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Alternatives to Antibiotics in Food Production Animals

The recently-issued FDA guidance has added more fuel to an already burning debate about the practices and long-term human consequences of antibiotic use in livestock. Are natural ingredients a viable solution?

by Joanna Cosgrove

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At a time when consumers have never been more inquisitive and discriminating about the origins of their food, the feed animal industry has faced a great deal of scrutiny regarding its use of antibiotics and antimicrobials, and the prospect of their trickle-down effects on human health. From a producer's point of view, antibiotics are an important part of managing disease and ensuring growth and production goals are met. From a consumer-safety point of view, there are legitimate fears that the overuse of antibiotics contributes to the evolution of "superbugs" that are resistant to standard antibiotic treatment. To that end, feed ingredient suppliers have worked to develop a variety of natural alternatives that deliver comparable results without the side effects.

Regulatory Overview: The Great Debate

The use of antibiotics in food production animals was originally intended for the purpose of keeping animals healthy. As the industry grew and adapted to meet the demands of feeding more people, traditional livestock farming could no longer keep pace. The current system of addressing animal health with feed-based antibiotics began in the late 1940s. By the late 1960s, scientists began raising concerns about the safety and implications of antibiotic use in feed animals, giving way to 1969's landmark Swann Report, which formally discussed the merits of the practice.

From a regulatory standpoint, the U.S. stance on the issue contrasts starkly with that of its global neighbors. Unlike the comprehensive ban on the use of antibiotics on food production animals in Europe, in late 2013, FDA eschewed formal regulations in lieu of self-governed guidance, citing a willingness to wait for concrete scientific proof linking feed animal antibiotic practices with effects on human health. The directive encouraged the voluntary elimination of antimicrobials and antibiotics used for growth purposes, and suggested a reduction in the use of antibiotics for treatment or therapeutic use in livestock.

The plan also established a three-year time frame to phase out antibiotics used for growth promotion, as well as calling for therapeutic and targeted-use antibiotics to be managed by greater veterinary oversight.

“Implementing this strategy is an important step forward in addressing antimicrobial resistance,” said Michael Taylor, FDA’s deputy commissioner for foods and veterinary medicine, in a statement. “The FDA is leveraging the cooperation of the pharmaceutical industry to voluntarily make these changes because we believe this approach is the fastest way to achieve our goal. Based on our outreach, we have every reason to believe that animal pharmaceutical companies will support us in this effort.”

As expected, the guidance ignited a fiery debate that included public health advocacy groups, lawmakers and others with vested interests. Some opponents of the guidance held that the 2013 Centers for Disease Control and Prevention (CDC) report¹ specifically called for the judicious use of antibiotics in food-producing animals in light of the “persistence and spread of antibiotic-resistant bacteria.”

The CDC report referenced “strong evidence” from scientists around the world that antibiotic use in food-producing animals can harm public health through the following sequence of events:

- Use of antibiotics in food-producing animals allows antibiotic-resistant bacteria to thrive, while susceptible bacteria are suppressed or die.
- Resistant bacteria can be transmitted from food-producing animals to humans through the food supply.
- Resistant bacteria can cause infections in humans.
- Infections caused by resistant bacteria can result in adverse health consequences for humans.

“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 wrote. “CDC encourages and supports efforts to minimize inappropriate use of antibiotics in humans and animals, including FDA’s strategy to promote the judicious use of antibiotics that are important in treating humans.”

Last year’s FDA guidelines were met with particular disdain by Rep. Louise Slaughter (D-NY), a microbiologist and vocal champion of public health issues, who termed the response to the “growing antibiotic resistant crisis caused by overuse of antibiotics on the farm” as “inadequate.”

“The FDA’s voluntary guidance is an inadequate response to the overuse of antibiotics on the farm with no mechanism for enforcement and no metric for success,” she commented in a statement. “Sadly, this guidance is the biggest

¹ CDC: *Antibiotic Resistance Threats in the United States, 2013*, p.36-37.

step the FDA has taken in a generation to combat the overuse of antibiotics in corporate agriculture, and it falls woefully short of what is needed to address a public health crisis.”

