Feed additives for swine

Introduction

Feed additives are compounds added to swine diets for the purpose of enhancing animal performance. This fact sheet focuses on compounds which provide minimal direct nutritional value to the diets. Such additives include antibacterial agents, antiparasitic compounds, metabolic modifiers, probiotics/prebiotics, acidifiers, enzymes and botanicals. Of these classifications, antibacterials metabolic modifiers, and antiparasitic agents are the major ones currently added to swine feeds. Some have been used extensively and successfully in swine production over the last 50 years.

Objectives

- Introduce different types of antibacterial agents and explain their benefit
- Present alternatives to antibacterial agents in swine diets
- Describe producer responsibilities when using feed additives

Antibacterial agents

Antibacterials (antibiotics and chemotherapeutics) are medicinals added to swine feeds to treat disease, to improve health, or to increase growth performance. A list of compounds and levels approved for specific purposes such as growth promotion, prevention of disease, and treatment of a specific disease are included in the Feed Additive Compendium [1]. Product and inclusion levels are approved by the Food and Drug Administration (FDA) after review of sponsor submitted scientific data which support claims that the compound is safe, effective, and properly labeled, and that food derived from treated animals is safe for human consumption.

Antibacterial agents may be included in feeds at levels for treatment or prevention of specific diseases, or to promote growth. In some cases the same active compound is approved at different inclusion levels and time limits for any or all of these categories. Antibacterial agents can be classified as antibiotics and chemotherapeutic agents. Antibiotics are compounds produced by bacteria or molds that inhibit the growth of other microorganisms. Many antibiotics have been discovered initially as occurring in nature. Chemotherapeutics may be chemically synthesized or naturally-occurring compounds that inhibit the growth of microorganisms. They may be used alone or in conjunction with antibiotics for the purposes of enhancing growth and feed efficiency, or for disease control in swine. Antibacterial products may be used for individual or in group treatment regimens. Generally feed additives are less effective for treatment of sudden onset disease conditions because the ill swine reduce daily feed intake. This inclination plus the historic FDA practice of approving feed additives at the dosage rates close to the minimum effective therapeutic level results in total daily drug consumption for ill swine that may not reach a useful level.
This factor coupled with the difficulty in rapidly changing diets in feed bins and feeders has favored the implementation of treatment programs that use water or individual treatment as the avenue of choice for acute disease treatment, rather than feed-based.

Where an outbreak is predictable or when using pulse medication programs to control chronic disease conditions, these concerns may be alleviated by timing strategic inclusions. Pulse medication (high drug levels for short and predetermined time periods) programs generally are used to control a disease organism for 1 to 3 weeks, as the swine develop immunity to the organism prior to the time it raises to disease-causing levels. Multiple pulses, at 3 to 4 week intervals, may be needed to accomplish such effects for selected organisms. Strategic applications of treatment drug concentrations prior to an anticipated disease onset or the use of pulse medication programs may be appropriate methods to reduce total medication levels, particularly in grow-finish swine. Veterinary advice to develop and maximize these intervention strategies is important to successful implementation.

Additions of antibacterials at non-treatment levels have been used as growth promoters generally and as preventatives for specific diseases in swine for over 50 years. The mechanism of action for growth-promotion has not been conclusively demonstrated, but has generally been considered to result from metabolic, nutritional or disease control effects in the animals. Most of the benefits have been ascribed to increased digestive tract function or improved general health of medicated swine. Antibacterials have maintained effectiveness since their introduction in the 1950’s. Hays [2] and Zimmerman [3] summarized the applicable studies on the effects of growth-promotants on pig performance during the periods of 1950 to 1977 and 1977 to 1985, respectively (Table 1).

Table 1. Improvements in pig performance fed antibacterials during years of 1950-1985. *Starter period from about 15 to 55 lb and grower-finisher from 55 to 200 lb body weight. †Hays [2], 15,689 pigs ‡Zimmerman [3], 10,083 pigs during the summer of 1999 (adapted from Rozeboom, [46]).

