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## Foreseeable Hazards in Animal Feed

Updated May 1, 2019

While the U.S. animal food supply has a history of safety, there are also instances where the presence of hazards has resulted in significant instances of animal illness and death and in some cases human illness. Examples of animal food hazards that have led to animal and human illness and death include: mycotoxins, dioxins, industrial chemicals such as melamine and cyanuric acid, nutritional deficiencies and toxicities, animal drugs, and microbial pathogens.

Below we will summarize the national and local (Oregon) knowledge of some of the hazards associated with animal feed. This is not an all-inclusive list. Feed manufacturers should use their own experiences to add to the list for their facility.

### What do we know about common feed hazards?

#### **Mycotoxins:**

A mycotoxin is a toxic secondary metabolite produced by organisms of the fungus kingdom and is capable of causing disease and death in both humans and other animals. The term 'mycotoxin' is usually reserved for the toxic chemical products produced by fungi that readily colonize crops. ([Wikipedia](#))

Aflatoxins, as an example of mycotoxins, are naturally occurring and are produced by many species of the fungus *Aspergillus* on certain agricultural commodities. Since their discovery in the early 1960's, aflatoxins have been shown to be toxic to animals and humans when consumed above certain levels. Aflatoxins have also been shown to be carcinogenic to laboratory test animals. When animals consume feed containing aflatoxins, they are metabolized by the liver to a reactive intermediate and eliminated as aflatoxin M1 in milk or as aflatoxicol in urine. High level aflatoxin exposure produces acute damage and cirrhosis of the liver as well as cancer of the liver. It appears that no animal species, including humans, is immune to the acute toxic effects of aflatoxins. In 2005, there was a major recall of dog food because it was contaminated with aflatoxins. The FDA received reports from 4 states of illness in over 40 dogs, including 23 deaths, associated with the consumption of the contaminated pet food. In addition, the company's contaminated pet food was exported to at least 29 foreign countries. The source of this contamination was traced to local corn, which had been contaminated with aflatoxins before entering the pet food facility.

ODA monitors mycotoxin levels in ingredients and finished feeds during drought years when stress on the crop is likely to increase toxins. We strongly encourage all feed manufacturers to

have a mycotoxin monitoring or mitigation plan and to communicate it to your suppliers. See materials on defensible sampling to formulate a robust detection system.

### **Dioxins:**

Dioxins, a collective term for a group of environmental contaminants that includes certain dioxin, furan, and dioxin-like PCB (polychlorinated biphenyl) congeners, are found throughout the world. Dioxins and furans are released into the air from combustion processes. The wide use of PCBs as dielectric and coolant fluids in the past has resulted in their presence in the environment. They bio-accumulate in fat tissues of animals.

Dioxins have been linked to adverse health effects in humans, such as cancer, immune suppression, and reproductive or developmental effects. Dioxin is a concern in food-producing animals because human dioxin exposure in the United States comes primarily from the consumption of animal products. In 1997, the USDA's Food Safety and Inspection Service, through their dioxin sampling survey, identified dioxins in poultry tissue. Through a multi-agency investigation, the FDA traced this contamination to high levels of dioxins present in an anti-caking agent (ball clay) used in animal food. That same year, FDA issued a statement to users of ball clay products in animal feed requesting those companies cease using the ball clay products in animal feeds and feed ingredients. In 2002, a foreign government identified high dioxin levels in a mineral product intended for animal food imported from the United States. The source of the dioxin was related to the high temperature used in the mineral manufacturing process. In 2003, another dioxin incident in minerals was identified as a result of an FDA food sampling assignment. In this case, the mineral premix manufacturer purchased a trace mineral that was a by-product of a metal smelting process. Dioxin contamination is not limited to the U.S. animal food supply. Incidents of dioxin contamination in Belgium in 1999 and Ireland in 2009 led to significant financial impacts due to the exposure of animals directly through consumption of the animal food and to humans who would consume the meat derived from the animals. These combined incidents were estimated to have a financial burden of over \$759 million. These incidents raised public awareness of the problem of dioxin contamination in animal food.

