

# Economics of Antibiotic Use in U.S. Swine and Poultry Production

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In the United States today, antibiotics are commonly used in food animals to promote growth and prevent disease, as well as to treat sick animals. The U.S. Food and Drug Administration (FDA) estimates that 14.6 million kg. (32.2 million lbs.) of antibiotics were sold for use in animals in 2012 (FDA, 2014), more than four times the 3.29 million kg. (7.3 million lbs.) of antibiotics sold for human use in 2011 (FDA, 2012). Antibiotics are used primarily in intensive swine, poultry, and feedlot cattle systems, with limited use in dairy cows, sheep, and companion animals.

The extensive use of antibiotics in livestock comes at a cost: it contributes to the increase in drug-resistant pathogens in animals that can potentially be transmitted to humans and negatively impact human health, even if the magnitude of the risk to human health is still debated (You and Silbergeld, 2014). Concerns about increasing antibiotic resistance led to bans on antibiotics for growth promotion (AGPs) in the European Union in 2006. In the United States, AGPs are not banned, but the FDA recently issued guidelines for the industry to voluntarily withdraw medically important antibiotics from growth promotion (FDA, 2013a). For policy makers, the challenge is to evaluate the benefits and costs of animal antibiotics to society. What is the economic value of antibiotics to the livestock industry versus the potential health cost of increasing resistance levels? What are the potential productivity and economic effects of a ban on AGPs for U.S. meat producers and consumers?

## Antibiotic Resistance: The Public Health Question

The discovery that antibiotics fed in subtherapeutic

concentrations to livestock can hasten their growth and prevent disease (Jukes et al., 1950; and Moore et al., 1946) came just as farmers in the United States were struggling to keep pace with demand for food and animal protein. Antibiotic use for growth promotion and disease prevention soon became an integral part of a new agricultural production model, despite early warnings about the potential risks of developing resistance (Starr and Reynolds, 1951). Numerous studies have demonstrated that food animals on farms using low levels of AGPs harbor a higher percent of resistant bacteria than farms that do not use AGPs (Marshall and Levy, 2011). Increased resistance to certain drugs (such as fluoroquinolones) in both animals and humans coincides with their addition to animal feed and their use in veterinary medicine (Endtz et al., 1991; Bager et al., 1997; and Nelson et al., 2007). Additionally, studies comparing resistance prevalence in both humans and animals before and after AGP bans have documented significant decreases in resistance (primarily in vancomycin-resistant enterococci following the ban of avoparcin as a growth promoter) (Aarestrup et al., 2001; Bager et al., 1999; Bogaard, Bruinsma, and Stobberingh, 2000; Klare et al., 1999; Pantosti et al., 1999; and Wegener et al., 1999).

Increasing levels of resistance in bacteria isolated from food-producing animals and retail meat sources have been reported by the National Antimicrobial Resistance Monitoring System (FDA, 2013b). FDA reported that resistance to third-generation cephalosporins rose among isolates from retail ground turkey between 2008 and 2011, and among certain salmonella serotypes in cattle between 2009 and 2011 (FDA, 2013b).

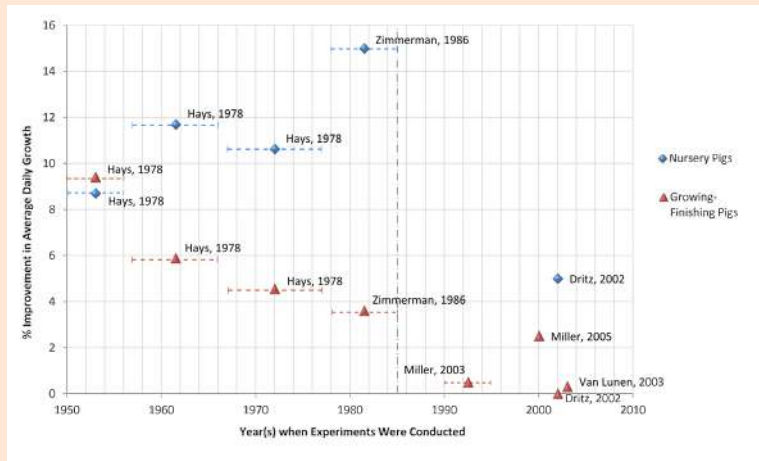
Most important from a public health perspective, extensive research has documented the spillover of resistance genes and resistant pathogens from food animals into human populations via three primary pathways: (1) the release of antibiotic-resistant bacteria into the environment (Campagnolo et al., 2002; Chee-Sanford et al., 2001; and Gibbs et al., 2006), (2) resistance transmission through the food chain (Jakobsen et al., 2010a; Jakobsen et al., 2010b; and Sørensen et al., 2001), and (3) the acquisition of resistant strains through direct contact with food animals (van Cleef et al., 2011a; van Cleef et al. 2011b; Graveland et al., 2010; Huber et al., 2011; Huijsdens et al., 2006; Khanna et al., 2008; Smith et al, 2009; and Voss et al., 2005).

How much these processes contribute to resistance of human pathogens to antibiotics is still unclear. Nevertheless, a report from the Centers for Disease Control and Prevention (CDC) states, “Because of the link between antibiotic use in food-producing animals and the occurrence of antibiotic-resistant infections in humans, antibiotics should be used in food-producing animals only under veterinary oversight and only to manage and treat infectious diseases, not to promote growth” (CDC, 2013).

### Evidence of Benefits in Swine Production

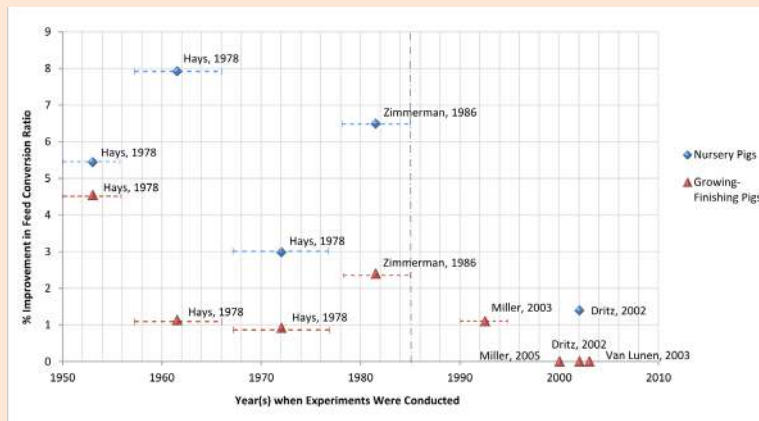
The major inputs in food animal production—feed, labor, and capital—can be improved on some operations by feeding antibiotics. AGP use can enhance the growth rate and the feed conversion ratio, the rate at which animals convert feed into weight gain (Dibner and Richards, 2005; Hays, 1977; and Zimmerman, 1986), and it can increase labor or capital productivity by substituting for hygiene management in animal housing or transportation (Key and McBride, 2014; and MacDonald and

