party certification. A guidance document, entitled "Voluntary Third-Party Certification Programs for Foods and Feeds" (<http://www.fda.gov/regulatoryinformation/guidances/ucm125431.htm>), was released in

January 2009 and provides more information on this topic. While third-party certification programs are not intended to take the place of inspections performed by a regulatory agency, if a firm is *participating* and compliant in a recognized third-party program, the firm is likely at lower risk for problems than a firm that is not participating. The final rule on third-party certification bodies was issued on November 27, 2015. The effective date was January 26, 2016. The regulation establishes a program for accreditation of third-party auditors for conducting food safety audits of foreign food facilities for human and animal food and issuing certifications.

Regulatory compliance efforts often rely on voluntary compliance with the law and regulations. When voluntary compliance and education are unsuccessful, the Agency has other options, such as Untitled Letters, Warning Letters, informal meetings, mediation, civil penalties, administrative hearings, injunctions, seizures, and criminal prosecutions. Enforcement action would not be taken based on information from third-party certifiers; however, an inspection by a regulatory agency could be used to follow-up and document violations for enforcement action. See Appendix IV to find more information about regulatory oversight.

FDA's animal feed safety program has not always included adequate attention to every sector of the feed industry. A new challenge will be to figure out how to adapt our regulatory approach to an evolving industry. Over the last 30 years, there has been a major shift in feed manufacturing as an increasing amount of feed is produced on the farm. Some on-farm operations, such as the large integrators, are making more feed than many commercial feed companies. Historically, regulatory oversight was focused principally on the commercial medicated feed manufacturing. But recent FDA efforts undertaken in response to the Food Safety Modernization Act (FSMA) and other legislation have given us some tools to help broaden our coverage. Adoption of the original BSE rule in 1997 caused us to expand our routine feed safety coverage significantly, pushing us to begin managing our resources using a risk-based approach to expand coverage. FSMA builds upon the risk-based concept. CVM is considering how inspectional and regulatory coverage can be expanded to include on-farm feed producers and other segments of the feed industry, such as importers and warehouse/storage facilities. Risk associated with these segments will be assessed to determine where the Agency will focus its limited resources.

One segment of the feed industry that had not been subject to FDA's regulatory attention was transportation. However, that changed in April 2016 when FDA finalized FSMA's final rule on Sanitary Transportation of Human and Animal Food. The rule establishes requirements for the use of sanitary practices by human and animal food shippers, loaders, and transporters/haulers that use motor or rail carriers.

### **Current Project Work**

**Project E1.** The FDA collaborated with AAFCO in developing Animal Feed Regulatory Program Standards (feed standards) for use by State feed control programs. FDA and AAFCO jointly announced the availability of the Program Standards in February 2014.

Since that time, FDA has been working on an implementation initiative to encourage States to implement the feed standards and to provide technical assistance during implementation. As of May 2016, 21 states are implementing the standards. Twelve of those 21 states are in their second year of implementation, with the other nine completing their first year.

Several work groups have been working on revising the current standards, and CVM has representatives on each of the work groups.

Implementation of the feed standards will promote uniformity and consistency among animal feed regulatory programs and provide a platform for mutual reliance within a national integrated food safety system. The standards do not apply to animal feed manufacturers. They were developed for and intended to be implemented under animal feed regulatory programs. The Program Standards are available on the FDA Website at: <http://www.fda.gov/ForFederalStateandLocalOfficials/AnimalFeedRegulatoryProgramStandardsAFRPS/default.htm>.

**Project E2.** Imported food products are required to meet the same safety standards as domestic food products. In September 2007, the President's Interagency Working Group on Import Safety reported the burdens facing border officials caused by the growth in the amount of imports and by an increased focus on security. The report noted that these officials must manage larger volumes of imports from countries that often have a less-developed regulatory system. In addition, border officials must consider more complex risk scenarios, use more sophisticated screenings and examinations, and employ new technologies to ensure product safety. The report made clear that new import oversight methods would be needed to ensure the safety of imported products used in the United States. The Agency has been working on methods to improve that oversight.

As part of FSMA, Congress directed FDA to expand its management of imported food. FDA has a presence in many foreign countries that produce and export food to the U.S.; however, the ability of the U.S. to establish a presence is limited by available resources and access restrictions. The resource limits of the Agency require us to rely upon stakeholders and partnerships. FSMA has provided FDA with the authority to establish requirements for importers of food and feed. The Agency's relationships with regulatory partners and industry stakeholders will be enhanced through the Foreign Supplier Verification Program and the Accredited Third-Party Certification rule. Both were published as final rules on November 27, 2015. FSMA also requires the establishment of a voluntary qualified importer program.

