

June 12, 2012

Honorable Louise Slaughter
Member of Congress
2469 Rayburn House Office Building
Washington, DC 20515

Dear Congresswoman Slaughter:

We are aware of the letters you sent in February to establishments throughout the food chain asking for information regarding their purchasing policies related to antibiotic use in food animals. Although we expect companies will respond to you directly, we would like to provide a scientific perspective on the use of antibiotics in food animals, and the risks and benefits it poses to both animal health and human health.

Antibiotics are stringently regulated and judiciously used

Antibiotics used in veterinary medicine are reviewed and approved by the Food and Drug Administration (FDA or the agency) pursuant to the Federal Food, Drug, and Cosmetic Act (FDCA), the same statute governing the approval of drugs used in human medicine. Drug sponsors must submit data to FDA showing the drug to be effective for treating the target pathogen or condition, safe for use in the intended animal, and sponsors must demonstrate the capability of manufacturing the drug while adhering to Good Manufacturing Practices (GMPs).

For animal antibiotics, the safety assessment is more stringent than that for human antibiotics in three ways:

1) If there are unacceptable risks to humans, FDA will not approve the antibiotic for animals.

While FDA conducts a risk-benefit assessment for human antibiotics, there is no similar consideration of benefits in reviewing antibiotics used in food animals. This means that the risk to human health for products under review must be extremely low because FDA does not consider any benefits to offset the risks.

2) FDA requires a food safety assessment to ensure that meat is safe.

The safety assessment for food animal antibiotics requires sponsors to submit toxicology and food residue studies to ensure that meat derived from animals treated with a certain antibiotic will be safe for human consumption. Data from

these studies are used to establish withdrawal periods, *i.e.*, periods prior to harvest during which antibiotics cannot be used in order to ensure that the final food product is free of residues above established tolerance levels.

3) FDA studies the pharmaceutical thoroughly to guarantee it does not increase the risk of antibiotic resistant bacteria in food. In 2003 FDA implemented Guidance 152, a qualitative risk assessment process that outlines a comprehensive, evidence based approach to preventing antimicrobial resistance that may result from the use of antimicrobial drugs in animals.¹ This process was a priority action item in the U.S. Public Health Action Plan (<http://www.cdc.gov/drugresistance/actionplan/actionPlan.html>).

At the end of the review process, FDA regulates the information sponsors must place on the label. This information includes the dose rate at which the drug is to be used and the efficacy claim allowed to be used. For food animal antibiotics, FDA uses four different label claims:

1. Disease treatment;
2. Disease control;
3. Disease prevention; and
4. Increases average daily weight gain or feed efficiency, which are typically referred to as “growth promotion” claims.

Drugs carrying any of these four claims may be administered to flocks or herds of animals via feed. So, for instance, an antibiotic used at a particular dose rate to treat a disease might be given to animals through the feed. Significantly, off-label or extra-label uses of antibiotics approved for use in feed are strictly prohibited. Veterinarians and producers using antibiotics approved for use in feed must follow the directions for use on the label.

Finally, the FDA regulatory requirements are becoming increasingly strict regarding antibiotics in feed. In April 2012 FDA released Guidance for Industry #209, which states that it is injudicious to use medically important compounds to improve production in food animals. Additionally, Guidance #209 provides that veterinary oversight must be demonstrated for therapeutic use of these same antibiotics. This Guidance in essence carries the weight of regulation and FDA has the authority to implement these provisions. The effect of Guidance #209 is that using medically important antibiotics in food producing animals for growth

promotion purposes will cease and the remaining therapeutic uses will be carried out under the guidance of a licensed veterinarian.