**Figure 1.** Percentage Improvement in Average Daily Growth of Pigs Fed Antibiotics over Time



Note: The x-axis refers to the year when the experiments were conducted. Hays, 1978 and Zimmerman, 1986 are reviews of studies conducted over a given time period. The horizontal lines represent the period during which the experiments were conducted. The vertical dashed line separates early vs recent studies as shown in Table 1.

**Figure 2.** Percentage Improvement in Feed Conversion Ratio of Pigs Fed Antibiotics over Time



Note: Notes associated with Figure 1 apply.

Wang, 2011). Using AGPs could also reduce variability in animal weights and sizes, avoiding financial penalties at markets for animals outside the range suited for mechanized processing (Liu, Miller, and McNamara, 2003).

The effects of subtherapeutic levels of antibiotic feed additives on growth rate and feed efficiency have been reported in cattle, swine, and poultry for more than 50 years (Jukes et al., 1950; Moore et al., 1946; and Salinas-Chavira et al., 2009), but

effect sizes vary widely among operations and over time (Figures 1 and 2). Rosen (1995) analyzed a database of more than 4,000 reports from 55 countries and found a high degree of variation for the effects on weight gain and feed conversion in broilers and pigs.

Results obtained in animal-level experiments likely reflect specific nutritional, environmental, and genetic conditions and cannot be generalized. Moreover, most animal-level experimental research on the

**Table 1. AGP Effects Found in Newer vs. Older Studies, by Age of Pigs**

	Early Studies: 1950–1985 Adapted from Hays (1977), Zimmerman (1986), and Cromwell (2002)			Modern Production System Adapted from Dritz et al. (2002)		
Parameter	Control	Antibiotic	Difference (%)	Control	Antibiotic	Difference (%)
<b>Starting Phase</b>						
Average Daily Gain (kg)	0.39	0.45	16.40%	0.436	0.458	5.00%
Feed Conversion Ratio	2.28	2.13	6.90%	1.44	1.42	1.4% (NSS)
<b>Growing Phase</b>						
Average Daily Gain (kg)	0.59	0.66	10.60%	n.a.	n.a.	n.a.
Feed Conversion Ratio	2.91	2.78	4.50%	n.a.	n.a.	n.a.
<b>Growing-Finishing Phase</b>						
Average Daily Gain (kg)	0.69	0.72	4.20%	0.78	0.778	0.2% (NSS)
Feed Conversion Ratio	3.3	3.23	2.20%	2.9	2.9	0%

Note: The data for 1950–1985 come from a meta-analysis conducted by Cromwell (2002) based on data from Hays (1977) for the period 1950–1977 and data from Zimmerman (1986) for the period 1978–1985. The meta-analysis includes data from 453, 298, and 443 experiments involving 13,632, 5,783, and 13,140 pigs, respectively, for the three phases. The results of the meta-analysis are weighted averages based on the number of replications. The data used in the right panel (modern production system) come from a single study Dritz et al. (2002) involving 3,648 and 2,660 pigs for the nursery and grow-finish phases, respectively.

growth-promoting effect of antibiotics has been performed by the manufacturing and feed industries with relatively few studies by independent research bodies (Thomke, 1998), and most of this research predates 2000.

A meta-analysis of more than 1,000 growth experiments performed in swine between 1950 and 1985 demonstrated that antibiotics in feed improved the daily weight gain in starter pigs (animals weighing 7 to 25 kg, or 15 to 55 lbs.) by an average of 16.4% and the feed efficiency by 6.9% (Cromwell, 2002). Antibiotics were most effective in improving growth in young pigs but were still effective for older growing and finishing pigs (Table 1). One hypothesis is that weanling and starter pigs are more susceptible to stress and sub-clinical diseases and, consequently, show a greater response to AGPs

(Hays, 1977).

Historical experiments have demonstrated that responses to AGPs are lower when production conditions are optimized, with good housing, hygiene, nutrition, and health (Hays, 1977). Early experiments concluded that the degree of response to antibiotics was inversely related to the general well-being of the experimental animals (Coates et al., 1951; Hill et al., 1953; and Speer et al., 1950). Greater antibiotic responses were demonstrated in pigs carrying a high disease load compared with pigs raised in environments with low disease loads, indicating that the growth-promoting effect is at least partially the result of bacteriostatic and bactericidal activity (Zimmerman, 1986). Greater responses were also shown if the antibiotics were added to an inadequate diet (Burroughs, 1959). Nutritional

stress and stress associated with relocation (such as movement of feeder pigs) or temperature extremes have been associated with greater responses to antibiotics (Hays, 1977; and Ryan et al., 1961). In addition to improving feed efficiency, adding antibiotics to swine feed was found to reduce the mortality rate by 50% in young pigs (2.0% vs. 4.3%) in trials conducted between 1960 and 1982 (Cromwell, 2002).

Because those results were obtained in animal experiments conducted decades ago, an important question is whether the growth response to antibiotics has changed over time, especially given the increasing levels of resistance among food animals. A review comparing results of animal-level experimental studies led between 1950–1977 and 1978–1985 concluded that the overall effectiveness of AGPs did not diminish between the 1950s and the 1980s (Zimmerman, 1986).

However, for post-2000 studies, the literature suggests that productivity gains from AGPs are lower than indicated by earlier research (Figures 1 and 2). For instance, Miller, McNamara, and Bush (2003) estimated that AGP use increased average daily weight by 0.5% and feed efficiency by 1.1%, much less than the two-digit improvements reported in the 1980s (Cromwell, 2002). Similar results were demonstrated in animal-level experiments, as shown in Table 1 (Dritz et al., 2002; and Van Lunen, 2003). Recent studies tend to show a small, significant growth response to AGPs for nursery pigs, but no significant response for finishing pigs (Dritz et al., 2002; Key and McBride, 2014; and McBride, Key, and Mathews 2008). After controlling for input levels, operator and farm characteristics, farm production practices, and location, a recent study analyzing data from the U.S. Department of Agriculture’s (USDA) Agricultural Resource Management Survey estimated that AGP

use improved output by 1.0% for feeder-to-finish hog producers, a statistically insignificant improvement (Key and McBride, 2014).

