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CHAPTER 5

Physical and Chemical Methods for the Reduction of Biological Hazards in Animal Feeds

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Introduction

Animal feeds consist of all food produced for the consumption by livestock and poultry animals and companion animals, including dogs and cats. Animal feed is specifically formulated to ensure that the necessary balance of nutrients is provided to the animal for proper growth, development, and maintenance. The feeding of manufactured animal feeds ensures that the animal receives all the required nutrients and supplements absent from the animal's natural diet. According to the American Feed Industry Association (AAFCO, Association of American Feed Control Officials) over 900 agricultural ingredients and co-products are used to produce animal feeds and pet foods. These ingredients include cereal grains (corn, oats, wheat, etc.), oilseeds and meals (canola meal, soybean meal, etc.), and various processing by-products (corn gluten meal, distillers products, wheat bran, etc.) (http://www.afia.org/howmade). In addition to plant-based ingredients, animal-based products make up a large portion of animal feeds and pet foods. Animal-based proteins can be derived from whole cuts after slaughter or from rendering of portions not used for human consumption (Sapkota et al., 2007). Rendered animal proteins and products include the portions not consumed by humans, including bones, fat, blood, feathers, and some internal organs (Meeker and Hamilton, 2006).

The production of finished feeds ready for consumption by the animal can occur on the farm, in a feed mill, or at a pet food manufacturing facility. In all cases, raw materials are received and included in species-specific formulations. Animal diet formulations take into account the required nutrients of the animal and the nutrients provided by the raw ingredients. The manufacture of raw ingredients into complete finished feeds can include multiple processes. These processes can include grinding, mixing, pelleting, and/or extrusion. Grinding can be done through a roller mill or hammer mill. The goal of grinding is to ensure all components for the finished feed have a similar particle size for uniform distribution during further

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processing and consumption. Following grinding, all ingredients must be mixed or blended for uniform distribution. Uniformly blended feeds can be further processed by pelleting or extrusion, both thermally intensive processes. During both pelleting and extrusion, the ground ingredients are passed through a mixing chamber and pushed through a die of a desired size. Pelleted and extruded products can increase bulk density and improve handling along with improving protein digestibility. The form of the complete finished diets can vary, from ground mash types to pelleted. Finished pet foods can also be in various forms, from kibbles to pate with gravy to jerky type.

The ingredients in complete animal feeds come from a wide range of raw materials, so it is not surprising that contamination with enteric pathogens, like *Salmonella*, occurs (Ge et al., 2013). The link between the spread of *Salmonella* from contaminated animal feed to both animals and humans causing illness has been well established (Jones, 2011; Crump et al., 2002). Along with *Salmonella*, food-producing animals have been identified as major reservoirs for many human pathogens, including *Campylobacter* spp., *Clostridium* spp., *Escherichia coli* (including O157:H7), *Yersinia* spp., and *Enterococcus* spp. (Mead et al., 1999; Crump et al., 2002). While pathogens of bacterial origin seem to be the most prevalent, viral pathogens should not be overlooked as possible hazards in animal feeds and pet foods. More recently the coronavirus, porcine epidemic diarrhea virus (PEDV) has been found to be transmitted via feed (Dee et al., 2014; Pasick et al., 2014). Although PEDV is not a human pathogen, it generated significant economic losses in North America after its introduction in 2013 (Cochrane et al., 2016a,b). In swine feeds, PEDV was the first substantial viral pathogen to be transmitted by feed and may not be the only. More recently mammalian orthoreovirus has been detected in swine feces and swine blood meal with contaminated blood meal found to be infective (Narayanappa et al., 2015). In addition to swine viruses being reported, a surge of highly pathogenic avian influenza (HPAI) was reported in many poultry flocks throughout the United States in 2015 (APHIS Report). However, no definitive proof-of-concept studies have established feed as a vector for HPAI, as of this publication.

