Institute for Agriculture and Trade Policy

Fueling Resistance?
Antibiotics in Ethanol Production

Fueling Resistance? Antibiotics in Ethanol Production

by Julia Olmstead
Institute for Agriculture and Trade Policy
Minneapolis, Minnesota

Published July 2009

The Institute for Agriculture and Trade Policy works locally and globally at the intersection of policy and practice to ensure fair and sustainable food, farm and trade systems.

Introduction

The epidemic of antibiotic resistance globally poses a severe threat to human and animal health. Deaths and infections caused by "superbugs," which are unresponsive to treatment with multiple antibiotics, are the human face of this problem.

The use and overuse of antibiotics is a key driver of resistance in hospitals as well as on farms.[1,2,3] For instance, the best available estimates are that about 84 percent of all antimicrobials in the U.S. are used in agriculture.[4]

Lately, there have been reports of a new and heretofore unrecognized source of unregulated antibiotic use: the ethanol industry.

For decades, ethanol producers have added antibiotics to the ethanol fermentation process to control bacterial outbreaks, and for most of that time, they have claimed the antibiotics dissipate or are rendered inactive during production. But in 2008, the Food and Drug Administration (FDA) began testing dried distillers grains—the nutrient-rich residue sold as livestock feed that is a co-product of ethanol production—for antibiotic residues. The test results came back positive for erythromycin, tylosin (a similar macrolide antibiotic that may also spur cross-resistance to erythromycin) and virginiamycin (a streptogramin antibiotic with an important human analogue, Synercid), which doctors also depend on for treating sick patients.

The National Academies of Science, among many others, have called for an end to the indiscriminate and unnecessary use of antibiotics. In addition, the FDA recently told Congress that it supports a ban on non-therapeutic use of antibiotics in the raising of food animals.[5] The ethanol industry—along with the livestock sector and other industrial users—needs to move quickly as a sector to end the use of antibiotics. Luckily, there are existing alternatives to antibiotics use for controlling bacteria and many ethanol producers are already putting these alternatives into practice. In this report, IATP looks at the implications of antibiotic use in ethanol production and points the way toward an antibiotic-free ethanol industry.

Why antibiotics?

In theory, starch-based ethanol production is relatively simple. Grind up a starchy feedstock like corn and add water to make a mash; add yeast, then sit back and watch as the yeast ferment the starch into ethanol and carbon dioxide. In practice, of course, it is much more complicated.

Ethanol fermentation tanks routinely become contaminated with bacteria. The most problematic is a class known as "lactic acid bacteria" that includes *Lactobacillus*, *Pediococcus*, *Leuconostoc* and *Weissella*.[6] Yeast converts starch to ethanol, but bacteria convert those same sugars to lactic or acetic acid. If the bacteria get out of control, ethanol production yields can drop significantly, an estimated 1-5 percent, which is no small economic problem for producers.[7]

Scientists and producers don't entirely understand where the bacteria come from, but suspect they enter on the feedstock (predominately corn) coming into the ethanol plant or are already present in the plant's environment. The bacteria often build up in places where the flow slows down in the fermenter, along turns in piping, heat exchangers or valves, for example. Cleaning and sanitation of the feedstock and fermentation tanks can help control bacterial populations, but when cleaning is not enough, ethanol producers often turn to antibiotics. Most commonly, they add penicillin, virginiamycin, erythromycin, tylosin or tetracycline to the fermenters, killing off the bacteria and leaving the yeast unharmed. All of these are identical or nearly so to antibiotics also used in human medicine.

As with any regularly used antibiotic, however, the doses become less and less effective as the bacteria become resistant. Producers are forced to continually increase dosage levels and cycle through different types of antibiotics to keep them effective. Recent research has identified several strains of bacteria living in ethanol fermentation tanks that are resistant to penicillin and virginiamycin, the most commonly used antibiotics in ethanol production.[8]

While human antibiotics can only be bought by prescription, those used in ethanol plants are available in bulk to anyone "over-the-counter" at farm and feed supply stores—or even over the Internet.[9] Many of these antibiotics come from overseas distributors. The amount of antibiotics added to the ethanol process also is under effectively no oversight or regulation. This makes it nearly impossible to estimate with any accuracy the amounts of antibiotics used by the ethanol industry.