In Denmark, which has an export-oriented, market-driven, and intensive production system, the use of AGPs was banned in finishing pigs in 1998 and in weaning pigs in 2000. The termination of AGPs had no major effect on productivity or feed efficiency in finishers but resulted in some loss of productivity in weaners (World Health Organization (WHO), 2002). Long-term swine productivity improved markedly between 1992 and 2008, suggesting that the ban on AGPs did not harm long-term productivity (Aarestrup et al., 2010). The effects of the ban on AGPs on antibiotic consumption are mixed. Between 1997 and 2008, the total consumption of antibiotics in the Danish swine production industry decreased from 81.2 mg/kg of pork produced to 48.9 mg/kg of pork produced (Aarestrup et al., 2010). Following the AGP ban, total antibiotic use was at its lowest level in recent years in 1999. However, the therapeutic use of antibiotics increased and the total antibiotic consumption for animal production increased by 36% during the period 2001 through 2009 (Jensen and Hayes, 2014). This led the Danish government to impose new restrictions on producers' uses of antibiotics, and total use has started decreasing again after 2009 (Aarestrup, 2012).

The growth response to antibiotics may have decreased over the past 30 years for several possible reasons. First, the growth response to antibiotics is less important when animal nutrition, hygiene, genetics, and health are optimal. The relative improvement in the growth rate resulting from supplementing the diet of pigs with antibiotics has been shown to be inversely related to the growth rate of animals not being fed antibiotics (Braude, Wallace, and Cunha,

1953; and Melliere, Brown, and Rath 1973). With changes in the livestock industry over the past 30 years, all of these factors have improved. Second, increasing levels of resistance in animals could be diminishing the overall effectiveness of AGPs, although data are lacking to evaluate this hypothesis.

The recommended dosage of subtherapeutic antibiotics has increased over time, from 10–20 g/ton in the early 1950s to 40–50 g/ton in the 1970s, and 30–110 g/ton today (Hays, 1977; and Thaler 2010), but there is no demonstrated relationship with increased resistance levels.

### Evidence of Benefits in the Poultry Industry

Relatively few studies address the productivity and economic benefits of AGP use in the poultry industry. Table 2 compares three studies on the

effects of AGPs on broiler production: one animal-level experimental study of the removal of AGPs on two U.S. broiler farms (Engster, Marvil, and Stewart-Brown, 2002), one farm-level observational study based on a poultry national survey (MacDonald and Wang, 2011), and one observational study with data from before and after the ban on AGPs in Denmark (Emborg et al., 2001).

For the broiler industry in Denmark, the mortality rate, the average weight gain, and productivity (defined as kg of broilers produced/m<sup>2</sup> per grow-out) for 1995 to 1999 were not affected by the ban on AGPs (Emborg et al., 2001). The feed conversion ratio did increase, by 0.016 kg/kg from 1995 to 1999, the same magnitude of increase as after the removal of AGPs, in two U.S. broiler farms (Engster, Marvil, and Stewart-Brown,

**Table 2. Production and Economic Effects of AGP Restrictions in the Poultry Industry, United States, and Denmark**

	U.S. Animal Level Experimental Research (Engster et al., 2002)	U.S. Farm Level Observational Research (MacDonald and Wang, 2011)	Denmark Observational Research Pre (1994-1997) and Post (1998-2000) Ban on AGPs (Emborg et al., 2001)
Change in feed conversion ratio, value (% change)	Site 1: +0.016 (0.8%*) Site 2: +0.012 (0.6%*)	No HACCP: +0.08 (4%) HACCP: +0.05 (2.6%)	+0.016 (0.9%)
Average weight differential grams (% change)	Site 1: -13.6 g (0.6%*) Site 2: -18.1 g (0.8%*)	2-7% production decline without AGPs when controlling for labor, capital and other inputs, <i>not statistically significant</i>	+ 53 g
Mortality rate	Differential: Site 1: -0.2% Site 2: -0.14%	With AGP: 3.95% No AGP, No HACCP: 5.01% No AGP, HACCP: 3.95%	Pre-ban: 4.1% Post-ban: 4.0%
Cost-effectiveness	Cf. Graham et al. study, based on Engster data:  Net effect of using AGP = lost value of \$0.0093 per chicken (savings in the cost of AGPs more than compensate the decrease in production).	Growers using no AGPs and with HACCP receive 2.1% more fees per kg than growers using AGPs, suggesting higher costs of production in the absence of AGP.  Non-AGP premium that would be paid to growers by integrators: \$22.5 million.	Calculations suggested that savings in the cost of APG almost exactly offset the cost of the decreased feed efficiency.  Potential substantial costs associated with modifications to the production systems (not evaluated).

Note: HACCP = Hazard Analysis and Critical Control Points (a food safety plan).

Sources: Emborg et al., 2001; Engster et al., 2002; Graham et al., 2007; and MacDonald and Wang, 2011.

2002) (Table 2). The end of AGP use in poultry production in Denmark appears to have caused a small decrease in feed efficiency, which was at least partly offset by savings in the cost of AGPs (WHO, 2002).

In the United States, MacDonald and Wang (2011) have demonstrated that suspending AGPs would have no statistically significant effect on production in broiler grow-out operations, once other factors that may affect production (labor, capital, and other inputs) are controlled. However, they also demonstrate that growers who do not use AGPs receive statistically significant higher contract fees than AGP users (+2.1%). These higher fees paid by integrators likely compensate growers for increased costs associated with production without AGPs since broilers produced without AGPs cannot be labeled as antibiotic-free (no antibiotic use at all), limiting the possibility for producers to sell these products for a premium price.

Graham, Boland, and Silbergeld (2007) estimated that the net effect of using AGPs was a loss of \$0.0093 per chicken, with the savings in the costs of AGPs more than compensating for the decrease in production. However, this economic analysis does not include veterinary costs or potential costs related to the increased variability in the weight of broiler chickens. Additionally, the added production was valued according to the fees paid to growers which is, in fact, an underestimation of the value of birds to the integrator.