In addition to bacterial and viral pathogens, transmissible spongiform encephalopathies (TSEs) have been identified as potential biological pathogens transmissible in feeds. TSE includes bovine spongiform encephalopathy (BSE) and chronic wasting disease (CWD). TSEs are hypothesized to be caused by an infectious proteinaceous entity called a prion. Prions are composed largely of a protease-resistant misfolding of proteins. BSE, also known as mad cow disease, was first linked to human illness of variant Creutzfeldt-Jakob disease (vCJD), a human neurodegenerative prion disease. vCJD was first described in the United Kingdom in 1995 in two teenagers. Further investigation into vCJD in humans indicated the causative prion of vCJD humans was also the causative prion of BSE in cattle. The introduction of infectious prions into the human population has been attributed to the consumption of contaminated meats. It is proposed that prions are introduced into animals via rendered animal products of diseased animals. Prions may be present in all tissues of diseased animals;

they are known to accumulate in central nervous system tissues, including skull, brains, eyes, parts of the vertebral column, spinal cord, trigeminal ganglia, and dorsal root ganglia. The aforementioned tissues with accumulated prions are referred to as specified risk materials (SRMs) and are banned from use in cattle and other ruminant feeds. However, SRMs are permitted in feeds for nonruminants, including poultry (Crump et al., 2002; Sapkota et al., 2007; Denton et al., 2005).

The prevention of biological hazards into animal feeds and pet foods has put manufacturers under increased scrutiny, especially with the recent implementation of the Food Safety Modernization Act (FSMA). One of the seven rules instituted by FDA is 21 CFR 507: Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls in Food for Animals. This rule must be followed by nearly all facilities that manufacture, process, pack, or hold animal food. It requires facilities to meet baseline standards for personnel, facility design, sanitation, and manufacturing conditions. In addition, facilities must identify potential hazards and evaluate if they need to be controlled to ensure the resulting animal food is safe.

Feed Manufacturing

Outside of feed manufacturing processes, overall feed mill and farm practices can influence the safety, from a biological hazard standpoint, of complete finished feeds. Nonprocessing factors include general sanitation of the processing facility, quality attributes of raw ingredients, and other biosecurity measures of the facility. The manufacture of complete finished feeds can occur in a feed mill or on-farm. Independent of location, many of the same processing steps occur. Raw ingredients are weighed or measured, mixed for uniformity, and stored until consumption. Processing of the feed can be minimal, as seen with mash-type diets or more heavily processed through conditioning, pelleting, and extrusion. Although the total elimination of biological hazards may not be possible, feed manufacturers do have options to reduce the risk of contamination in finished feeds. These include physical and chemical methods for the reduction of contamination.

Physical Methods

Physical methods to reduce the risk of biological hazards in finished feeds can be categorized in two ways: programs or standard operating procedures (SOPs) to prevent the contamination and physical processing methods, like thermal treatment. Although one specific program or SOP will not completely prevent the introduction of biological hazards into finished feed or a feed manufacturing facility, they can contribute to overall risk reduction. Programs and SOPs can include a feed mill biosecurity plan, following current good manufacturing practices (CGMPs), prerequisite supplier programs, sanitation, and pest management.

The implementation of a feed mill biosecurity plan will help reduce the risk of biological hazards from being introduced and spread throughout the feed manufacturing facility. Biosecurity plans are multifaceted and can help control the spread of feedborne diseases. In general, a biosecurity plan requires all aspects of the feed manufacturing process to be evaluated. This includes identifying all ingredients and process steps occurring at the feed manufacturing facility. This allows for the identification of potential points of entry into the facility, opportunities for cross-contamination within the facility, and potential points of control of biological hazards. Following biological hazard identification, all identified hazards must be evaluated for the hazard's severity and probability of occurrence within the facility. Based on the hazard's severity and probability, hazard mitigation steps can be implemented. Hazard mitigation can imply prevention of hazard entry along with potential elimination during further processing or chemical inclusion.

A major component of a feed mill biosecurity plan includes prevention of biological hazard entry into the facility. Preventative measures can range from approved suppliers to sanitation to control people within and outside of the facility. Ingredient receiving is one of the main routes of entry for biological hazards into a feed manufacturing facility. Although real-time testing of all ingredients for all potential biological hazards is not possible, implementation of preventative programs can help reduce the risk of receiving contaminated ingredients. These preventative programs include development of purchase specifications with suppliers. All safety specifications and expectations of ingredients should be clearly communicated with suppliers to ensure the safety of inbound ingredients. Verification of ingredient–supplier protocols and on-site manufacturing facility can also be implemented. Once specifications are in place, it is important to maintain enforcement with routine audits when possible. Ensuring suppliers follow CGMPs can also be another barrier in reducing contamination risks.