Distillers grains and antibiotic residues

The ethanol fermentation process uses only the starch from the corn or other feedstock. What's left—the protein, fiber and oil—can be processed and sold as "dried distillers grains with solubles" (DDGS), a nutrient-rich animal feed that is regularly added to or substituted in for corn- and soybean-based feed for beef and dairy cattle and for poultry. DDGS play a significant role in keeping an ethanol plant afloat financially—on average, sales of DDGS make up about 20 percent of a plant's revenue stream.[10]

In 2008, the FDA tested 60 DDGS samples for residues of virginiamycin, tylosin and erythromycin. Of the 45 samples analyzed, 24 came back positive, according to Dr. Daniel McChesney, director of the FDA/Center for Veterinary Medicine's Office of Surveillance and Compliance. Fifteen of the samples contained residues of virginiamycin, 12 contained residues of erythromycin, and five contained residues of tylosin. Some were detected at levels considered significant, according to the FDA, including residue levels exceeding 0.5 ppm, the limit established for virginiamycin, the sole antibiotic the FDA regulates in DDGS.

Residue	Number (45 samples total)	Percent
Any antibiotic	24	53%
Virginiamycin	15	33%
Erythromycin	12	27%
Tylosin	5	11%

Source: National Grain and Feed Association[11]

The FDA has not commented on what their study results might mean for human and animal health, has not made their study results public, and has not pledged any regulatory action against those that exceeded the limit.

The trouble with antibiotic overuse

Antibiotics are perhaps the greatest medical advance of the last century. But their waning effectiveness means many infections we currently consider little more than a nuisance could become a good deal more serious, even deadly.[12] The culprit is our overuse.

Non-human antibiotics are a major source of antibiotic overuse. More than 70 percent of all U.S. antimicrobials are added to animal feed not used for treating disease, but rather as feed additives for healthy beef cattle, pigs and poultry to promote growth and to help manage the stresses on animals posed by confinement housing.

Strong and compelling evidence now implicates this routine and widespread antibiotic use in livestock with rising antibiotic-resistant bacterial infections in humans.[13,14] Antibiotic use in ethanol production compounds this problem, as the drugs, we now know, can exit the plant through the DDGS and be fed to cattle, pigs or poultry.

There are alternatives

The biggest news about antibiotics and ethanol is not the antibiotic residues in distiller grains, however. The biggest news is that there are effective, economical alternatives to antibiotics already being used by a large percentage of the ethanol industry.

Of the 170 ethanol production facilities in the U.S., we estimate nearly 45 percent already are avoiding antibiotic use through a readily available alternative. Dozens more of these facilities are running trials of one of these alternatives, based on our extensive conversations with ethanol plant producers and vendors of antimicrobial alternatives.

Kerry Nixon, general manager of the Central MN Ethanol Co-op (CMEC), has been antibiotic-free since 2007. CMEC uses what is known as "stabilized chlorine dioxide" for bacterial control.

"Stabilized chlorine dioxide" (sold under the DuPont brand name "Fermasure") is actually buffered sodium chlorite, a salt with antimicrobial properties activated by the fermenter's own bacteria. The acidic nature of the bacteria converts the sodium chlorite to chlorine dioxide, a powerful disinfectant used frequently in water treatment facilities, which degrades to a nontoxic residue of chloride and sodium ions (salts). No free chlorine or dioxins are produced in the process.

Nixon says that two years ago his fermenter was nearly overrun with bacteria. "We were fighting an infection from June to November," said Nixon. "We tried switching antibiotics companies, brand names, types, and it just wouldn't go away."

Six months and thousands of dollars later, a Fermasure representative showed up and offered CMEC a free trial of the antibiotic alternative. Nixon decided he had nothing to lose.

"It knocked it out the first time," said Nixon. Since then, CMEC has been antibiotic-free and has only had to use Fermasure three times, resulting in significant cost savings for the co-op.

Stabilized chlorine dioxide isn't the only alternative. More than 40 producers have switched from antibiotics to an enzyme derived from hops, the same type of hops used in breweries. Hops extract is a natural antimicrobial, and the makers of IsoStab, the brand name for a hops extract produced for the ethanol industry by BetaTec, Inc., say adding the right hops-based enzymes not only controls bacteria, but also creates conditions under which yeast thrive.

Rob Carson, Director of Operations at ESE Alcohol, Inc., an ethanol plant in Leoti, Kan., said ESE has used the hops-based product since 2006. "It's cost competitive," said Carson. Ethanol yields are higher than when they used antibiotics, he said, and residues from the hops-based product are not a concern.

A number of other antimicrobials have gone on the market recently or are under development, offering ethanol producers several effective, economical alternatives to antibiotics.

Kerry Nixon says CMEC has saved thousands since they stopped using antibiotics. But there is more to it than simply saving money. “Our industry has had enough negatives,” said Nixon. “This gave us a chance to solve our problem and solve it safely. We never did like using antibiotics all the time.”