One of the major current benefits of AGP use may be maintaining animal health in older facilities, where hygiene management is less efficient. U.S. farms that produce broilers with AGPs tend to have older houses, with less modern equipment, and are less likely to follow a plan for managing food safety hazards (MacDonald and Wang, 2011). As is the case for swine, AGPs may have smaller benefits when

production conditions are optimized: Coates et al. (1951) demonstrated significantly smaller response in chicks to chlortetracycline and penicillin in new environments compared to previously used environments.

In terms of food security, there is a balance to find between using antibiotics to control animal disease and prevent the transmission of zoonotic pathogens from animals to humans, and limiting the emergence and the spread of antibiotic resistance. Some studies highlight that antibiotics added to animal feed or drinking water can decrease the bacterial contamination of animal carcasses and products (Hurd et al., 2008; and Singer et al., 2007). However, improved biosecurity, better hygiene management

practices, or vaccinations offer the opportunity to control infectious disease of food animals without increasing levels of resistance.

### Potential Economic Cost of a Ban

As described by a few authors (McBride, Key, and Mathews, 2008; and MacDonald and Wang, 2011), a ban on AGPs in the United States would affect producers differentially, according to location, farm size, contracting arrangements, production practices, species, and stage of production. The effect of a ban would also depend on management variables and health and sanitation practices, as shown in studies describing the Swedish experience after that country's 1986 AGP ban (Wierup, 2001).

**Table 3. Potential Economic Effects of AGP Restrictions at Animal, Farm, and Market Levels**

Potential Economic Effects of Withdrawing AGPs	
Potential Costs	Potential Benefits
Potential Animal-Level Effects	
Decreased growth rate, decreased feed efficiency	—
Short term higher mortality rate (especially of young animals), increased morbidity	Long term improvement in health status of animals after investing in biosecurity measures. Potential preservation of antimicrobial efficiency to treat animals.
Fewer animals born per litter	—
Increased variability of product	—
Potential Farm-Level Effects	
Increased time to market and decreased stocking densities	—
Increased input costs: feed (non AGP), young animals purchased	Decreased input costs: saving in AGP cost
Cost of more biosecurity measures and adjustments in housing to compensate for AGP termination	Long term improvement in health status of animals. Decrease in transmission of all diseases, including diseases which are not prevented by antimicrobials (e.g. viral diseases, respiratory tracts infections).
Increased veterinary costs (more treatment of disease)	Decreased veterinary costs (less disease outbreak after having invested in biosecurity measures)
Higher labor costs if alternatives to AGP are more labor-intensive	—
Increased variability of product	—
Potential Market-Level Effects	
Supply side: less output for each level of input, increase in wholesale and retail price of meat, variation in producers revenues (increase or decrease)	Supply side: Potential increase in producers revenues (increase in wholesale price of meat)
—	Demand side: increased consumer confidence and demand for product; increased access to export markets that previously rejected U.S. products because of AGP use

Source: Adapted from Sneeringer, 2014.

Incentives for U.S. food animal producers to use AGPs include improved animal performance and overall health, higher profits, and reduced production risks. Table 3 summarizes the potential economic effects of a restriction on AGPs at the animal, farm, and market levels.

Several studies have sought to estimate the potential economic effect of a ban on AGPs in the U.S. swine industry and found large differences in production cost increases: \$0.59/pig and a 9% decrease in net profits (Miller, McNamara, and Bush, 2003); \$1.37/pig (Miller et al., 2005); \$2.33/pig and a 2% increase in production costs (Brorsen and Lehenbauer, 2002); and \$4.50/pig in the first year and a 4.5% increase in overall production costs (Hayes and Jensen, 2003).

An evaluation conducted by a WHO panel on the effects of AGP termination in Denmark estimated the net increase in costs associated with removing AGPs at €1.04 (about the same in 2002 U.S. dollars) per pig produced and zero for poultry. This translates into an increase in pig production costs of just over 1%. Results from a general equilibrium model of the Danish economy suggest that pig production is around 1.4% per annum lower than might be expected and poultry production 0.4% per annum higher. There was no obvious effect on pork prices in Denmark in the years following the ban (WHO, 2002).

Recent USDA estimates of the market-level effects of a ban on AGPs in U.S. hog and broiler production also indicate limited effects (Sneeringer, 2014): the quantity produced would, at most, decrease by 1.08% in the hog industry and 1.12% in the broiler industry (assuming a 3% reduction in supply due to discontinuation of AGPs). The consequent increase in wholesale prices would range from less than 1% to at most 2.6%. The total value of production

would increase (0.54% for hogs and 1.45% for broilers), with a gain in value of production for producers not using AGPs before the ban, and a potential loss or gain for producers using AGPs before the ban, depending on assumptions. Since farmers receive about a third of the retail value of pork, consumers would likely see even smaller changes in price. These results are long-term effects; some short-term effects could be negative, as was the case in Denmark after the ban. An AGP ban in the United States could also increase access to export markets that have more stringent regulations on AGPs, such as the European Union, Mexico, and Taiwan (Maron, Smith, and Nachman, 2013).

### Policy Issues

The scientific evidence seems to suggest that it is possible for both the swine and the poultry industries to maintain production without AGPs, provided other disease prevention measures are implemented as AGPs are being phased out. Alternative strategies to prevent and control disease in livestock—vaccination, segregation of herds or flocks by age, sanitary protocols, ventilation systems, adjustments in feed rations, and physical biosecurity measures—offer the opportunity to control infectious diseases in food animals without increasing levels of resistance.

Such strategies will incur costs, which could ultimately raise wholesale meat prices. To our knowledge, there are no published estimates of the cost of investing in production systems with better biosecurity and hygiene, and no estimates of the potential benefits of such investments, which are likely to decrease in the transmission of viral diseases and respiratory tract infections, as well as diseases that are prevented by antimicrobials.