**Project E3.** CVM along with states within FDA's Minneapolis District (Wisconsin, Minnesota, North Dakota, and South Dakota) and FDA's Minneapolis District Office participated in a pilot project for assigning inspections based on risk factors. During the first year of the 3-year project, the participants identified and ranked health-related risk factors, which were used to rank the feed facilities in each State as either high-risk or low-risk. The majority of high-risk facilities were inspected by State or District inspectors. A few low-risk facilities were also inspected. After gaining experience from

the first year of inspections, the program developers reduced the number of risk-ranking criteria to simplify the process and modified the weights assigned to each criterion used to determine the potential for impacting animal or human health. We are beginning to use this approach to risk-rank firms in preparation for inspections that will be done under the new FSMA rules. A final project report is being drafted.

## **COMPONENT F – Education and Outreach**

For a comprehensive regulatory approach to be successful, cooperation between FDA and State regulatory programs is essential. In addition, the timely development and distribution of educational materials and guidance documents for feed companies and producers will be necessary as portions of the AFSS and FSMA are implemented. It is critically important to have program and inspection staff well trained in all facets of the Agency's feed safety program and an industry that knows what is required by FDA rules to prepare, distribute, and use feeds in a safe manner. However, such education and outreach initiatives need to be timely, informative, understandable, and available to those needing the information.

The AFSS places heavy emphasis on developing and implementing education and outreach programs, which it uses in conjunction with inspection and enforcement activities to bring about compliance with safe feed rules and policies.

The introduction of a new regulatory feed program or the modification of an existing one requires training to ensure that FDA and State personnel understand the new or modified program and that they are capable of carrying out the program's mandate. Furthermore, it is essential for the Agency to prepare and distribute materials to aid the industry in achieving compliance, because voluntary compliance by industry means less compliance effort by regulatory agencies.

One key to success with these outreach and education efforts is timing. The information must reach the users when they need it.

Delivering the message using formats familiar to the industry and other stakeholders is another key to success. A significant step in this effort occurred during 2013 when FDA launched a new easy to find and use animal feed web page ([www.FDA.gov/SafeFeed](http://www.FDA.gov/SafeFeed)) that has links to all pertinent feed safety information scattered throughout the FDA Website. Further, the information was arranged based on a user's needs. For example, the page has a navigational button for anyone who wants more information about feed ingredients, or about manufacturing feed. Regulatory information is on that page, too. And, to make the information even more available, the page was developed so that it will properly display on a mobile device as well as on a computer screen. Feed manufacturers and regulators can access information without having to return to an office computer to look it up.

Also, CVM has developed a web-based system that houses the most up-to-date approved Blue Bird labels for Type B and C medicated feeds. The system, which was made available in June 2009 for a number of approved drugs, provides the medicated feed industry with the best opportunity to ensure that accurate labeling is developed and used. In addition, by using resources available on the Internet, licensed medicated feed mills will be operating in compliance with the requirement of 21 CFR 515.10 by having in their possession current approved Type B or Type C medicated feed labeling before they receive Type A medicated articles. CVM continues to add new Blue Bird labels to the system.

### **Current Project Work**

**Project F1.** It has been several decades since FDA pet food regulations have been updated. On the other hand, the AAFCO model pet-food regulations have been amended nearly each year since they were adopted in 1967 by AAFCO's membership. Because the AAFCO regulations were aimed to keep pace with industry desires and public interests, they became the de facto accepted standard, even though they have not been adopted by every State. The public, pet food industry, government agencies, and AAFCO agree that current Federal pet food labeling can be improved to provide more meaningful information to pet owners about the nutrition and safe use of the food they purchase for their pets.

FDAAA also requires updated labeling standards for pet food. Congress is requiring a regulation that includes standards for nutritional and ingredient information on the label. The Agency established a docket (#2007-N-0442) about this topic. A public meeting was held on May 13, 2008, to receive comments from interested parties. A proposed regulation is being drafted for public comment.

**Project F2.** CVM has made use of the internet by placing videos about feed safety and U.S. feed standards on it, thus making the information available to international as well as domestic audiences. The information is available at any time to anyone with a computer and an Internet connection.

In 2010, the first video, which highlighted various safe animal feed and pet food principles, was released. The 5-minute video highlighted the role of feed manufacturers and animal feeders in ensuring the safety of food derived from animals. The video, "Safe Animal Feed," is available on the FDA's website and was also recorded on disks for distribution at trade shows and other meetings.