In 2017 the Oregon Department of Agriculture sampled an anti-caking agent commonly added to poultry feed and tested it for dioxin. Lab results revealed over 17ppt of dioxin in the product. This is about 11 times more than several regulatory bodies allow. The department embargoed the product and after a court case the firm agreed not to sell the product in Oregon.

Poultry are the bell weather species for dioxin accumulation in the food chain. Poultry feed manufacturers should consider monitoring ingredient suppliers for dioxin-like compounds.

### **Melamine and Cyanuric Acid:**

Melamine is a chemical compound that has a number of industrial uses, including the production of laminates, glues, dinnerware, adhesives, molding compounds, coatings and flame retardants. Melamine is a name used both for the chemical and for the plastic made from it. In this event, all references are to the chemical. There are no approved direct food uses for

melamine. Melamine is illegally added to inflate the apparent protein content of food products. (FAO)

Cyanuric acid or 1,3,5-triazine-2,4,6-triol is a chemical compound with the formula  $(\text{CNOH})_3$ . Like many industrially useful chemicals, this triazine has many synonyms. This white, odorless solid, finds use as a precursor or a component of bleaches, disinfectants, and herbicides. ([Wikipedia](#))

In 2007, there was a massive pet food recall due to adulteration of pet food with melamine and cyanuric acid. These substances were intentionally added to imported wheat gluten and rice protein concentrate for economic reasons. Melamine was added to wheat gluten and rice protein concentrate by the suppliers to create a falsely high estimate of protein in their products. While melamine by itself is relatively nontoxic to mammals, the melamine used to adulterate the wheat gluten and rice protein concentrate in this incident had been combined with cyanuric acid, creating a mixture that became toxic. When the animals ingested the adulterated food, the mix of these two chemicals was absorbed into the blood stream and ultimately created an accumulation of crystals in the tubules of the animals' kidneys, leading to kidney failure and death in many animals. The addition of these substances to pet food affected a large number of pet food facilities in the United States and created a nationwide problem by causing illness and death in many dogs and cats. During the investigation to find the root cause of the illnesses, the investigation found that products containing these adulterants had also been incorporated into the diets of food-producing animals (swine and aquaculture fish). These situations with food-producing animals emphasized the potential link between adulterated animal food (and ingredients) and the potential for adverse effects on human health.

The adulterated Rice Protein Concentrate was imported into Oregon. ODA spent months working with FDA to track product distribution and destruction. Among the lessons learned was to keep good production records of all ingredient movement and to have a personal visit with each supplier. Trust but verify.

### **Nutritional deficiencies and toxicities:**

Many animals consume one food as their sole source of nutrition. Therefore, the food that they consume must be nutritionally adequate and balanced. If not nutritionally adequate and balanced, the food presents a safety hazard to the animals. Nutrient deficiencies or excesses can raise safety concerns. Because different species have different nutritional needs, certain quantities of a nutrient that are needed by one species of animal could pose a health risk to another species of animal. Therefore, animal food hazards include both nutrient deficiencies and toxicities. There is a history of animal food incidents resulting in recall of the animal food and in animal illnesses and deaths from nutrient deficiencies or toxicities. Examples of nutrient related hazards in animal food include low levels of thiamine in cat food; high levels of vitamin D in dog food; low levels of vitamin D in food for swine; high levels of vitamin D in food for guinea pigs, fish, and other animal species; high levels of calcium and phosphorus in food for broiler chickens and turkeys causing the death of several hundred young birds; high levels of salt in food for broilers; high levels of protein/urea in food for cattle; and high levels of copper

in food for sheep. Many of these animal foods with nutrient imbalances (deficiencies or toxicities) resulted in a recall of the affected animal food, and in some cases serious illness or death in the animals consuming the food. Because food for food-producing animals is often sent in large batches, if a batch is deficient in a required nutrient or has excess of a nutrient that can lead to a toxic condition, the result can have a significant impact to a single farm. Nutrient deficiencies and toxicities in livestock food tend to be localized events with potential for serious impacts. However, nutrient deficiencies and toxicities in pet food can be national events due to the distribution pattern, and small package sizes, common to pet food.