A potentially important factor is consumer demand for antibiotic-free

meat and poultry. The use of AGPs may be declining in the United States driven, in part, by consumer preferences. Several major companies (including McDonald's, the fast food chain) have mandated the removal of AGPs from broiler production (MacDonald and Wang, 2011). In September 2014, Perdue Foods, the third-largest broiler company in the United States, announced that it had removed all antibiotics from its chicken hatcheries after phasing out the use of AGPs in its chicken production in 2007 (Perdue Foods, 2014). Some estimates indicate that 44% of U.S. broiler production no longer used AGPs in 2006, compared with 2% in 1995 (Chapman and Johnson, 2002; and MacDonald and Wang, 2011). USDA data suggest that the use of subtherapeutic antibiotics in hog production declined between 2004 and 2009—among farrow-to-finish operations, the use of antibiotics fed to finishing hogs for growth promotion dropped from 60% to 40% of market hog production between 2004 and 2009, and from 53% to 40% for nursery pigs (McBride and Key, 2013). However, there is no clear definition for “antibiotic-free” meat and poultry. USDA specifies that the label “no antibiotics added” may be used for meat or poultry products “if sufficient documentation is provided by the producer to the Agency demonstrating that the animals were raised without antibiotics.” This ambiguity led to the withdrawal in 2008 of the label “raised without antibiotics,” which USDA had approved for Tyson Foods in 2007, after disclosure that the company had used antibiotics for disease prevention in hatcheries.

Definitions of antibiotic use for growth promotion and disease prevention are even less clear. The term “subtherapeutic antibiotics” can include both growth promoters and antibiotics used for disease prevention, since some prophylaxis happens at low doses. Medicated feed additives can be authorized by FDA for

different purposes and are classified in two main categories: therapeutic uses and production purposes: “FDA considers uses that are associated with the treatment, control, and prevention of specific diseases to be therapeutic uses that are necessary for assuring the health of food-producing animals” (FDA, 2013a). Since many of the antibiotics approved for use in feed additives in the United States are authorized for both production purposes (growth promotion) and disease prevention, there is a risk that antibiotics could be reclassified from growth promotion to prophylaxis without actual changes in antibiotic use patterns. The Pew Charitable Trusts (2014) reviewed the labels of the 287 antibiotics covered by the FDA guidelines and identified that about one-quarter (66 of 287) of medically important antibiotics can be used in at least one species for disease prevention at levels fully within the range of growth promotion dosages and with no limit on the duration of treatment. Additionally, the FDA guidelines target only antibiotics classified as “medically important antimicrobials;” several antibiotics that are currently not considered medically important may still be used as growth promoters, even though they may indirectly contribute to resistance in human pathogens because of mechanisms of cross-resistance and co-selection.

The voluntary guidelines published by FDA in 2013 may be a first step towards more restrictions on antibiotic use in food animals. In creating the Task Force for Combating Antibiotic-Resistant Bacteria, a White House executive order in September 2014 specified that FDA, in coordination with USDA, “shall continue taking steps to eliminate the use of medically important classes of antibiotics for growth promotion purposes in food-producing animals” (U.S. Executive Office of the President, 2014).

If the benefits of AGPs (in terms of increased productivity) have diminished, then it becomes reasonable to be cautious and avoid the potential public health costs (in terms of increased resistance) rather than wait for a complete understanding of the ecology of gene flow between the animal, the environment, and human reservoirs. The use of antibiotics should principally be the last resort rather than a substitute for biosecurity, hygiene, and other good practices (Wierup, 2001). Antibiotics are not needed to promote growth, but they are essential to treat infectious diseases and maintain animal health. Since new antibiotic classes will likely not be available to veterinary medicine, it is in the best interests of food animal producers to preserve the effectiveness of existing veterinary antibiotics through antibiotic stewardship (Bengtsson and Greko, 2014). The challenge for policy makers is to find that balance between allowing use of antibiotics to control animal diseases and restricting their use to limit the emergence and spread of antibiotic resistance.

#### For More Information

- Aarestrup, F.M. 2012. “Sustainable Farming: Get Pigs off Antibiotics.” *Nature* 486:465 – 466.
- Aarestrup, F.M., V.F. Jensen, H.D. Emborg, E. Jacobsen, and H.C. Wegener. 2010. “Changes in the Use of Antimicrobials and the Effects on Productivity of Swine Farms in Denmark.” *American Journal of Veterinary Research* 71: 726–33.

- Aarestrup, F. M., A.M. Seyfarth, H.D. Emborg, K. Pedersen, R.S. Hendriksen, and F. Bager. 2001. “Effect of Abolishment of the Use of Antimicrobial Agents for Growth Promotion on Occurrence of Antimicrobial Resistance in Fecal Enterococci from Food Animals in Denmark.” *Antimicrobial Agents and Chemotherapy* 45 (7): 2054–59. doi:10.1128/AAC.45.7.2054-2059.2001.
- Bager, F., F.M. Aarestrup, M. Madsen, and H.C. Wegener. 1999. “Glycopeptide Resistance in Enterococcus Faecium from Broilers and Pigs Following Discontinued Use of Avoparcin.” *Microbial Drug Resistance* 5 (1): 53–56.
- Bager, F., M. Madsen, J. Christensen, and F.M. Aarestrup. 1997. “Avoparcin Used as a Growth Promoter Is Associated with the Occurrence of Vancomycin-Resistant Enterococcus Faecium on Danish Poultry and Pig Farms.” *Preventive Veterinary Medicine* 31 (1-2): 95–112.
- Bengtsson, B., and C. Greko. 2014. “Antibiotic Resistance—Consequences for Animal Health, Welfare, and Food Production.” *Upsala Journal of Medical Sciences* 119 (2): 96–102. doi:10.3109/03009734.2014.901445.
- Bogaard, A. E. van den, N. Bruinisma, and E.E. Stobberingh. 2000. “The Effect of Banning Avoparcin on VRE Carriage in The Netherlands.” *Journal of Antimicrobial Chemotherapy* 46 (1): 146–48. doi:10.1093/jac/46.1.146.
- Braude, R., H.D. Wallace, and T.J. Cunha. 1953. “The Value of Antibiotics in the Nutrition of Swine; a Review.” *Antibiotics and Chemotherapy* 3 (3): 271–91.