Since that video was produced, CVM has also produced others about how pet food is regulated ("FDA and Pet Food"), how to safely handle pet food in the home ("Pet Food and Treats in your Home"), and two videos about medicated feed labels ("Helping Animal Producers Understand Medicated Feed Labels," and "Medicated Feed Labeling for Manufacturers – Getting it Right"). And it produced one video about the role of feed manufacturers in producing safe medicated animal feed ("Medicated Feed Rules for Animal Feed Manufacturers"). More recently, CVM has produced two videos about

reporting feed problems to FDA (“Mandatory Reporting of Animal Food Problems” and “Voluntary Reporting of Animal Food Problems”) and added a video about BSE (“U.S. Measures to Protect Against BSE”).

More videos are planned. Videos are in development that will explain the VFD rule and how it affects animal producers, veterinarians, and animal feed distributors.

In addition, a video is near completion highlighting the Guidance for Industry #203, *Ensuring Safety of Animal Feed Maintained and Fed On-Farm*.

### **COMPONENT G – Research**

CVM’s Office of Research conducts research to support of CVM in areas such as ensuring the safety of animal feed in this country. The Office of Research, which is located in Laurel, MD, on a 167-acre plot of land, has facilities to house several types of animals and fish. The Office of Research is a multidisciplinary organization with a scientifically staff trained to work on a wide array of issues.

The three main areas of work are:

- analytical research for compounds that pose a health risk if found in animal tissue or animal feed;
- applied and basic research in animal health and medicine in support of current and evolving regulatory issues; and
- applied and basic research regarding microorganisms potentially harmful to animals and humans.

More information on the Office of Research is available on the CVM website.

### **Current Project Work**

**Project G1.** Current FDA regulatory methods for determining selenium levels in feeds are obsolete. Incorporation of the analysis for selenium into multi-elemental analysis will allow FDA’s Office of Regulatory Affairs and State regulatory laboratories to more efficiently test feeds for selenium. A method exists in the FDA Elemental Analysis Manual for quantifying several elements by inductively coupled plasma-mass spectrometry (ICP-MS) with microwave assisted digestion (including arsenic [As], cadmium [Cd], chromium [Cr], lead [Pb], mercury [Hg] and others) in food and related products. The proposed research will expand the ICP-MS method to include selenium in animal feed along with method-specific figures of merit (LOD, LOQ, etc.).

### **Appendix I**

#### **Processes:**

1. Food Additive Petition; FDA (21 CFR 571)
2. New Animal Drug Application (NADA); FDA (21 CFR 514)
3. Generally Recognized As Safe (GRAS) Petition - FDA (21 CFR 570); GRAS Notification proposed rule 62 FR 18938 (CVM and CFSAN are accepting notifications now under a pilot program)
4. Color Additive Petition; FDA (CFSAN) (21 CFR 71)
5. AAFCO Ingredient Definition Process (2016 Official Publication; pp 355-359)
6. Common or Usual Name Recognized by the Secretary/Director/Commissioner of Agriculture; FDA and AAFCO (21 CFR 502 and AAFCO Model Regulations; Regulation 6(a), 2016 OP p.132)
7. Bioengineered Plants – CFSAN Guidance document, October 1997 - consultation process with FDA
8. Drugs, Biologics, and Medical Devices Derived From Bioengineered Plants for Use in Humans and Animals (FDA Draft Guidance #153)
9. AAFCO Feed Labeling Model Regulations and Guides (food-producing animals and pet animals) – 2016 Official Publication; pp 107-239

#### **Ingredient/Additive Listings:**

1. Food Additives Permitted in Feed and Drinking Water for Animals -21 CFR 573
2. New Animal Drugs for Use in Animal Feeds - 21 CFR 558
3. Generally Recognized of Safe (GRAS) Substances - 21 CFR 582 & 584
4. Color Additives - 21 CFR 73 & 74
5. Feed Ingredient Definitions - AAFCO 2016 OP (pp 372 – 486)
6. Substances Prohibited for Use in Food and Feed (21 CFR 589)
7. Bioengineered Plants - CFSAN home page <http://www.fda.gov/Food/default.htm> and 9 CFR 340
8. Animal Food Labeling - 21 CFR 501, 21 CFR 201
9. Compliance Policy Guide 7126.08 - Common or Usual Names for Animal Feed Ingredients
10. Indirect Food Additives Resulting from Packaging Materials for Animal and Pet Food – 21 CFR 181 and 174 through 179 as cited by 21 CFR 570.13 and 570.14

#### **Other Products Approved for Use in Feed**

1. EPA Tolerances and Exemptions for Pesticide Chemical Residues in Food - 40 CFR 180
2. Biologic Products Approved by USDA for Use in Animal Feed - 9 CFR 101-123

## **Appendix II**

**Processes:** Procedures for establishing limits for contaminants in feed and feed ingredients include the following:

1. Setting tolerances, action levels and regulatory limits for feed contaminants are described in 21 CFR 509.4 through 509.7.