The process of ingredient receiving is also at an increased risk of entry of biological hazards. At most facilities, multiple ingredients are received in a day and by multiple inbound trucks. All drivers and visitors should be instructed of appropriate security measures with an emphasis on reducing the amount of foot traffic in and out of the facility and even within the facility. Proper biosecurity plans should address the activities of inbound drivers during receiving. If at all possible, all drivers should not exit the vehicle during delivery. If that is not possible, disposable foot covers for boots should be provided to drivers to reduce the risk of transferring hazards from footwear. While not applicable at all facilities, covers over ingredient pits should remain in place until the truck is ready to unload. In addition, all trucks entering the facility for pit unloading should have all mud and debris removed prior to entering. Documentation is also a key component. When possible, all pertinent information regarding ingredients being delivered should be collected. This includes date, time, and lot number. Additionally, inbound truck information should be collected, including previous loads and the clean-out/disinfection schedule. Other precautions when receiving bulk ingredients through a pit include the use of cone or funneling devices to limit the quantity of material spilled during

unloading and prevent spilled material from being swept into the ingredient pit. All spillage should be discarded and not swept into the pit as the area around the pit can easily be contaminated. Special precautions should also be made when receiving high-risk ingredients.

Ingredient receiving in general is a high-risk activity, but movement of people is also a high risk for introduction of contamination and often overlooked. Everyone who enters the feed manufacturing facility, including workers, drivers, subcontractors, and visitors, have the ability to inadvertently carry in biological hazards on clothing and footwear. This risk is even higher if the person has recently been on an animal farm or other feed manufacturing facility. As mentioned previously, drivers should remain in the vehicle whenever possible or wear disposable boot covers. Areas of high risk, like receiving, should be restricted from nonemployee access when possible. Additionally, the foot traffic of mill employees should be monitored. When and where possible, those workers responsible for handling raw ingredients should avoid finished production areas and vice versa. Segregating employees by stage of production can greatly reduce the risk of inadvertent cross-contamination from footwear and clothing.

In the event where biosecurity or other programs fail, biological hazards that do enter the facility can be very difficult to remove from the facility and lead to cross-contamination of finished products (EFSA, 2008). The spread of contamination throughout the facility can occur due to the spread of contaminated dust, foot traffic of employees and visitors, or movement of equipment. Cross-contamination can also occur within equipment that is considered clean. Many times, residual organic material can remain on equipment after production of a product has been completed. Equipment with the highest risk of cross-contamination includes screw conveyers, pellet coolers, storage bins, and bucket elevator boot pits (Cochrane et al., 2016a,b). Residual material found in these high-risk types of equipment is primarily due to their design. The use of flushing and sequencing of diets has been suggested as a method to help reduce the risk of cross-contamination from occurring. Flushing typically consists of running an ingredient, usually an abrasive type of material, through the system between batches to flush out any residual material. Sequencing requires the order of production, storage, and distribution to be preplanned to reduce the carryover of high-risk ingredients to sensitive diets. Flushing and sequencing have been utilized for years by the feed manufacturing industry to reduce the risk of batch-to-batch drug carryover. More recently, these principles have been applied to biological hazard mitigation but have limited reports of efficacy in the literature.

Sanitation practices within the facility can also greatly influence cross-contamination issues during production. Traditionally, floor sweepings from production areas have been added back to feed. Dust and aggregate materials that accumulate in production areas should be properly disposed of and not added back into the feed production system. This also includes all organic material collected from dust collection systems, all floor sweepings, and aggregate

materials that accumulate on or around equipment. All dust and collected materials should be considered high risk and disposed of accordingly (Cochrane et al., 2016a,b).

Another avenue of cross-contamination that can occur at a feed manufacturing facility is during loadout and delivery of finished feeds. The principle sequencing used in feed production can also be used during storage, loadout/packaging, and delivery of finished feeds. During the loadout of delivery trucks, cross-contamination could occur due to residual material on truck exteriors and interiors. All organic material on delivery trucks should be removed prior to loadout at the feed mill. In addition, all delivery trucks should maintain a log of shipments to improve traceability. As previously mentioned, truck drivers should remain in the vehicle when possible to avoid tracking potential contaminated materials on footwear. When drivers are required to exit the vehicle, shoe covers should be worn and hands sanitized before reentering the truck. Drivers should also avoid contact with animals and avoid areas around exhaust fans, animal disposal sites, and livestock contact areas, like loadout chutes (Cochrane et al., 2016a,b).