Risks of Antibiotic Use

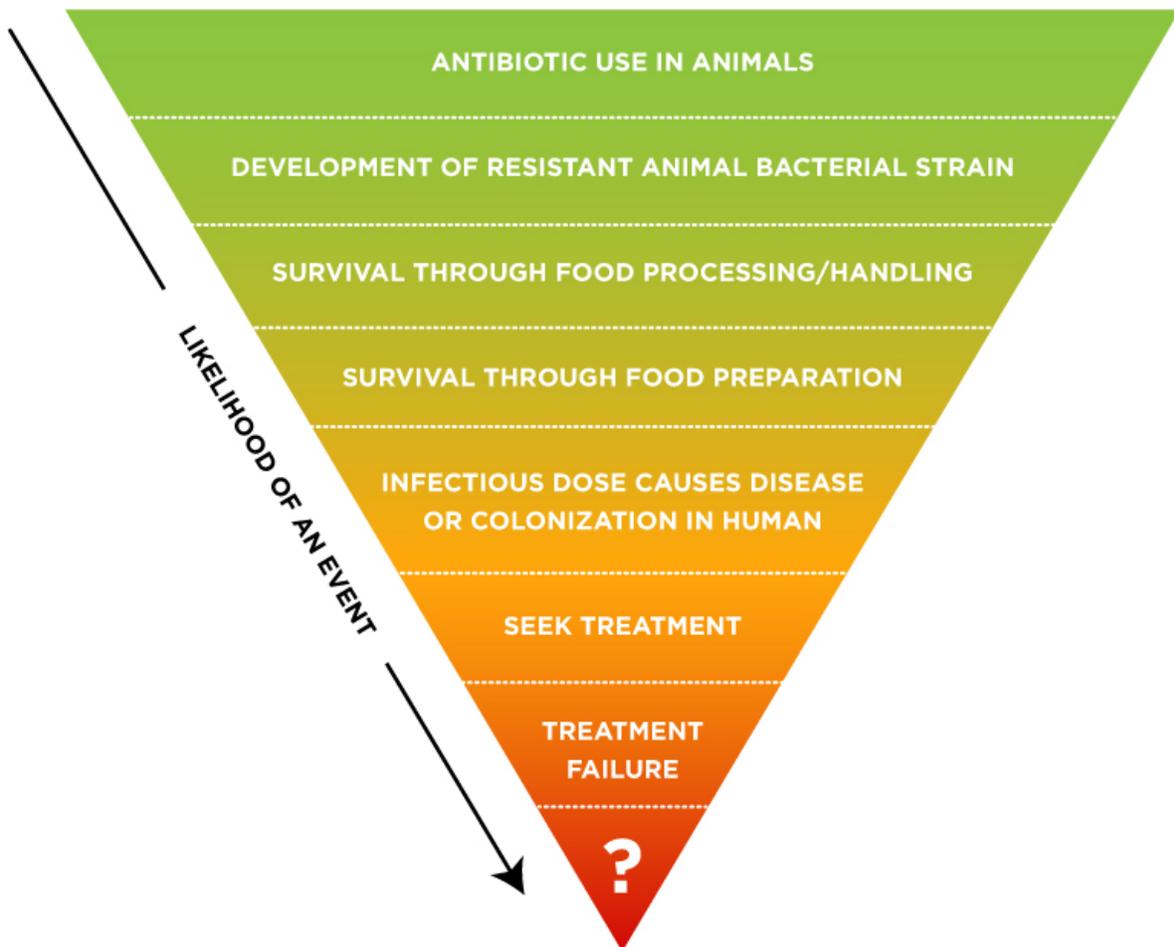
The chart in Figure 1 demonstrates the potential pathway through which antibiotic use in food animals might impact public health. The public policy question is, to what extent does the use of antibiotics in food animals result in the threat of treatment failure when antibiotics are administered to humans?

Risk assessment is the proper tool to answer this question. Several published, peer-reviewed risk assessments have demonstrated that the risk to human health is vanishingly small.

- Assessment of the impact on human health of resistant *Campylobacter jejuni* from fluoroquinolone use in beef cattle. *Anderson SA, et. al., Food Control 2001; 12(1):13-25*. A Georgetown University risk assessment on the use of fluoroquinolones in beef cattle and the resulting human health risk of fluoroquinolone-resistant *Campylobacter* on beef estimated the risk to humans to be 40 additional hospitalizations and 1 case of mortality over the course of 10 years.
- Public Health Consequences of Macrolide Use in Food Animals: A Deterministic Risk Assessment. *Hurd, et. al., Journal of Food Protection, Vol. 67, No. 5, pgs. 980-992*. According to an Iowa State University study, the probability of someone in the U.S. experiencing a treatment failure due to the acquisition of resistant food borne bacteria from eating meat from animals treated with macrolide antibiotics (tylosin, tilmicosin) is less than one in 10 million for resistant *campylobacter*, and less than one in 3 billion for resistant *Enterococcus faecium*. As one of the scientists said; “People would be more likely to die from a bee sting than for their antibiotic treatment to fail because of macrolide-resistant bacteria in meat or poultry.”
- Assessing Potential Human Health Hazards and Benefits from Subtherapeutic Antibiotics in the United States: Tetracyclines as a Case Study. *Cox and Popken, Risk Analysis, 2010*. An assessment of the risk of using tetracycline in food animals concluded that reducing tetracycline use in food animals in the United States should not be expected to cause any improvements in human health or to reduce the risks of tetracycline-resistant infections.