Oregon has had its share of animal deaths due to nutrient imbalances. Over the last 20 years we have lost sheep and dairy cattle to excess copper, hogs to excess selenium, rabbits to excess vitamin D, dairy cattle to excess sulfur and sick horses due to excess salt.

It's important that farmers insist on proper feed labeling so formulation and intent are well communicated. Oregon is the only state that requires both the minimum and maximum amount of selenium in a product is disclosed. Since this change there has been very few selenium toxicity cases.

We also require a guarantee of sulfur levels (min and max) whenever a finished feed or ingredient is over 0.5% Sulfur. Sulfur is very active in binding other minerals and disrupting proper body functions. Highly variable sulfur levels can be found in many ingredients including water & corn distillers.

### **Animal drugs:**

In the United States, animal drugs require approval by FDA before they can be marketed for administration to animals. While animal drugs can be safely and effectively used in accordance with their regulations, animal drugs can be chemical hazards introduced into animal food such as through an ingredient containing residues or through drug carryover or cross contamination during manufacturing. Drugs can be approved for one species but have toxic effects if included in food for a different species. For animal drugs used in food-producing animals, FDA establishes a tolerance for the drug residue in human food as part of the approval process. Animal drug residues detected in food derived from food-producing animals (i.e., animal tissues such as meat, milk, and eggs) are considered a hazard for human food if an established animal drug tolerance is exceeded.

An example of an ingredient-related hazard is drug contamination in an animal food resulting from using a raw material that contains drug residues. Depending on the chemical property of the drug, residues of certain drugs may become concentrated during animal food manufacturing and processing. Two examples of types of drugs that can become concentrated during manufacturing are antibiotics and pentobarbital. In 2013, two companies recalled various pet treats after antibiotic residues were found upon testing of the treats by a regulatory laboratory. In 2014, FDA issued an import alert for poultry jerky-type treats due to the presence of antibiotic and/or antiviral residues as a result of positive test results for these residues in jerky treats from certain countries. Pentobarbital is a component of euthanasia solutions that

are used to humanely kill animals. Pentobarbital is stable in tissue, aqueous environments, and resists degradation at rendering temperatures. There are reports of pentobarbital toxicosis in domestic species, zoological animals, and wildlife. In 2015, cases of toxicosis linked to pentobarbital in horsemeat resulted in the death of two animals and illness of a third in a wildlife preservation center in the United States. In 2017, pentobarbital in dog food resulted in illness in four dogs and the death of a fifth dog.

Many feed mills manufacture animal food that contains one or more approved animal drugs. These medicated feeds are subject to 21 CFR part 225 – Current Good Manufacturing Practice for Medicated Feeds, which require, in part, that facilities making medicated feed take steps to ensure adequate cleanout of their equipment in order to maintain proper drug levels and to avoid unsafe contamination of animal food with drugs. Flushing of equipment and sequential production of medicated feed are two commonly practiced procedures for preventing unsafe contamination from drug carryover. Failure to perform proper equipment cleanout procedures or failure to adequately follow the procedures could result in contaminated animal food that may cause illness or death in animals. For example, incomplete clean-out from a previous batch of animal food manufactured with monensin (which is particularly toxic to horses) has been the source of contamination in animal food. In 2014 and 2015, monensin contamination of animal food resulted in the death of horses and layer hens.