<table>
<thead>
<tr>
<th>Years</th>
<th>Production Stages</th>
<th>Improvement, %</th>
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<tbody>
<tr>
<td></td>
<td>Daily gain</td>
<td>Feed/gain</td>
</tr>
<tr>
<td>1950-1977b</td>
<td>Starter</td>
<td>16.1</td>
</tr>
<tr>
<td></td>
<td>Grower-finisher</td>
<td>4.0</td>
</tr>
<tr>
<td>1978-1985c</td>
<td>Starter</td>
<td>15.0</td>
</tr>
<tr>
<td></td>
<td>Grower-finisher</td>
<td>3.6</td>
</tr>
</tbody>
</table>

Additions of antibacterials at non-treatment levels have been used as growth promoters generally and as preventatives for specific diseases in swine for over 50 years. The mechanism of action for growth-promotion has not been conclusively demonstrated, but has generally been considered to result from metabolic, nutritional or disease control effects in the animals. Most of the benefits have been ascribed to increased digestive tract function or improved general health of medicated swine. Antibacterials have maintained effectiveness since their introduction in the 1950’s. Hays [2] and Zimmerman [3] summarized the applicable studies on the effects of growth-promotants on pig performance during the periods of 1950 to 1977 and 1977 to 1985, respectively (Table 1).

Many individual antibacterial agents and combinations are approved for use in swine diets. The more common additives and their withdrawal times are listed in Table 2. Selection of a specific feed additive and the level necessary for optimal response is dependent on several factors including: intended purpose—treatment, prevention or growth promotion, the stage of production, disease pressures within the herd, and required withdrawal time. Use levels of feed additives must comply with FDA approvals and the manufacturer’s directions. Producers must know the approved use levels and withdrawal periods of the products they use. Extra-label usage (unapproved levels or indications) of antibacterials in feeds is specifically prohibited by the Animal Medicinal Drug Use Clarification Act (AMDUCA) passed by Congress in 1995.

Growth promotants are routinely used in weaned pigs to assist with the stresses associated with weaning and changes in diets. The NAHMS 2000 swine survey indicated that 80.1% of sites containing wean to market pigs used antibacterials in feeds. Their use is less common in grower-finish diets. Table 1 demonstrates the relative production improvements expected in these age classes. In addition, more variable responses may be seen as swine achieve heavier weights. Such experiences have enabled many producers to determine that growth promotants through-out the production cycle were not cost-effective under their management systems. Under these conditions producers have removed them from grow-finish use, while maintaining use in the nursery-early grower stages.

Generally, benefits from antibacterials in gestation diets other than during the breeding period are minimal, therefore use has been limited. A summary of nine research trials showed that a high level (0.5 to 1.0 gram/ sow/day) of an absorbable antibiotic (tetracyclines) fed prior to and at breeding improved farrowing rate by 7% to 10% and litter size by 0.4 to 0.5 pig/ litter at the subsequent farrowing [4]. Table 3 suggests that weaning weights and pig survival are increased slightly when absorbable antibacterials are included in prefarrowing and lactation diets [4].

A major concern has been raised in food-animal systems over the use of antimicrobials also effective in human disease control. The emergence of drug-resistant microbial populations in humans and animals, and the potential for cross-contamination between populations have resulted in public health
officials world-wide requesting a sharp reduction of growth-promoting antibacterials in food animals. Governmental and industry responses have varied between countries based on different regulatory approaches and consumer pressures. The European Union has banned growth promotants in feeds of food animals. These issues, as well as the issues of antimicrobial resistance in food animals and its public health importance continue to be studied in other countries. These examinations may result in actions to reduce the use of antimicrobial growth-promotants through legislative or regulatory routes. Increased scrutiny by consumers may also result in the development of sizable markets for swine raised without growth-promoters as a consumer safety and quality issue. Producers should remain vigilant for changes in consumer demands or regulatory approaches. Recent experiences in Denmark have demonstrated that traditional growth-promotants could be removed from grow-finish swine diets without substantially compromising swine health or performance. However, when these withdrawals were expanded to the nursery production many producers experienced substantial decreases in swine health and productivity, which required substantive management changes and an increase in use of treatment level drugs. Similar experiences could be expected under North American production systems.

Natural chemotherapeutic agents

Copper sulfate and zinc oxide have been identified as naturally occurring chemotherapeutic agents that have growth promoting effects in grow-finish swine diets. Both copper and zinc are required for normal growth at low inclusion levels in swine diets. Elemental copper at 6 to 11 ppm and zinc at 75 to 125 ppm meet these nutritional requirements. Copper possesses antibacterial and antifungal properties and is an effective growth promant when fed at concentrations of 100 to 250 ppm in the diet [5,6]. The combination of copper and a growth promotant antibiotic results in a greater growth response than the feeding of copper or antibiotics alone in the starter rations [4,7], (Table 4). Zinc oxide at levels of 1500 to 3000 ppm fed for 2 to 3 weeks after weaning has been found useful for non-specific control of post-weaning diarrheas. Use of these compounds for extended periods at high levels may result in environmental contamination of ground where manure is spread. Copper toxicity in sheep is attained at low levels (3.5-20 mg/kg BW daily consumption), particularly on low molybdenum containing pastures. Therefore caution when applying high copper manure to pasture lands is required. Zinc compounds will also raise soil levels but most animals are less susceptible to toxicosis. Inclusion of high levels of zinc oxide for longer than 3 to 4 weeks or of levels higher than 250 ppm of copper sulfate for extended periods may cause direct toxic effects in pigs. Therefore, producers should check with their feed manufacturer about the concentrations of copper, iron, and zinc present in commercial feeds or mineral mixes before providing copper or zinc suplementations to feeds, and should avoid excessive inclusion rates or extended feeding periods. In several European countries, to minimize soil build-up of copper or zinc, public concerns have mandated restricted usage of these products in diets.