- Burroughs, W. 1959. "Five-Year Summary of More than 400 Experimental Comparisons of Feed Additives in Beef Cattle Rations at College Experimental Stations." American Society of Animal Production Extension Section Meeting, November.
- Brorsen, B.W. Brorsen, and T. Lehenbauer. 2002. "Economic Impacts of Banning Subtherapeutic Use of Antibiotics in Swine Production." *Journal of Agricultural and Applied Economics* 34 (3): 489–500.
- Campagnolo, E.R., K.R. Johnson, A. Karpati, C.S. Rubin, D.W. Kolpin, M.T. Meyer, and J.E. Esteban. 2002. "Antimicrobial Residues in Animal Waste and Water Resources Proximal to Large-Scale Swine and Poultry Feeding Operations." *The Science of the Total Environment* 299 (1-3): 89–95.
- Chapman, H.D. and Z.D., Johnson. 2002. "Use of antibiotics and roxarsone in broiler chickens in the USA: analysis for the years 1995 to 2000." *Poultry Science* 81(3):356-64.
- Chee-Sanford, J.C., R.I. Aminov, I.J. Krapac, N. Garrigues-Jeanjean, and R.I. Mackie. 2001. "Occurrence and Diversity of Tetracycline Resistance Genes in Lagoons and Groundwater Underlying Two Swine Production Facilities." *Applied and Environmental Microbiology* 67 (4): 1494–1502. doi:10.1128/AEM.67.4.1494-1502.2001.
- Coates, M.E., C.D. Dickinson, G.F. Harrison, S.K. Kon, S.H. Cummins, and W.F.J. Cuthbertson. 1951. "Mode of Action of Antibiotics in Stimulating Growth of Chicks." *Nature* 168 (4269): 332–332. doi:10.1038/168332a0.
- Cromwell, G.L. 2002. "Why and How Antibiotics Are Used in Swine Production." *Animal Biotechnology* 13 (1): 7–27. doi:10.1081/ABIO-120005767.
- Dibner, J.J., and J.D. Richards. 2005. "Antibiotic Growth Promoters in Agriculture: History and Mode of Action." *Poultry Science* 84 (4): 634–43.
- Dritz, S.S., M.D. Tokach, R.D. Goodband, and J.L. Nelssen. 2002. "Effects of Administration of Antimicrobials in Feed on Growth Rate and Feed Efficiency of Pigs in Multisite Production Systems." *Journal of the American Veterinary Medical Association* 220 (11): 1690–95.
- Emborg, H., A.K. Ersboll, O.E. Heuer, and H.C. Wegener. 2001. "The Effect of Discontinuing the Use of Antimicrobial Growth Promoters on the Productivity in the Danish Broiler Production." *Preventive Veterinary Medicine* 50: 53–70.
- Endtz, H.P., G.J. Ruijs, B. van Klingeren, W.H. Jansen, T. van der Reyden, and R.P. Mouton. 1991. "Quinolone Resistance in *Campylobacter* Isolated from Man and Poultry Following the Introduction of Fluoroquinolones in Veterinary Medicine." *The Journal of Antimicrobial Chemotherapy* 27 (2): 199–208.
- Engster, H.M., D. Marvil, and B. Stewart-Brown. 2002. "The Effect of Withdrawing Growth Promoting Antibiotics from Broiler Chickens: A Long-Term Commercial Industry Study." *The Journal of Applied Poultry Research* 11 (4): 431–36. doi:10.1093/japr/11.4.431.
- Gibbs, S. G., C.F. Green, P.M. Tarwater, L.C. Mota, K.D. Mena, and P.V. Scarpino. 2006. "Isolation of Antibiotic-Resistant Bacteria from the Air Plume Downwind of a Swine Confined or Concentrated Animal Feeding Operation." *Environmental Health Perspectives* 114 (7): 1032–37. doi:10.1289/ehp.8910.
- Graham, J.P., J.J. Boland, and E. Silbergeld. 2007. "Growth Promoting Antibiotics in Food Animal Production: An Economic Analysis." *Public Health Reports* 122 (1): 79–87.
- Graveland, H., J.A. Wagenaar, H. Heesterbeek, D. Mevius, E. van Duijkeren, and D. Heederik. 2010. "Methicillin Resistant *Staphylococcus Aureus* ST398 in Veal Calf Farming: Human MRSA Carriage Related with Animal Antimicrobial Usage and Farm Hygiene." Edited by Michael Otto. *PLoS ONE* 5 (6): e10990. doi:10.1371/journal.pone.0010990.
- Jensen, H.H. and D.J. Hayes. 2014. "Impact of Denmark's Ban on Antimicrobials for Growth Promotion." *Current Opinion in Microbiology* 19: 1-7.
- Hayes, D.J. and H.H. Jensen. 2003. "Lessons from the Danish Ban on Feed-Grade Antibiotics." Center for Agricultural and Rural Development Iowa State University. Available online: <http://www.card.iastate.edu/publications/dbs/pdf/03bp41.pdf>.
- Hays, V.W. 1977. "Effectiveness of Feed Additive Usage of Antibacterial Agents in Swine and Poultry Production." Lexington: University of Kentucky. Available online: <https://archive.org/stream/effectivenessoff00hays#page/n3/mode/2up>.
- Hill, D.C., H.D. Branion, S.J. Slinger, and G.W. Anderson. 1953. "Influence of Environment on the Growth Response of Chicks to Penicillin." *Poultry Science* 32 (3): 462–66. doi:10.3382/ps.0320462.