Aside from biosecurity plans and preventative measures, other physical methods of mitigating biological hazards include irradiation and thermal processing. Irradiation using gamma, ultraviolet (UV), or electron beam radiation has been demonstrated to reduce PEDV load by 3-log (Trudeau et al., 2016). Wilson et al. (2015, 2016) demonstrated the feasibility of using infrared radiation to decontaminate raw pet food ingredients; depending on initial moisture content of the ingredients, infrared heating intensity, and tempering duration, up to 3-log of mycotoxigenic fungi was reduced.

Thermal processing of food for humans and animals is commonly used as a method for mitigation of biological hazards. Thermal processing of animal feeds is traditionally done via pelleting, whereas pet foods are commonly produced via extrusion. Thermal processing parameters, including temperature and time, greatly influence the lethality of processing on biological hazards (Jones, 2011). In addition to time and temperature parameters, the feed matrix can also influence biological hazard lethality. It is important to note that thermal processing of animal and pet foods can greatly reduce or eliminate biological hazards but is only a point-in-time strategy and does not reduce or eliminate the possibility of postprocessing contamination.

Pelleting of animal feeds includes three stages: mixing of steam with the mash feed (conditioning), pressing of the conditioned feed through the pellet die (pelleting), and cooling of finished pellets in a pellet cooler. The culmination of these events produces the final pelleted product. During conditioning, temperatures and residence time can be modified based on feed formulation, as some ingredients are heat labile. Other factors influencing the pelleting process include equipment design and maintenance, equipment operating procedures, supporting equipment (steam generator), and environmental conditions. Although most processes can be controlled, not all parameters can be precisely manipulated.

During the conditioning step of pelleting, heat and moisture of the mash are increased and can reduce the microbial load (Jones, 2011). Temperature, residence time at a given temperature, and moisture are the major factors influencing the microbial lethality during the conditioning process. Estimates of reduction of *Salmonella* in animal feed indicate roughly 10^3 colony-forming units (cfu) per 100 g are destroyed starting at temperatures of 71°C (Stott et al., 1975). Both time and temperature are crucial for reduction or elimination of biological pathogens, like *Salmonella*. Several researchers have determined target temperatures of 80–85°C during conditioning to destroy *Salmonella* (Jones and Richardson, 2004; Veldman et al., 1995). More recently the minimum temperature for destruction of PEDV was noted to be at 54°C during pelleting. Pelleting temperatures of 38 and 43°C were found to not sufficiently destroy PEDV and led to infection in a piglet bioassay (Cochrane et al., 2015a,b). The residence time during conditioning can range from seconds to minutes, depending on the equipment involved. However, with the development of new equipment, conditioning temperatures and times have been enhanced to improve lethality to microbial contaminants (Jones, 2011). The use of expanders in the pelleting process have increased conditioning temperatures to 115–125°C and pressures up to 1200 psi for periods of 10–20 s. The reported reduction in bacterial load with the use of expanders was 10^5 to 10^6 cfu/g (Francher et al., 1996). In addition to temperatures reached during conditioning, the physical action of the pellet mill rollers pushing the conditioned feed through the die results in a temperature increase due to friction. This increase in temperature is a minimal amount of 1–2°C. This minimal increase in temperature likely has no impact on destruction of microorganisms as the increased temperature is applied to feed for a fraction of a second (Jones, 2011). The final stage of the pelleting process, cooling, removes heat and moisture via large volumes of air. Air temperature and flow must be closely monitored to ensure proper cooling of pellets. Condensation can form within the pellet cooler when the temperature of the top and walls of the cooler drops below the dew point of the entering air. Generated condensation can create an environment conducive for *Salmonella* or other biological hazard growth (Jones, 2011).