Antiparasiticides

Swine are susceptible to infection by numerous species of internal and several species of external parasites. These parasites vary widely in their life cycle, and extent of injury capacity for swine. Feed has been used to provide effective administration for many anthelminthic products for many years. In most applications the drug is used for a prescribed interval and dosage rate.

<table>
<thead>
<tr>
<th>Additive</th>
<th>Withdrawal time before slaughter, days</th>
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</thead>
<tbody>
<tr>
<td>Bacitracin, methylene disalicylate</td>
<td>none</td>
</tr>
<tr>
<td>Bacitracin, zinc</td>
<td>none</td>
</tr>
<tr>
<td>Bambermycins</td>
<td>none</td>
</tr>
<tr>
<td>Chlortetracycline</td>
<td>none</td>
</tr>
</tbody>
</table>
| Oxytetracycline                               | none
table 2. Withdrawal time for antibacterials in swine feeds.  

*a Feed Additive Compendium [1]  
*b At 500 g/ton use level, withdraw 5 days before slaughter  
*c Withdraw from feed 20 days before slaughter when neomycin base inclusion is 140 g/ton and 5 days before slaughter when neomycin base is below 140 g/ton.  
*d In combination with pyrantel tartrate withdraw 10 weeks (70 days) before slaughter.
This regimen purges the adult parasites and may kill developing larvae depending on the product selected. Once the drug is withdrawn the animal is again able to become infected upon exposure to contaminated environment or animals. Two dewormers (pyrantel tartrate and hygromycin B) are approved for continuous inclusion in the diet. Pyrantel tartrate has been marketed for control of ascarid (large round worm) larval by continuously feeding at low inclusion levels to post-weaned pigs. A combination of routine exposure to ascarid eggs and suppression of larval transport through the body enable protection against parasite damage to be achieved during the feeding period and some level of immunity developed to protect from future infections. The introduction of feed-grade mange and lice control formulations has facilitated the year-round control of these parasites, limited the need for individual treatment or use of insecticide sprays, and made whole-herd eradication programs more feasible. The wide range of products available, the varied life cycles, withdrawal times (Table 5), and the environmental and regional impacts of these parasites makes it advisable to obtain professional veterinary assistance when formulating a parasite control or eradication program.

Metabolic modifiers

Metabolic modifiers have been proposed to modulate physiologic processes to improve animal productivity. In swine initial efforts centered around modifying protein and fat deposition in finishing swine using several different metabolic pathways. In the USA, a beta-agonist compound, Ractopamine hydrochloride has been approved for use in finishing feeds to increase protein and reduce fat deposition in finishing swine. Research has been reported that inclusion in the diet for the last five weeks of finishing increased the fat-free lean by up to 3.8%, increased loin eye area by 5.0%, reduced 10 rib back fat by 18%, and increased protein production by 2.4% without adversely effecting meat quality traits [8]. Dosage levels and timing are approved as part of the label instructions. Beta-agonist compounds use in food animals has been prohibited by regulatory actions in other countries because of human health concerns. Some specialty markets in the USA and all pork exports to the European Union have precluded usage. In response USDA-AMS has developed a certification and auditing system and USDA-FSIS has developed rapid tests to detect ractopamine HCL residues in an effort to guarantee swine have not received this product when so claimed.

Alternatives to antimicrobial feed additives

Probiotics/prebiotics. Probiotics are a class of feed additives consisting of living bacteria and/or yeast cultures fed to improve desirable microflora balance within the small and large intestine. Numerous product formulations are available for inclusion in swine feeds [9]. Most common mixtures contain one or more of the Lactobacillus species, Bacillus subtilis, Streptococcus faecium, Saccharomyces cerevisiae and other commenseal species. To be effective, the desirable microbes must establish as normal inhabitants of the intestinal tract of healthy animals by surviving and flourishing in the gut environments. These mixtures are thought to work by either directly excluding harmful bacteria or by reducing intestinal pH to indirectly favor the development of other desirable health-promoting microorganisms which compete with harmful bacteria to reduce their presence in the gut. The desired effect is to improve weight gain and feed efficiency by improving gut digestion and reducing pathogenic organism loads.