Figure 1

Flow Chart of Antibiotic Resistant Bacteria



- Human health Risk Assessment of Penicillin/Aminopenicillin Resistance in Enterococci Due to Penicillin Use in Food Animals. *Cox, et. al., Risk Analysis, Vol. 29, No. 6, 2009*. A risk assessment of penicillin used in animal feeds concluded that the use of these drugs were unlikely to seriously impact human health from antibiotic-resistant bacteria.

Additionally, FDA's own studies reinforce the results of these and other independently conducted risk assessments. For example, [FDA's risk assessment on the use of Virginiamycin](#), a commonly used antibiotic, found that "assuming a food pathway attribution of 10 percent, the average risk to a random member of the U.S. population of having SREF (streptogramin-resistant *e. faecium*) attributable to animal uses of virginiamycin and that may result in impaired Synercid therapy ranges from 7 chances in 1 billion to 14 chances in 100 million in one year."

Another indication that animal use contributes little, if anything, to the burden of human antibiotic resistance is an examination of the specific resistant bacterial challenges that are the biggest problems in clinical and healthcare settings. The following list is taken from the Infectious Disease Society of America's "Facts About Antibiotic Resistance" and demonstrates the lack of a pathway from antibiotic use in animals to these human resistance challenges.

- **Staphylococcus infections (MRSA)** are mainly hospital nosocomial infections but have been found in communities associated with schools and athletic facilities. These infections are a result of human to human transmission or contact with contaminated materials. IDSA says that 1% of people carry MRSA in their nasal passages. CDC investigates cases of MRSA and has concluded that animal contact is not a risk factor for these infections. Furthermore, CDC also has concluded that MRSA is not a foodborne infection and cannot be acquired by eating meat.
- **Acinetobacter baumannii** is an opportunistic pathogen associated with a high rate of infections in soldiers wounded in Iraq. It is most often associated with wound infections in hospitals and other medical facilities. It is inherently resistant to many antibiotics and has no connection to food animals or antibiotic use in food animals.
- **Vancomycin Resistant Enterococcus (VRE)** is another hospital nosocomial infection that has developed resistance due to extensive use of vancomycin in U.S. hospitals. Vancomycin, or drugs in its class, has never been approved for or used in food producing animals in the U.S.
- **Pseudomonas aeruginosa** is another opportunistic pathogen found in intensive care units that has become resistant to fluoroquinolone antibiotics. It occurs uncommonly in food producing animals where it can cause mastitis in dairy cows. Fluoroquinolones are not approved for use in dairy cows and furthermore Pseudomonas is not a foodborne pathogen.
- **Streptococcus pneumoniae** resistant to several classes of antibiotics is strictly a human pathogen that causes respiratory infections. This organism has no known connection to food producing or companion animals.

- **Neisseria gonorrhoea** is strictly a human pathogen that causes venereal infections transmitted through human sexual contact. Resistance develops because of poor patient compliance with the prescribed course of antibiotic therapy. There is no connection with animals or antibiotic use in animals.
- **Drug resistant tuberculosis, Clostridium difficile, and Klebsiella species** are other bacteria that are mentioned in the IDSA fact sheet. There is no known connection between these pathogens and food producing animals.