Oregon has had multiple cases of monensin poisoning in horses, feedlot cattle and dairy calves. Firms using this drug need to increase their diligence in monitoring monensin to be certain residue levels in manufacturing machinery does not exceed levels deemed safe for all species, especially horses and chickens. An emerging issue is low level of contamination of antimicrobials important to human and animal medicine. This is thought to be contributing to antimicrobial resistance. It is currently being studied at the international and national level.

Oregon occasionally samples for low-level drug contamination in non-medicated feeds.

### **Microbial pathogens:**

Microbial contamination of animal food is also a high concern, not only for animals consuming the contaminated food, but also for humans that handle that contaminated animal food. Microbial contamination is primarily a concern with pet food because it has the potential to be directly contacted by humans. There have been reported outbreaks in which people have become ill, and even hospitalized, from microbial contamination of pet food. Two examples of Salmonella illness in humans that were linked to pet food occurred in 2007 and 2012. In 2007, a rare serotype of Salmonella, *S. Schwarzengrund*, was identified as being the cause of human illness and the Salmonella source was linked to a pet food. After the initial recall and stoppage of production for five months, there were additional reports of illness in humans from the pet food. This led to a larger recall of approximately 23,109 tons of dry pet foods, representing 105 brands. While no pets were reported sick, 79 people in 21 states were reported ill due to the handling of pet food contaminated with this Salmonella strain. In April 2012, epidemiologic and laboratory investigations conducted by officials in local, state, and federal animal and human health agriculture, and regulatory agencies linked a *Salmonella Infantis* outbreak to

contaminated dry dog food produced by a single production facility. A total of 49 people (47 individuals in 20 states and 2 individuals in Canada) were reported infected with *Salmonella Infantis*. Among the 24 human patients with available information, 10 were hospitalized. The results from product testing by multiple agencies along with production codes provided by ill persons, led to multiple recalls by several companies with animal food products manufactured at the implicated production facility. The recalls included 17 brands representing over 30,000 tons of dry dog and cat food produced at the facility. This was the second documented outbreak of human salmonellosis linked to dry pet food in the United States.

Oregon pet food manufacturers have been involved in some of the above cited adulteration cases. The problems of Salmonella, e coli h157 and Listeria m. seem to persist in pet foods brought into the home. Industry needs to continue to find ways to reduce pathogens. Consumers need to be aware of the microbial hazards and handle pet food appropriately. ODA is contributing time to a national effort to modernize pet food labeling including safe handling statements.

### **Endophytes:**

Endophytes are problematic throughout the world but of special concern in Oregon due to its large grass seed industry. They are toxins produced by fungus growing on grass seed. They are very similar to mycotoxins. As one of the worlds largest grass seed producers, Oregon also is one of the largest producers of grass seed screenings (and straw). The major toxins are Lolitrem B and Ergovaline. Typical symptoms are abortions, lameness, and loss of blood circulation.

Manufacturers of grass seed screenings are required to put warning statements on the label not to exceed 30% of the animals' diet in order to minimize potential intake of excessive toxins.

### **Anti-Nutritional Factors:**

Lots of plants have natural defense mechanisms that have to be overcome with processing prior to feeding an ingredient. Soy beans are a good example. They need processing to remove a proteinase inhibitor. Unprocessed Lima Beans contain linamarin, which if not removed, can metabolize into the toxic chemical hydrogen cyanide. Lima Bean Poisoning has occurred a couple times in Oregon, most recently in dairy goats.

### **Botulism**

Botulism is a rare but serious illness caused by a neurotoxin that attacks the body's nerves and causes difficulty breathing, muscle paralysis, and even death. This toxin is made by *Clostridium botulinum* and sometimes *Clostridium butyricum* and *Clostridium baratii* bacteria. These toxins cause serious illness and even death in humans and animals. Humans can get botulism through improperly processed food (especially home-canned food) and through ingestion of contaminated milk. Animals contract botulism through contaminated feed, decomposing carcass material or water poisoned with a rotting carcass. (CDC)

There has been at least one animal feed related case in Oregon linked to improper storage of barley malt sprout products stored in a contaminated silage pit. Botulism may also occur in hay if small animals/wildlife accidentally get pulled into a hay baler and compressed in a hay bale.