Slaughter referenced her proposed legislation—the Preservation of Antibiotics for Medical Treatment Act (PAMTA)—as a mandatory measure that would protect eight classes of antibiotics for use on humans and sick animals only. She said that although PAMTA is currently backed by more than 450 medical and consumer advocate groups, it has been met with strong opposition by the agribusiness and pharmaceutical industries that FDA expects to comply with the voluntary guidance.

Slaughter pointed to trends in Europe that she said were proof that voluntary directives were not effective in stopping the overuse of antibiotics on the farm. “In 2006, the European Union issued a directive urging agriculture companies to limit the use of antibiotics in food animals, but therapeutic antibiotic use increased to compensate,” she said. “Agricultural antibiotic use only declined in countries that instituted their own limits, like the Netherlands, [which] saw a steep decline in 2009 when fines were instituted for noncompliance.”

The regulatory atmosphere in Europe is decidedly more hard-lined. “The Europeans have decided that if antibiotics have any potential risk of transferring resistance to humans, they shouldn’t be used in animals,” explained Aidan Connolly, vice president of Alltech, a supplier of natural animal nutrition technologies. “The Europeans use the term ‘precautionary principle,’ which means that even if antibiotics are important for human health, they believe it’s not wise to allow their use in animal nutrition—particularly if they are going to be used in human health to treat diseases.”

Approximately 40 countries have introduced restrictions on sub-therapeutic antibiotics (those that are used to keep an animal healthy, as opposed to treating a disease), including the countries in the EU, Brazil, Argentina, Middle East countries, India, Japan and Korea.

Outside of the United States, there’s a greater inclination for transparency. In 1995, the Danish Ministry of Food, Agriculture and Fisheries and the Danish Ministry of Health established the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme. DANMAP’s goals were to monitor the consumption of antimicrobial agents for food animals and humans, and the occurrence of antimicrobial resistance in bacteria isolated from food animals, food of animal origin and humans; to track associations between antimicrobial consumption and antimicrobial resistance; and to identify routes of transmission and areas for further research studies.



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"In the late 1990s, [the Danes] were the first to remove antibiotics from their feed and only allowed them to be used if the animal was sick," Connolly said. "Their findings are published annually online [and have led] other countries like Germany and The Netherlands to start publishing their own reports as well. The U.K. has also talked about doing it, too."

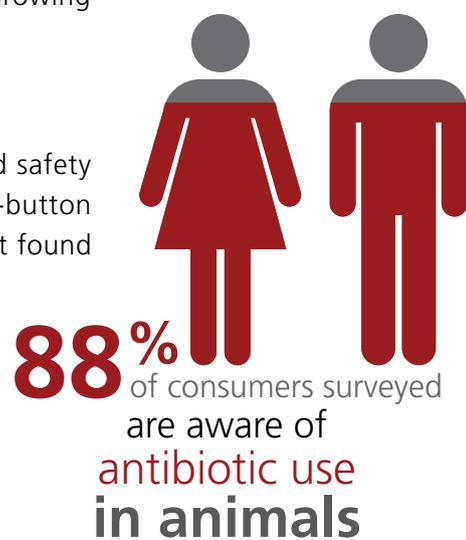
Interestingly, the International Federation for Animal Health (IFAH) expressed its support of the FDA guidance, commenting that "antibiotics are a vital tool in any veterinarian's toolbox."

Mike McGowan, IFAH's acting executive director, stated, "The responsible use of antibiotics, including the principle 'as much as necessary, as little as possible,' and under the supervision of a veterinarian, needs to be further encouraged." He continued, "Animal health is inextricably linked to human health, nutrition and well-being, so ensuring that animals get the therapy they need, when they need it, is vital for all concerned."