2. Setting guidance levels are described in FDA's Good Guidance Practices Regulations, 21 CFR 10.115.

**Contaminant Limits:** FDA has established Limits on contaminants in food and feed,

1. Aflatoxin action levels (FDA's "Compliance Policy Guide" (CPG) 683.100);
2. Pesticide tolerances (EPA's *Code of Federal Regulations* (CFR), Title 40, Part 186 and FDA's CPG 575.100);
3. Pesticide action levels (FDA's CPG 575.100 & *Federal Register* (FR), Vol. 55, No. 74; April 17, 1990);
4. Temporary tolerances for PCB's (FDA's 21 CFR 509.30);
5. Guidance levels for Fumonisin (FDA's Guidance for Industry #112);
6. Guidance for Industry and FDA: Advisory Levels for Deoxynivalenol (DON) in Finished Wheat Products for Human Consumption and Grains and Grain By-Products used for Animal Feed;
7. Substances prohibited from use in animal food or feed (FDA's 21 CFR 589);
8. Tolerances established for drugs in food (FDA's 21 CFR 556);
9. Guidance levels for trace mineral contaminants (AAFCO's 2016 Official Publication; pg 320);
10. Salmonella in Food for Animals (FDA's CPG.690.800); and,
11. Draft Guidance for Industry: Testing for Salmonella Species in Human Foods and Direct-Human Contact Animal Foods; Availability (*Federal Register*, Vol. 76, No. 56, Wednesday, March 23, 2011, 16425

### Appendix III

#### Operations/Manufacturing Process Listings:

1. Medicated Feed cGMPs (21 CFR 225)
2. Type A Medicated Article cGMPs (21 CFR 226)
3. Current Good Manufacturing Practice and Hazard Analysis and Risk-Based Preventive Controls for Food for Animals (21 CFR 507)
4. AAFCO Feed Manufacturing Regulations 2016 OP pp 230-239
5. Low acid canned food regulations (21 CFR 500.23)
6. Codex Code of Practice for Good Animal Feeding  
<http://www.codexalimentarius.org/search-results/?cx=018170620143701104933%3Ai-zresgmxec&cof=FORID%3A11&q=Codex+Code+of+Practice+for+Good+Animal+Feeding&siteurl=http%3A%2F%2Fwww.codexalimentarius.org%2F>
7. HACCP; (seafood 21 CFR 123 and juice 21 CFR 120)
8. SSOP (21 CFR 120.6 and 123.11)

### Appendix IV

**Inspection and Enforcement Descriptions:** Inspections (FD&C Act Subchapter 701)

1. Enforcement (FD&C Act Subchapter 704-706; IOM Chapter 2)  
<http://www.fda.gov/ICECI/Inspections/IOM/default.htm> (under Chapter 7)
2. Federal-State Cooperation (IOM Chapter 3)  
<http://www.fda.gov/ICECI/Inspections/IOM/default.htm> (under Chapter 3)
3. Regulatory Procedures Manual  
[http://www.fda.gov/ora/compliance\\_ref/rpm/default.htm](http://www.fda.gov/ora/compliance_ref/rpm/default.htm)
5. Audits conducted by FDA of State inspections  
<http://www.fda.gov/ForFederalStateandLocalOfficials/PartnershipsContracts/StateContracts/AuditReportsonStateFoodContractInspections/default.htm>

### **Inspection and Enforcement Listings:**

1. Administrative actions refer to 21 CFR, particularly parts 12, 511, 514, and 571  
FDA and AAFCO Enforcement Guidelines (CVM Policy and Procedure Guide 1240.3600)  
<http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/PoliciesProceduresManual/ucm046222.htm>
2. Federal and State Audits (FDA Field Management Directive #76)  
<http://www.fda.gov/downloads/ICECI/Inspections/FieldManagementDirectives/UCM384257.pdf>
3. Inspection priorities (BSE Compliance Plan 7371.009)  
<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/UCM113437.pdf>
4. FDA Compliance Program Guidance Manual, Program 7371.003 Feed Contaminant Program;  
<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/ucm113409.pdf>
5. FDA Compliance Program Guidance manual, Program 7371.004 Feed Manufacturing Compliance Program;  
<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/ucm113430.pdf>