- Huber, H., N. Giezendanner, R. Stephan, and C. Zweifel. 2011. "Genotypes, Antibiotic Resistance Profiles and Microarray-Based Characterization of Methicillin-Resistant Staphylococcus Aureus Strains Isolated from Livestock and Veterinarians in Switzerland: Further Characterization of MRSA Strains." *Zoonoses and Public Health* 58 (5): 343–49. doi:10.1111/j.1863-2378.2010.01353.x.
- Huijsdens, X.W., B.J. Van Dijke, E. Spalburg, M.G. van Santen-Verheul, M.E. Heck, G.N. Pluister, A. Voss, W.J.B. Wannet, and A.J. De Neeling. 2006. "Community-Acquired MRSA and Pig-Farming." *Annals of Clinical Microbiology and Antimicrobials* 5 (1): 26.
- Hurd, H.S., J. Brudvig, J. Dickson, J. Mirceta, M. Polovinski, N. Matthews, and R. Griffith. 2008. "Swine Health Impact on Carcass Contamination and Human Foodborne Risk." *Public Health Reports* 123 (3): 343–51.
- Jakobsen, L., A. Kurbasic, L. Skjøt-Rasmussen, K. Ejrnaes, L.J. Porsbo, K. Pedersen, L.B. Jensen. 2010a. "Escherichia Coli Isolates from Broiler Chicken Meat, Broiler Chickens, Pork, and Pigs Share Phylogroups and Antimicrobial Resistance with Community-Dwelling Humans and Patients with Urinary Tract Infection." *Foodborne Pathogens and Disease* 7 (5): 537–47. doi:10.1089/fpd.2009.0409.
- Jakobsen, L., D.J. Spangholm, K. Pedersen, L.B. Jensen, H.-D. Emborg, Y. Agersø, F.M. Aarestrup, A.M. Hammerum, and N. Frimodt-Møller. 2010b. "Broiler Chickens, Broiler Chicken Meat, Pigs and Pork as Sources of ExPEC Related Virulence Genes and Resistance in Escherichia Coli Isolates from Community-Dwelling Humans and UTI Patients." *International Journal of Food Microbiology* 142 (1-2): 264–72. doi:10.1016/j.ijfoodmicro.2010.06.025.
- Jukes, T.H., E.L.R. Stokstad, R.R. Taylor, T.J. Cunha, H.M. Edwards, and G.B. Meadows. 1950. "Growth-Promoting Effect of Aureomycin on Pigs." *Archives of Biochemistry* 26 (2): 324–25.
- Key, N., and W.D. McBride. 2014. "Sub-Therapeutic Antibiotics and the Efficiency of U.S. Hog Farms." *American Journal of Agricultural Economics* 96 (3): 831–50. doi:10.1093/ajae/aat091.
- Khanna, T., R. Friendship, C. Dewey, and J.S. Weese. 2008. "Methicillin Resistant Staphylococcus Aureus Colonization in Pigs and Pig Farmers." *Veterinary Microbiology* 128 (3-4): 298–303. doi:10.1016/j.vetmic.2007.10.006.
- Klare, I., D. Badstübner, C. Konstabel, G. Böhme, H. Claus, and W. Witte. 1999. "Decreased Incidence of VanA-Type Vancomycin-Resistant Enterococci Isolated from Poultry Meat and from Fecal Samples of Humans in the Community after Discontinuation of Avoparcin Usage in Animal Husbandry." *Microbial Drug Resistance* 5 (1): 45–52.
- Liu, X., G.Y. Miller, and P.E. McNamara. 2003. "Do Antibiotics Reduce Production Risk For U.S. Pork Producers?" 2003 Annual meeting, July 27-30, Montreal, Canada 22026. American Agricultural Economics Association Available online: <http://ideas.repec.org/p/ags/aaea03/22026.html>.
- MacDonald, J.M., and S.-L. Wang. 2011. "Foregoing Sub-Therapeutic Antibiotics: The Impact on Broiler Grow-out Operations." *Applied Economic Perspectives and Policy* 33 (1): 79–98. doi:10.1093/aapp/ppq030.
- Maron, D., T. Smith, and K. Nachman. 2013. "Restrictions on Antimicrobial Use in Food Animal Production: An International Regulatory and Economic Survey." *Globalization and Health* 9 (1): 48.
- Marshall, B.M., and S.B. Levy. 2011. "Food Animals and Antimicrobials: Impacts on Human Health." *Clinical Microbiology Reviews* 24 (4): 718–33. doi:10.1128/CMR.00002-11.
- McBride, W. and N. Key. 2013. *U.S. Hog Production From 1992 to 2009: Technology, Restructuring, and Productivity Growth*. U.S. Department of Agriculture, Economic Research Service, Economic Research Report-158, October.
- McBride, W.D., N. Key, and K.H. Mathews. 2008. "Subtherapeutic Antibiotics and Productivity in U.S. Hog Production." *Applied Economic Perspectives and Policy* 30 (2): 270–88. doi:10.1111/j.1467-9353.2008.00404.x.
- Mellièrè, A.L., H. Brown, and R.P. Rath. 1973. "Finishing Swine Performance and Response to Tylosin." *Journal of Animal Science* 37: 286.