As for what the future might hold for additional U.S. action, Rick Phillips, president and CEO, Anitox, said politics and the potential for litigation will most certainly be the driving undercurrent. "In general, FDA and USDA have had a tendency to not over-respond in a legislative format. They encourage companies to move in a certain direction through basic regulation maneuvers and then put litigation on top of it, letting the consumer make the decision," he commented. "Like we saw with the veterinary feed directive—it's voluntary that the pharmaceutical companies change the use of the products. You can imagine if they don't and someone makes a case against them, there's a tremendous litigation potential. Companies are going to move away from it; they're not going to wait for the legislation," he continued. "Consumer perception is that antibiotics are bad in animals and there's a growing market for non-antibiotic use."

Sizing Up Consumer Attitudes

The consumer mindset as it relates to feed animal health and safety has ebbed and flowed in recent decades. Right now, it's a hot-button issue. Midan Marketing recently conducted a consumer poll that found 88 percent of consumers were aware of antibiotic use in animals—and 60 percent had concerns about it. After hearing/reading about the use of antibiotics and growth hormones in livestock, 17 percent said they stopped buying meat when they thought antibiotics and/or growth hormones were used, and 46 percent said they started paying more attention to meat packaging.²



² Midan Marketing, *Antibiotics and Growth Hormones: The Consumer Mindset*, 2013.

There were some noteworthy misconceptions though, according to Danette Amstein, principal of Midan Marketing. “Worth considering is the fact that 86 percent of our respondents did not recognize the following statement as true: ‘By the time fresh meat is sold at the grocery store, there is no longer any antibiotics in it,’” she said. “This is a very clear indication that consumers have not been properly educated about antibiotic use in livestock and are not getting the right information.”

Amstein said the takeaway of their research was that communication and transparency are paramount. “Given the level of consumer awareness and concern around the use of antibiotics in livestock, those of us in agriculture must take note and do a better job of explaining the use,” she said. “We have to also understand that public outcry is often fueled by a source, and if we remain silent and don’t take the time and energy to explain why antibiotics are used, that source ends up with a loud, unchallenged platform.”

So given the CDC’s warnings about antibiotic resistance, plus the prevalence of media reports about food-borne pathogens such as *E. coli* and *Salmonella*, is the consumer worry about the use of antibiotics in food supply livestock justified?

Anitox’s Phillips thought the overall response was politically “over-hyped.” “From a veterinary perspective, if we look at the empirical data and medical science, I think the risk and concern are very minimal,” he said.

“If you look at antibiotics and what they’re used for, it hasn’t really been to treat; it’s been prophylactic use for growth promotion,” he continued, and stressed that antibiotics should not be confused with growth hormones. “Antibiotics are put in the feed and consumed by the animal to modify the good intestinal flora in the gut [and] prevent bad bacteria from overwhelming the intestinal tract. You’re basically treating the animal in the gut with an antibiotic.”

Anitox markets a portfolio of feed additives formulated to control feed microbe contaminants to increase feed values and improve livestock performance. One of its top products is Termin-8®, an FDA-approved, pathogen-controlling feed additive that’s licensed for use in 64 countries around the world. A key component in Termin-8 is formaldehyde—an ingredient that may raise eyebrows among some ardent label readers.

Phillips explained that the formaldehyde, a potent disinfectant and microbe killer, maintains a 14-day window in the feed—beginning during the manufacturing phase and lasting through the storage phase—after which it subsequently breaks down into formic acid before being consumed by the



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animal. “A lot of the problems we have with respect to food safety get into the operations in different ways and one way is feed,” he said. “It usually comes in after the feed is made through recontamination by birds, insects and handling.”

As for the safety of the formula, Phillips said that although “formaldehyde” implies an undesirable undertone, it’s essentially harmless. “The level of formaldehyde we use in our feed is very similar to eating two apples—we consume formaldehyde every day,” he said. “It’s a very safe product; the problem is formaldehyde has a negative connotation to it.”

But in an industry where perception is a driving force, Phillips said Anitox is prepping to launch a new formula in May 2014 that’s similar to Termin-8 but formaldehyde free. Trials have shown comparable results in the control of *Salmonella*, *E.coli* and *Clostridia*.