Although probiotics have been commercialized and available for more than 50 years, documented evidence of their therapeutic and nutritional value has been quite variable. Possible reasons for the lack of consistent results are low or variable viability of microbial cultures, strain differences in cultures selected, dose level and frequency of product feeding, antimicrobial and feed ingredient interactions which reduce/neutralize viable colonies before feeding, and composition of diet. Further research may refine the products and conditions of use which will ensure reproducible results.

Prebiotics may be defined as food/feed substances that beneficially affect the host by selectively stimulating growth or activity of favorable bacterial species in the gut. They represent an emerging area of research interest with potential for inclusion in feed rations of swine. Current prebiotics are primarily derived from oligopolysaccharide compounds. These compounds provide nutrient substrates for beneficial
bacteria and may be used to selectively boost the colonization of acid-producing bacteria. Many of the advantaged bacteria are similar to those found in probiotic mixtures. Therefore combination regimens of selected prebiotics and probiotic compounds may arise to improve gut health and pig performance. Further research may refine these products, interactions with other compounds, and identify use conditions which will result in reproducible beneficial results when added to feeds.

Acidifiers in feeds. Acidified feeds may help improve the digestive processes in swine through a variety of mechanisms, although the mode(s) of action are not fully understood. Consumption of acidified feeds may decrease the stomach pH which results in increased pepsin activity and slowing of stomach emptying. Both of these actions generally should assist to increase protein digestion and utilization. Reduced stomach pH may provide a more hospitable gut environment for beneficial microbes (see probiotics above) and reduce growth of E. coli, Salmonella and other gut-associated pathogens. Organic acids applied to feeds may reduce feed degradation and microbial loads. Fumaric, citric and propionic acids and mixtures of organic and inorganic acids are commercially available for use in swine diets. In production systems utilizing liquid feeds, pre-feeding fermentation processes have been developed to reduce feed pH and increase diet digestibility. Newly weaned pigs appear to gain the greatest benefits from inclusion of acidified feeds. Grow-finish performance may be more variable. Fermentation of liquid feeds has demonstrated benefit in reducing Salmonella carriers at the farm level. Inclusion rates for acidifiers vary with the product selected. Generally to be effective a 1 to 3% inclusion rate is required. Under specific production conditions these inclusion levels may be economically justified.

Botanicals. Botanicals are compounds derived from roots, leaves, bark, flowers or other parts of plants. A number of herbaceous compounds have been proposed to possess useful antimicrobial, antiparasitic or antioxidant properties. Botanicals have been reported to increase feed intake, stimulate secretion of digestive juices and the immune system, provide direct antibacterial activity and improve oxidative stability in animal products. Recent interest has focused on the potentials for botanicals to express antimicrobial or antioxidant properties, and to act as alternatives to antimicrobials in feeds [10]. Oils of various spices may contain natural antioxidants, generally tocopherols or phenoles. Problems associated with potency evaluation of unrefined products, standardization of active ingredient extraction, and determination of appropriate inclusion levels for specific effects are current limitations to widespread use. Additional research to screen various botanicals, to identify and quantify active ingredients for useful characteristics, and to develop inclusion regimens for antibacterial, antiparasitic or antioxidant effects for products currently available is required before science-based recommendations can be made. There have been a limited number of controlled trials reported to support/quantify proposed benefits of botanical inclusions in swine diets, but given the world-wide commercial interest in these compounds additional information should be forthcoming.

Other additives. Flavors may be added to diets to enhance the aroma or taste of the feed. Most research data suggest flavors are of limited benefit unless one is attempting to mask off-odors or off-flavors in feeds.

Enzymes may be included in feeds for the purpose of assisting in the digestive process. Little benefit from enzyme supplementation can be expected in traditional grain-based diets fed in the USA, but may be beneficial where non-traditional feedstocks are used. Exceptions to this observation are beta-glucanase and phytase. Beta-glucanase has been shown to enhance utilization of barley that is rich in beta-glucans. This complex carbohydrate interferes with the pig’s ability to efficiently digest and utilize barley nutrients.

Swine, like other monogastric animals, possess virtually no inherent phytase digestive activity, and consequently have poor utilization of phosphorus in plant-based diets. When added to these diets, the phytase enzyme aids in the digestion of phytate phosphorus; therefore, increasing plant-based phosphorus availability for the monogastric animal. Use of phytase reduces the amount of supplemental inorganic phosphorus required in diets to meet the pig’s dietary phosphorus requirements. Additionally there is evidence indicating that phytase positively affects the availability of calcium and other minerals such as manganese, zinc, copper, iron, and utilization of energy and amino acids that are phytate bound.