### **Blister beetles**

Blister beetles are found in Hay. Oregon had their first case in Southern Oregon a few years ago. Beetles are easily seen and cause lesions in horses' mouths and gastrointestinal tracts, causing sickness and potentially resulting in death.

There are several developmental stages of blister beetles, the larvae may ingest other insects or even grasshopper eggs, while adult blister beetles may feed on flowers or leaves of plants such as alfalfa, particularly when in substantial bloom (> 20%). Blister beetles often swarm and if they are feeding on alfalfa in the field, they may be harvested with the hay.

Blister beetles are typically abundant during the mid-summer months, so the second cutting of alfalfa is the stage that is most likely to be consumed by beetles and a potential threat to horses. In general, early and later cuttings of hay are less likely to have beetles present. The first and fourth (if the crop permits a fifth cutting this should be okay as well) are considered safer cuttings. It is important that the individual purchasing the hay speak with the farmer regarding the cutting of hay and the method used for harvesting. When the hay is cut and crushed at the same time, generally with a crimper, this makes it harder for the beetles to escape the harvesting process. Therefore, it is ideal to purchase alfalfa where a crimper was not used. This means the hay was cut and left to dry then baled at a later time. This staging of the harvest provides the beetles time to escape, making it less likely they will be baled in the hay.

*From: <https://www.vet.k-state.edu/vhc/services/equine/timely-topics/blisterbeetle.html>*

### **BSE (Bovine Spongiform Encephalopathy)**

Bovine Spongiform Encephalopathy (BSE) belongs to the unusual group of progressively degenerative neurological diseases known as transmissible spongiform encephalopathies (TSEs). TSE diseases are characterized by long incubation periods ranging from several months for transmissible mink encephalopathy, to several years for BSE. During the incubation period there is no visible indication of the disease. In the late 1980's and early 1990s, BSE spread within the United Kingdom and then to other countries through the practice of using rendered bovine origin proteins as an ingredient in cattle feed. Since then, feed restrictions put in place by countries that may have imported infected cattle or contaminated feed ingredients have been highly effective in reducing the number of BSE cases worldwide.

BSE can be passed to humans that consume high-risk materials from infected cattle. It causes a similarly fatal disease in humans. Infection occurs at a very low level of people exposed to infected cattle.

In 1997, FDA published a final regulation 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 rule 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 manufacture or transport. FDA strengthened the 1997 rule in 2008 by prohibiting the use of the highest risk cattle tissues in ALL animal feed. These high-risk materials include the brains and spinal cords from cattle 30 months of age and older and non-inspected cattle carcasses over 30 months without the brain and spinal cord removed.

To date, four cases of BSE have been detected in the United States. The first case was detected in 2003 in a cow imported from Canada. Three cases have since been detected in U.S. born cattle, but laboratory evidence suggests that these cases had atypical strains of BSE, that is not the same strain that caused the large outbreak in the United Kingdom.

### **Emerging hazards**

**Viruses:** We do not have any known experience in Oregon yet with these but they are hard to detect. They are being studied nationally. African Swine Fever has demonstrated survivability in soybean meal during shipment. Porcine Reproductive & Respiratory Syndrome (PRRS) and avian influenza – feed trucks may be the carry infection between farms if biosecurity precautions are not followed.

Other hazards that are monitored are **pesticide residues** and **heavy metal** contamination. These rarely occur but should not be ignored when setting up an ingredient purchasing contract or investigating an animal death case.

These are just some of the hazards that have the potential to be associated with animal food. Feed manufacturers should incorporate their historical knowledge of local ingredients, water and forages and their physical plant when evaluating hazards.