Citing the power of the media-driven consumer voice, he summed up why companies have begun embracing alternative solutions: “When a tailwind becomes a headwind—just like our formaldehyde—the energy, time and money it would take to fight that are better spent in R&D to come up with a better solution.”

Natural Alternatives

Despite the assurance of various groups and authorities, consumers continue to be decidedly skeptical about the ripple effect of antibiotics used in livestock. In response, natural ingredient suppliers have stepped up to the challenge of offering a variety of significant alternatives ranging from essential and functional oil-based formulas to those including beta-glucans and pre- and probiotics.

“The public is demanding a cleaner, safer product [and] the all-natural, antibiotic-free revolution is ready to start,” said Chris Lester, vice president of operations, Advanced Ag Products, makers of By-O-reg+.

By-O-reg+ is a natural chicken feed additive comprised of encapsulated oregano oil (5 percent carvacrol) blended with cassia oil (part of the cinnamon family, containing an aldehyde cinnamaldehyd), beta-glucans and vitamin C that work in concert to help control disease and stimulate the animal’s immune system. The carvacrol is encapsulated to help prevent oxidation, and to ensure the concentrated essential oil is delivered to the digestive tract. The company is also testing a version of the formula that includes cranberry for added health benefits.

Lester asserted natural alternatives are more economical than traditional solutions. He also said when the immunity of a livestock animal is improved, the animal is better equipped to combat unexpected illnesses, presumably eliminating the need for antibiotics. “A major side benefit is that the healthier animal is better able to process the feed it consumes,” he said. “This healthier animal is then passing on these benefits to its young, creating a healthier, heavier hog that is significantly cheaper to raise.”

Lester said, however, that changing long-held mindsets is never easy. “It’s extremely hard to get the nutritionists and veterinarians to think outside the box and try a new product,” he said. “The new generation of veterinarians and nutritionists are just starting to break in and change the mindset of the industry.”

Farm owners are equally difficult converts. However, in an interview with *The New York Times*, Scott Sechler, president of the Bell & Evans poultry product company, suddenly became the movement’s foremost cheerleader about the antibacterial benefits his chickens experienced after implementing feed that included oregano oil.

Lester said Sechler’s experience is critical to the organic community. “His use of By-O-reg+ in his broilers, and the sale of these birds at organic food mecca Whole Foods, is the push that the organic revolution needs in overcoming the corporate reliance upon drugs and growth hormones,” he said.

Orego-Stim®, another oregano-based natural feed additive containing natural bioflavonoids, was recently launched by Meriden Animal Health. According to the company, Orego-Stim is a non-encapsulated product because its “unique aroma produced by these oils reinforces the appetite, leading to improved feed consumption.”

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For animals such as pigs, which have a well-developed olfactory-glossopharyngeal response, the scent stimulates appetite and increases the production of saliva and digestive enzymes, improving both feed intake and digestion. Meriden stated its Orego-Stim is not absorbed through the intestines, so it can focus its unique mode of action on the entire length of the gastrointestinal tract, conveying protection against parasitic species such as *Eimeria*, which can induce necrotic enteritis in chickens.

Clostat™ from Kemin Industries is also indicated for the reduced risk of necrotic enteritis in poultry. The ingredient contains the proprietary *Bacillus subtilis*, PB6, which was developed to maintain microflora balance to ensure gut integrity.

“Research shows that Clostat reduces pathogenic *Clostridium perfringens* while maintaining the growth of beneficial bacteria such as *Lactobacilli* and *Bifidobacterium*,” said Dr. Raju Chanthirasekaran, global product manager, Kemin Industries in an interview with *Feed Info News Service* earlier this year. “Furthermore, Clostat does not create antibiotic resistance or residue concerns, so it is becoming widely adopted in poultry diets.”

He explained Clostat is stable at common pelleting temperatures, safe for animal consumption and human handling, and compatible with commonly-used feed additives. The ingredient has received full European Commission approval to use the ingredient for the fattening of piglets, chickens, turkeys and other minor poultry species.