Pet food kibbles are typically manufactured through the process of extrusion, rather than pelleting. Although pelleting and extrusion are similar, extruded diets typically have higher moisture contents and subjected to higher shear and pressure levels. During extrusion, feed is guided by a single or double screw through a barrel with increasing restrictions and forced through a die. This process generates heat and pressure. Sudden expansion of the product also occurs as the product exits the die due to the pressure differential generated. Feed composition, moisture content, processing temperature and pressure, and retention time can all influence product expansion at the die exit. Studies validating extrusion as a kill step for *Salmonella* or other pathogens are limited. For process validation, the specific production equipment should be used to conduct validations. Benchtop or pilot-scale equipment may vary in replication of industrial processes. Generally, industrial or production-scale equipment is not available for controlled validation studies with pathogens. Introduction of pathogens

into a pet food manufacturing facility for validation would have a significant impact on food/feed safety. To compensate for the inability to use actual pathogens for testing, surrogate microorganisms that pose no risk to human or animal health can be used. However, not all microorganisms behave in a similar fashion, so translation of processing temperatures and time from the surrogate to actual pathogen may not be correct. To date, *Enterococcus faecium* has been used as a *Salmonella* surrogate during processing of almonds, extrusion of a balanced carbohydrate-protein meal, and a poultry feed (Jeong et al., 2011; Bianchini et al., 2012; Cochrane et al., 2015a,b). Some have also suggested the use of microorganisms with a higher heat tolerance to ensure process robustness. However, the conditions to achieve inactivation of heat-resistant organisms can be misleading and much higher than needed for pathogen destruction or within reason for the feed and feed industries (Okelo et al., 2006, 2008). Of the studies that have evaluated the inactivation of pathogens during extrusion, the temperature and retention times are varied. Evaluation of *Clostridium sporogenes* in a mixture of mechanically deboned turkey and white corn flour by twin-screw extrusion resulted in a 4- to 5-log reduction at 115.6°C and a 2-log reduction at 93.3°C (Li et al., 1993). Inactivation of *Streptococcus thermophiles* in whey protein isolate occurred in twin-screw extrusion with a 4.2-log reduction at 143°C and a 4.9-log reduction at 135°C (Queguiner et al., 1989). Reduction of *Salmonella* in controlled extrusion studies has been variable. Temperatures of 93.3–176.8°C were found to completely eliminate *Salmonella* in feed samples with 25%–35% moisture (Crane et al., 1973). Other studies revealed that the elimination of *Salmonella* serovar Typhimurium occurred at 83°C in feed with 28.5% moisture (Okelo et al., 2006). As with pelleting, extrusion offers only a point-in-time mitigation and does not prevent finished product cross-contamination following processing.

Chemical Methods

While the goal of implemented biosecurity and preventative programs is to prevent the contamination of biological hazards into feed, however, this is also not possible. Physical methods, like irradiation and thermal processing, have the capacity to mitigate biological hazards once they are present but only offer a point-in-time mitigation. Following finished feed irradiation or thermal processing, cross-contamination at multiple points can lead to contamination. The inclusion of chemical additives, either alone or in combination with other mitigation techniques, has become of more interest and may help decrease the risk of cross-contamination. Common chemical additives include organic acids and formaldehyde, with more recent research evaluating essential oils, medium chain fatty acids, and acidulants like sodium bisulfate.

The most common organic acids incorporated into feed include propionic, formic, lactic, and acetic acids. All these organic acids have been shown to be effective at reducing *Salmonella* in various feed and food matrices (Amado et al., 2013; Anang et al., 2007; Koyuncu et al., 2013; Menconi et al., 2013). Propionic acid has been shown to destroy 90% of the cell

population within 1 h and formic acid within 3 h of treatment (Cherrington et al., 1991). The combination of propionic and formic acids in a blend evaluated by Carrique-Mas et al. (2007) performed similarly to a combination of lactic, propionic, formic, and benzoic acids by Cochrane et al. (2016a,b) in the mitigation of *Salmonella* in feed. The proposed mode of action of organic acid treatment to mitigate *Salmonella* contamination suggests that organic acids penetrate the cell membrane and enter the bacterial cell's cytoplasm, where they dissociate causing the pH of the cell to increase, causing cell atrophy (Brul and Coote, 1999). There are further advantages to organic acid treatments compared to formaldehyde because organic acids are proposed to be relatively stable in feed and can occur naturally in living organisms and therefore may have greater consumer appeal when listed on an ingredient label (Wales et al., 2010).