- Miller, G.Y. P.E. McNamara, and E.J. Bush. 2003. "Productivity and Economic Effects of Antibiotics Used for Growth Promotion in Pork Production." *Journal of Agricultural and Applied Economics* 35: 469-482.
- Miller, G.Y., X. Liu, P.E. McNamara, and E.J. Bush. 2005. "Farm-Level Impacts of Banning Growth-Promoting Antibiotic Use in U.S. Pig Grower/Finisher Operations." *Journal of Agribusiness* 23 (2). Available online: <http://econpapers.repec.org/article/agsjloagb/59680.htm>.
- Moore, P.R., A. Evenson, T.D. Luckey, E. McCoy, C.A. Elvehjem, and E.B. Hart. 1946. "Use of Sulfasuxidine, Streptothricin, and Streptomycin in Nutritional Studies with the Chick." *Journal of Biological Chemistry* 165 (2): 437-41.
- Nelson, J.M., T.M. Chiller, J.H. Powers, and F.J. Angulo. 2007. "Fluoroquinolone-Resistant *Campylobacter* Species and the Withdrawal of Fluoroquinolones from Use in Poultry: A Public Health Success Story." *Clinical Infectious Diseases* 44 (7): 977-80. doi:10.1086/512369.
- Pantosti, A., M. Del Grosso, S. Tagliabue, A. Macri, and A. Caprioli. 1999. "Decrease of Vancomycin-Resistant Enterococci in Poultry Meat after Avoparcin Ban." *Lancet* 354 (9180): 741-42. doi:10.1016/S0140-6736(99)02395-8.
- Rosen, G.D. 1995. "Antibacterials in poultry and pig nutrition." In Wallace R.J. and A. Chesson, ed. *Biotechnology in Animal Feeds and Animal Feeding*. Wiley-VCH Verlag GmbH, Weinheim, Germany. doi: 10.1002/9783527615353.ch8.
- Ryan, F.A., L.M. Potter, E.P. Singen, and L.D. Matterson. 1961. "The Continuous Feeding of an Antibiotic to Laying Hens." *Poultry Science* 40 (5): 1142-51. doi:10.3382/ps.0401142.
- Salinas-Chavira, J., J. Lenin, E. Ponce, U. Sanchez, N. Torrentera, and R.A. Zinn. 2009. "Comparative Effects of Virginiamycin Supplementation on Characteristics of Growth-Performance, Dietary Energetics, and Digestion of Calf-Fed Holstein Steers." *Journal of Animal Science* 87 (12): 4101-8. doi:10.2527/jas.2009-1959.
- Singer, R.S., L.A. Cox Jr., J.S. Dickson, H.S. Hurd, I. Phillips, and G.Y. Miller. 2007. "Modeling the Relationship between Food Animal Health and Human Foodborne Illness." *Preventive Veterinary Medicine* 79 (2-4): 186-203. doi:10.1016/j.prevetmed.2006.12.003.
- Smith, T.C., M.J. Male, A.L. Harper, J.S. Kroeger, G.P. Tinkler, E.D. Moritz, A.W. Capuano, L.A. Herwaldt, and D.J. Diekema. 2009. "Methicillin-Resistant *Staphylococcus Aureus* (MRSA) Strain ST398 Is Present in Midwestern U.S. Swine and Swine Workers." Edited by U. Dobrindt. *PLoS ONE* 4 (1): e4258. doi:10.1371/journal.pone.0004258.
- Sneeringer, S. 2014. "The Economics of Sub-Therapeutic Antibiotic Use in U.S. Livestock Agriculture." Paper presented at the Antibiotic Resistance at the Animal-Human Interface Workshop, Princeton University NJ, May 13.
- Sørensen, T.L., M. Blom, D.L. Monnet, N. Frimodt-Møller, R.L. Poulsen, and F. Espersen. 2001. "Transient Intestinal Carriage after Ingestion of Antibiotic-Resistant Enterococcus Faecium from Chicken and Pork." *The New England Journal of Medicine* 345 (16): 1161-66. doi:10.1056/NEJMoa010692.
- Speer, V.C., R.L. Vohs, D.V. Catron, H.M. Maddock, and C.C. Culbertson. 1950. "Effect of Aureomycin and Animal Protein Factor on Healthy Pigs." *Archives of Biochemistry* 29: 452-53.
- Starr, M.P., and D.M. Reynolds. 1951. "Streptomycin Resistance of Coliform Bacteria from Turkeys Fed Streptomycin." *American Journal of Public Health and the Nations Health* 41 (11 Pt 1): 1375-80.
- Thaler, B. 2010. "Feed Additives for Swine - 2010 National Swine Nutrition Guide." South Dakota State University. Available online: <http://bit.ly/1wS9Roc>.
- The Pew Charitable Trusts. 2014. "Gaps in FDA's Antibiotics Policy." November 30. Available online: <http://bit.ly/1uElZLZ>.
- Thomke, E. 1998. "Growth Promotants in Feeding Pigs and Poultry. I. Growth and Feed Efficiency Responses to Antibiotic Growth Promotants." *Annales de Zootechnie - Animal Research* 47 (2): 85-97. doi:10.1051/animres:19980201.
- U.S. Centers for Disease Control. 2013. *Antibiotic Resistance Threats in the United States, 2013*. Available online: <http://www.cdc.gov/drugresistance/threat-report-2013/index.html>.
- U.S. Executive Office of the President. 2014. "Executive Order—Combating Antibiotic-Resistant Bacteria." The White House. Available online: <http://www.whitehouse.gov/node/298751>.

- U.S. Food and Drug Administration. 2012. *Drug Use Review*. Available online: <http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM319435.pdf>.
- U.S. Food and Drug Administration. 2013a. *Guidance for Industry #213: New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209*. Available online: <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf>
- U.S. Food and Drug Administration. 2013b. *National Antimicrobial Resistance Monitoring System – Enteric Bacteria: 2011 Executive Report*. Available online: <http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm409035.htm>.
- U.S. Food and Drug Administration. 2014. FDA Annual Summary Report on Antimicrobials Sold or Distributed in 2012 for Use in Food-Producing Animals. Available online: <http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm416974.htm>.
- Van Cleef, B.A.G.L., H. Graveland, A.P.J. Haenen, A.W. van de Giesen, D. Heederik, J.A. Wagenaar, and J.A.J.W. Kluytmans. 2011a. “Persistence of Livestock-Associated Methicillin-Resistant *Staphylococcus Aureus* in Field Workers after Short-Term Occupational Exposure to Pigs and Veal Calves.” *Journal of Clinical Microbiology* 49 (3): 1030–33. doi:10.1128/JCM.00493-10.
- Van Cleef, B.A.G.L., D.L. Monnet, A. Voss, K. Krziwanek, F. Allerberger, M. Struelens, H. Zemlickova. 2011b. “Livestock-Associated Methicillin-Resistant *Staphylococcus Aureus* S in Humans, Europe.” *Emerging Infectious Diseases* 17 (3): 502–5. doi:10.3201/eid1703.101036.
- Van Lunen, T.A. 2003. “Growth Performance of Pigs Fed Diets with and without Tylosin Phosphate Supplementation and Reared in a Biosecure All-in All-out Housing System.” *The Canadian Veterinary Journal* 44 (7): 571–76.
- Voss, A., F. Loeffen, J. Bakker, C. Klaassen, and M. Wulf. 2005. “Methicillin-Resistant *Staphylococcus Aureus* in Pig Farming.” *Emerging Infectious Diseases* 11 (12): 1965.
- Wegener, H.C., F.M. Aarestrup, L. Bogø Jensen, A.M. Hammerum, and F. Bager. 1999. “Use of Antimicrobial Growth Promoters in Food Animals and Enterococcus Faecium Resistance to Therapeutic Antimicrobial Drugs in Europe.” *Emerging Infectious Diseases* 5 (3): 329.
- Wierup, M. 2001. “The Swedish Experience of the 1986 Year Ban of Antimicrobial Growth Promoters, with Special Reference to Animal Health, Disease Prevention, Productivity, and Usage of Antimicrobials.” *Microbial Drug Resistance* 7: 183–90.
- World Health Organization (WHO). 2002. *Impacts of antimicrobial growth promoter termination in Denmark*. Report WHO/CDS/CPE/ZFK/2003.1, November.
- You, Y., and E.K. Silbergeld. 2014. “Learning from agriculture: understanding low-dose antimicrobials as drivers of resistome expansion.” *Frontiers in Microbiology* 5:284.
- Zimmerman, D.R. 1986. “Role of Sub-therapeutic Levels of Antimicrobials in Pig Production.” *Journal of Animal Science* 62 (Supplement 3): 6–16.

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