Another alternative ingredient with promise is Farmatan® from Prinova, an EU-approved alternative to pharmaceutical antimicrobials. An all-natural, hydrolyzable tannin extract from Slovenian sweet chestnut trees, polyphenol-rich Farmatan was found to deliver antimicrobial, antifungal, antioxidant and anticoccidial benefits to chickens.

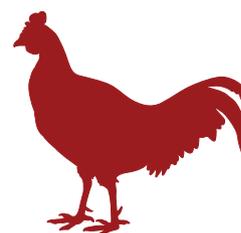
At the heart of Oligo Essential, a functional oil ingredient from World Ag Associates LLC, are natural castor oil and cashew nut shell liquid, which provide beneficial ricinoleic acid (anti-inflammatory), antioxidant cardol and cardanol. Oligo Essential is a multifunctional feed additive with antimicrobial, anti-inflammatory and antioxidant activities—all of which are supported by various academic and research based publications,” said Garrett Goto, the company’s technical director. “Our feed additive can be included in the diet at any age for all poultry, swine and/or ruminant species.”

A deeper understanding of the effect of natural alternatives is also warranted, said Roger Clemens, DrPH, chief scientific officer, Horn Animal Wellness, a distributor of a range of ingredients for animal health. “Every animal is unique and they don’t all respond the same way to different ingredients,” he said. “Every model of animal places an important emphasis on the totality of understanding ingredients like lactoferrin, oligosaccharide and beta-glucan—which represent the future of how we possibly can reduce the use of antibiotics and perhaps involve some vaccines, while at the same time provide better health for our animals.”

Alltech’s Connolly stressed that in most cases, the use of one ingredient isn’t as critical as a total program approach (which usually includes three to five interventions). “Going in with a single intervention typically does not provide anywhere near the benefit as doing multiple things at the same time,” he said.

And any program is best started as early as possible. “In the case of chickens, they need to drink three to four times as much as they eat, so you need to look at what you can do through their water—and typically, the use of water that is more acidic is better because it helps favor the good bacteria,” he said. “The feed must also be made to be as digestible as possible.”

He went on to explain the great potential for crossover treatments between human and animal fields. “Some of the things you hear about in the human field—prebiotics, probiotics, natural coccidiostats—we have clear research in animals demonstrating



Chickens
need to *drink*



3-4x
as much as they

EAT



how they work and how to use them cost-effectively," he said, noting that the use of probiotics in livestock can have particular caveats. "You have to be very careful using probiotics; they have to be live organisms, and must be delivered in the right number at the right time. It's also clear that animals do better with multiple strains of probiotics, not a single strain."

Alltech focuses on prebiotics, "technological sugars" (not simple fructose) called mannan-rich fractions, which are inert sugars that can be heat-treated without the threat of compromised viability. The company actively participates in trials with universities and research institutions around the world. "We have a huge database of information and are the number two investor in U.S. agricultural research after the U.S. government," Connolly said.

As the industry begins its transition to adopt FDA's guidance on livestock antibiotics during the next three years, Connolly said there will likely be a cost impact transferred to consumers due to all of the pieces that are in play. "Based on what we've seen in other countries, we will see prices increase in the cost of meat, milk and eggs," he predicted. He also noted that without the use of antibiotics as growth promoters, it would take approximately 2 percent more product to feed an animal—or the animal would produce 2 percent less for the same amount of feed. "To overcome that, you in essence need to look at other processes, including management improvements (only selecting the most professional farmers or producers), and really controlling disease right away when it happens," he stated.

Connolly concluded by saying although therapeutic antibiotics will always have a place in livestock disease control, natural technologies are the logical choice to fill other voids. "There will be a lot of embracing of natural technologies," he said. "Some new non-antibiotic technologies are more effective than others, but they're certainly going to be looked at by a lot of people who want to try to overcome what they could lose." □

Joanna Cosgrove is a freelance writer who has been covering the dynamic facets of the dietary supplement, functional food and beverage, and animal wellness industries for more than 15 years. Her work has appeared in a variety of respected industry publications.



We will see
prices increase
in the cost of
**meat, milk
and eggs**

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