<table>
<thead>
<tr>
<th>Additive</th>
<th>None</th>
<th>Copper*</th>
<th>Antibacterials*</th>
<th>Both</th>
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</thead>
<tbody>
<tr>
<td>Daily gain, lb</td>
<td>0.46</td>
<td>0.57</td>
<td>0.55</td>
<td>0.62</td>
</tr>
<tr>
<td>Feed/gain</td>
<td>1.98</td>
<td>1.87</td>
<td>1.81</td>
<td>1.75</td>
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<tr>
<td>Survival, %</td>
<td>95</td>
<td>100</td>
<td>93</td>
<td>98</td>
</tr>
</tbody>
</table>

Table 4. Effects of copper and antibacterial additions on performance of weanling pigs. *Two trials involving 256 pigs from 4 to 8 weeks of age (15 to 30 lb) **55 ppm chlortetracycline in one experiment, 27 ppm of virginiamycin in a second experiment.
Phytase inclusion stimulates better utilization of total dietary phosphorous in the gut, enabling producers to reduce total phosphorous levels in the diet while meeting intake requirements. These dietary changes result in substantial decreases in residual phosphorus in manure, and offer the potential for reduced feed costs. As land applications of manure become more regulated using a phosphorous-based standard, this additive should receive greater attention.

**Producer responsibilities in feed additive usages**

Participation in the Pork Quality Assurance Program-Level III [1] of the National Pork Board will provide valuable information in managing the use of medicated feed additives. Producers should follow directions for each feed additive as provided by the manufacturer on the product label to obtain maximum benefit. When using medicated feed additives adherence to these instructions are required by law. Consultation with a veterinarian or nutritionist about the cost-effective and beneficial use of the various feed additive classifications above may improve pork product quality and provide competitive advantages.

When using medicated feeds producers must:
1. Read the feed tag to assure the additive is being fed at approved concentrations and indications. Use medicated feeds only as approved by FDA (label directions). Comply with the published withdrawal times to avoid residues.
2. Maintain mixing and distribution records to demonstrate that appropriate actions to avoid cross-contamination and product abuse were taken, including identification of the responsible party when additives are used. (see PQA- Level III booklet p.87 for sample records)
3. Provide appropriate clean-out, sequencing and bin/feeder identification procedures to avoid cross-contamination or mis-delivery in feed mixing, delivery or storage devices.
4. Obtain professional advice on the selection and use of medication regimens in feed.

Approved use concentrations and indications, instructions for use in feed, and withdrawal times for antimicrobial compounds are regulated by the FDA. USDA-FSIS (United States Department of Agriculture Food Safety and Inspection Service) has the responsibility to monitor pork carcasses at packing plants for evidence of harmful chemical residues. As specialty markets expand some otherwise approved products may be precluded by the specialty market production requirements. Every pork producer must take precautions to abide by FDA required pre-slaughter withdrawal times for feed additives and other medications, and to understand the markets into which her/his product is being sold. Disregarding these regulations or market requirements could result in a sizable monetary loss to individual producers.

**Summary**

Feed additives available to producers include antibacterial agents, antiparasiticides, metabolic modifiers, acidifiers, probiotics/prebiotics, botanicals, flavors, and enzymes. Research and historical experience have demonstrated that antibacterials provide the most consistent generalized improvements in growth rate and feed efficiency of the feed additives above. Alternatives to these compounds are actively being sought because of the increased consumer concerns about antimicrobial resistance in food animals. To maximize returns, producers should develop a tailored feed additive program based on specific production needs and current research information. Consultation with a practicing veterinarian and an animal nutritionist to formulate effective medication and feed additive programs will benefit producers and consumers of pork.

**Literature Cited**


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<thead>
<tr>
<th>Chemical Name</th>
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<tbody>
<tr>
<td>Dichlorvos</td>
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</tr>
<tr>
<td>Fenbendazole</td>
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</tr>
<tr>
<td>Pyrantel Tartrate</td>
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</tr>
<tr>
<td>Levamisole Hydrochloride</td>
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<tr>
<td>Ivermectin</td>
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<tr>
<td>Hygromycin B</td>
<td>15</td>
</tr>
<tr>
<td>Thiabendazole</td>
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Table 5. Withdrawal time for anthelmintics in swine feeds. Feed Additive Compendium [1]


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