CMEC is now able to market its DDGS as “antibiotic-free,” a term that has played well with Nixon’s DDGS customers, many of whom became concerned about antibiotic residues after hearing recent news reports on the FDA’s residue testing. It is also a qualification that is necessary for any producer hoping to export DDGS to Europe. Since 2005, the EU has banned antibiotic residues in DDGS used for feed.

Eric Sumner, market development manager for DuPont’s Fermasure, says the feed industry is paying close attention to antibiotics in ethanol. “Given current trends,” said Sumner, “I’d be surprised if anyone is using antibiotics 10 years from now.”

Policy recommendations

1. **The ethanol industry should enact a voluntary, immediate ban on antibiotic use.**

   Antibiotic overuse poses a severe threat to human and animal health. Non-human antibiotic use is a major contributor to this problem and antibiotic use in ethanol production com pounds it. Antibiotic alternatives exist for ethanol production—alternatives proved viable and economical by dozens of producers already. Given these alternatives, there are no good arguments for continued antibiotic use in ethanol production.

2. **As part of its renewed commitment to transparency, the FDA should make public its antibiotic residue testing results and commit to strict regulation of antibiotic resi dues in DDGS.**

   If the ethanol industry is unwilling to ban antibiotics, the FDA must act swiftly to forcefully regulate antibiotic residue in DDGS. Full results from the FDA’s 2008 DDGS antibiotic residue tests, along with any future residue test results, should be made public immediately.

3. **The FDA should restrict all non human-health uses of antibiotics.**

   To address the threat of decreased antibiotic effectiveness, the FDA must take action to restrict antibiotic use not only in ethanol production, but throughout agriculture and other industrial applications—particularly non-therapeutic use of antibiotics. Decreasing antibiotic use in human health care will do little if inappropriate animal and agriculture uses are not addressed as well.

References

[1]Levy SB. The challenge of antibiotic resistance. *Scientific American*. 1998; 278:32-39.

[2]Smolinski MS, Hamburg MA, Lederberg J. (eds). *Microbial threats to health: Emergence, detection, and response*. Washington, DC: Institute of Medicine, National Academies Press; 2003.

[3]Van den Bogaard AE, Stobberingh EE. Epidemiology of resistance to antibiotics: Links between animals and humans. *International Journal of Antimicrobial Agents*. 2000; 14:327-335

[4]Mellon M, Benbrook C, Benbrook KL. *Hogging it! Estimates of antimicrobial abuse in livestock*. Washington, DC: Union of Concerned Scientists; 2001.

[5]Sharfstein, Joshua. Principal Deputy Commissioner on Food and Drugs. U.S. Food and Drug Administration. Testimony before the House Committee on Rules. Available at: http://www.rules.house.gov/111/oj/hr5419/statements/sharfstein_hr1549_111.pdf. Accessed July 13, 2009.

[6]Bischoff KM, Liu S, Leathers TD, Worthington RE, Rich JO. Modeling bacterial contamination of fuel ethanol fermentation. *Biotechnology and Bioengineering*. 2009; 103:117-122.

[7]Narendranath NV, Hynes SH, Thomas KC, Ingledew MW. Effects of lactobacilli on yeast-catalyzed ethanol fermentations. *Applied Environmental Microbiology*. 1997; 63(11):4158-4163.

[8]Lushia W, Heist P. Antibiotic-resistant bacteria in fuel ethanol fermentations. *Ethanol Producer Magazine*. May 2005.

[9]See, for example, http://farm-and-pet.hardwarestore.com/110-614-antibiotic-drug-dairyand-beef.aspx; or http://lakelandvetonline.com/?gclid=CMTx77_vwZsCFQ4MDQodoWEUBA.

[10]Moen M. The Whole Kernel: Building a market for a byproduct of corn-based ethanol. *Solutions*. 2009; Available at: http://www.cfans.umn.edu/solutions/kernel.htm. Accessed July 13, 2009.

[11]National Grain and Feed Association. FDA sampling detects antibiotic residues in ethanol distillers products. *NGFA Newsletter*. 2009; 61(2):1

[12]Varma JK, Molbak K, Barrett TJ, et al. Antimicrobial-resistant nontyphoidal salmonella is associated with excess bloodstream infections and hospitalizations. *Journal of Infectious Diseases*. 2005; 191:554-561.

[13]Silbergeld EK, Graham J, Price LB. Industrial food animal production, antimicrobial resistance, and human health. *Annual Review of Public Health*. 2008; 29:151-169.

[14]Smith DL, Dushoff J, Morris G Jr. Agricultural antibiotics and human health. *PLoS Med*. 2005; 2(8):e232.

2105 First Avenue South | Minneapolis Minnesota 55404 | USA | 612.870.0453 | Fax 612.870.4846 | iatp.org