Finally, real world experience shows that reducing antibiotic selection pressure in animals has no impact on human resistance levels. In the U.S., for instance, levels of fluoroquinolone-resistant *Campylobacter* have changed little since the use of fluoroquinolones in all poultry was discontinued in 2005, indicating resistance levels in humans are due to selection pressure from something other than use in poultry. Similarly, according to a September 2011 GAO report, Danish officials report that “Denmark’s resistance data have not shown a decrease in antibiotic resistance in humans after implementation of the various Danish policies, except for a few limited examples.” These policies include reducing use by banning the use of antibiotics as growth promoters.

Benefits of Antibiotic Use

While FDA does not consider benefits in the review process for food animal antibiotics, it is important to factor benefits into the public health discussion. Producers and veterinarians take seriously their responsibility for ensuring good animal welfare and antibiotics that are used carefully and judiciously by producers and veterinarians to treat, control, or prevent disease improve animal health and welfare. Animal welfare describes how well an animal is coping with the conditions in which it lives and antibiotics are among the many tools used by producers to provide good welfare to their flocks and herds. Proper housing, management, diet and nutrition, genetics, responsible care, and humane handling are other such tools.

Antibiotic use is also among the several tools used to help enhance food safety. Many steps in meat and poultry processing are designed to eliminate foodborne pathogens. Meat processors seek to reduce incoming pathogen levels from animals and those processors utilize interventions to limit pathogens because it reduces the risk of contamination in the final product. To that end, healthy animals typically have fewer pathogens that need to be removed, which makes other removal steps more effective. Thus, the careful use of antibiotics to keep animals in top health is an important first step in providing the safest possible meat supply. More specifically, a growing body of published research demonstrates that judicious antibiotic use can aid food safety efforts and provided below are citations to research supporting that conclusion.

- Georgia professor Dr. Scott Russell tracked the outcome in the processing plant of birds affected by airsacculitis, a common infection caused by *E. coli*. Presence of the disease increases levels of fecal contamination at the plant and leads to more errors in processing because birds varied in weight, leading to increased levels of *Campylobacter* contamination. According to Dr. Russell, subclinical disease in chickens affects carcass contamination, and subclinical disease can be reduced by antibiotics. (Russell SM. The effect of airsacculitis on bird weights, uniformity, fecal contamination, processing errors, and populations of *Campylobacter* spp. and *Escherichia coli*. *Poult Sci.* 2003 Aug;82 (8): 1326-31)
- Similar research by Dr. Scott Hurd at Iowa State University regarding the presence of carcass lesions, which indicates subclinical disease, was associated with increased levels of *Campylobacter* contamination in swine. (Hurd HS, Brudvig J, Dickson J, Mirceta J, Polovinski M, Mathews N, Griffith R. Swine Health Impact on Carcass Contamination and Human Foodborne Risk. *Public Health Reports*, 2008 May-June Vol 123:343-351.)
- A model constructed by Dr. Randall Singer at the University of Minnesota linking changes in animal illness to possible changes in human foodborne illness observed large increases in human illness days each year as a result of small increases in animal illness levels. “Because the potential human health benefits from continued animal antibiotic use may outweigh the potential increase in human health risks, further clarification of the net human health impact from interventions should be carefully assessed prior to implementation of changes in antibiotic use policy,” wrote the authors. (Singer RS, Cox LA Jr, Dickson JS, Hurd HS, Phillips I, Miller GY. Modeling the relationship between food animal health and human foodborne illness. *Prev Vet Med.* 2007 May 16; 79 (2-40): 186-203.)

All public health professionals, including veterinarians, are serious about reducing the risks of antibiotic resistance. It is vital that public policy decisions about the use of these products be made on the basis of science and risk assessment. The research is clear that the contribution of using antibiotics in food animal production to the human burden of antibiotic resistance is quite small, if it exists at all. We are encouraged by the steps being taken by FDA to extend veterinarian involvement in all uses of antibiotics in food animals and believe FDA’s action will be yet another risk mitigation step to ensure the careful and judicious use of antibiotics in food animals.

We appreciate your interest in this issue and hope we can work with you and your staff in protecting both human and animal health.

Respectfully submitted,

American Farm Bureau Federation
American Feed Industry Association
American Meat Institute
Animal Health Institute
American Veterinary Medical Association
National Cattlemen's Beef Association
National Chicken Council
National Meat Association
National Milk Producers Federation
National Pork Producers Council
National Turkey Federation