Formaldehyde has been approved as a feed additive to control *Salmonella* and mold in animal feed (Formaldehyde, 2003). Data have demonstrated that formaldehyde is effective at mitigating *Salmonella* in animal feed (Cochrane et al., 2016a,b; EFSA, 2009). However, it requires specialized equipment for successful application, carries potential worker health concerns, and may be perceived negatively by consumers (Jones, 2011).

Many essential oils have been found to have antimicrobial properties, including the essential oils of oregano, rosemary, garlic, turmeric, and capsicum. Oregano and rosemary oils have been found to cause a 1- to 2-log reduction in *Salmonella* in various human foods (Gunduz et al., 2010; Skandamis et al., 2002). Garlic and oregano have both been shown to be effective at mitigating *Salmonella* and have minimum inhibitory concentrations of 729 and 417 ppm and maximal tolerated concentrations of 52 and 104 ppm, respectively (Dussault et al., 2014). Rosemary has also been shown to be effective against *Salmonella* contamination with a minimum inhibitory concentration of 0.3% v/v and minimal bactericidal concentrations of 0.5% v/v against *E. coli* contamination (Jiang et al., 2011). The phenolic compounds in essential oils are proposed as essential to their mode of action as bactericidal compounds (Rasooli et al., 2006). Some essential oils can contain phenol compounds that are thought to interact with and disrupt the cell membrane of bacteria, causing the cell to lose functional properties and leak the inner cell materials (Rasooli et al., 2006). More recently, a combination of garlic oleoresin, turmeric oleoresin, capsicum oleoresin, rosemary extract, and wild oregano essential oils was shown to be effective at mitigation of *Salmonella* Typhimurium in avian blood meal (Cochrane et al., 2016a,b).

Meanwhile, medium chain fatty acids, such as capric and caprylic acid, have been shown to be effective against *E. coli* and *Salmonella* growth (Kim and Rhee, 2013). Caprylic acid added to feed has been shown to decrease the quantity of *Salmonella* colonization in broiler chicks (Johny et al., 2009). A combination of caproic, caprylic, and capric acids has also been shown to be effective in the mitigation of *Salmonella* Typhimurium in feather meal, avian blood meal, porcine meat and bone meal, and poultry by-product meal (Cochrane et al., 2016a,b).

Sodium bisulfate has been used in a variety of food matrices for pH reduction. Sodium bisulfate has also been used in the animal industry for inclusion in feeds to reduce enzyme activity in poultry feed and bacterial loads in bedding of dairy cattle (Kassem et al., 2012; Sun et al., 2008). Additionally, the pet food industry has utilized sodium bisulfate for reduction of struvite formation in cats (Knueven, 2013). Inclusion of sodium bisulfate in various animal feed matrices, including poultry by-product meal and meat and bone meal, was effective at reduction microbial contamination.

Although this is not an exhaustive list of chemical additives capable of mitigating *Salmonella* or other biological hazards in animal feeds, it does give manufacturers an additional option to ensure finished product safety.

Conclusions

Livestock and companion animal feeds can be manufactured through many processes including grinding, mixing, pelleting, and/or extrusion. These specially formulated blends of plant- and animal-based ingredients provide all the essential nutrients for the intended species. Due to the wide range of raw materials used to make complete feeds, there is potential for contamination of various enteric pathogens, like *Salmonella*. The contamination of livestock animal feeds and pet foods with pathogens can lead to the colonization of livestock and companion animals, ultimately leading to human illness. Contamination is not only limited to bacterial pathogens but can also be contaminated with viral pathogens (PEDV) and TSEs (BSE and CWD). With the recent implementation of the FSMA, animal feeds and pet foods have come under more scrutiny and require manufacturers to specifically identify potential hazards and evaluate control measures to ensure animal food safety. Control measures to ensure the manufacture of safe finished animal foods include physical and chemical intervention methods. Physical intervention can include prevention (implementing a feed mill biosecurity plan), thermal processing (pelleting and/or extrusion), and irradiation (gamma, UV, or electron beam). Chemical interventions can include the use of various chemical additives (organic acids, formaldehyde, medium chain fatty acids, and essential oils). Additionally, a combination of physical and chemical methods can mitigate the risk of contamination of finished feeds even more. Although the risk of contamination by biological hazards in animal feeds cannot be completely eliminated, feed manufacturers have multiple methods to help reduce the risk.

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