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**Committee on Energy & Commerce
Subcommittee Health**

Antibiotic Resistance and the Use of Antibiotics in Animal Agriculture

July 14, 2010

Chairman Pallone, Ranking Member Shimkus, and members of the Subcommittee:

Thank you for holding this hearing on antibiotic resistance and the use of antibiotics in animal agriculture. I am Dr. Richard Carnevale. I am a veterinarian by training with a degree from the University of Pennsylvania, and I am here today on behalf of the Animal Health Institute, a trade association that represents companies that make medicines for animals. Prior to joining AHI about 15 years ago, I served as Deputy Director for the Office of New Animal Drug Evaluation at FDA's Center for Veterinary Medicine and later as Assistant Deputy Administrator for the Office of Science at USDA's Food Safety & Inspection Service. AHI companies work to provide products to livestock and poultry producers that help keep their animals healthy. By doing this, companies contribute to public health and food safety. Research shows that the first link in the chain of producing safe meat, milk and eggs is keeping animals free from disease. AHI companies also develop products that are used for the health and welfare of our companion animals, but today my remarks are focused on the objective of this hearing and animal agriculture.

Food safety starts on the farm, and our companies spend millions of research and development dollars to find new and innovative products to keep farm animals healthy. Some animal health products are used to treat and prevent or control disease in animals while others are used for nutritional efficiency. More recently, products are being developed that will contribute to food safety by reducing bacteria that do not make animals sick but have the potential to make people sick.

Animal health products are subject to stringent, science-based review processes at three federal agencies: pharmaceutical and feed additive products are reviewed by the Food and Drug Administration (FDA) under the Federal Food, Drug and Cosmetic Act, biologic products, or vaccines, are regulated by United States Department of Agriculture (USDA) under the Virus, Serum, Toxins and Analogous Products Act, and animal pesticides are regulated by the Environmental Protection Agency (EPA) under the Federal, Insecticide, Fungicide, and Rodenticide Act (FIFRA). All products are reviewed for safety and efficacy: efficacy, which protects producers by ensuring the products deliver the benefits they promise; and safety, to ensure the products are safe for the animal being administered the drug or vaccine and to ensure the meat from the animal is safe for human consumption and safe for the environment.

One class of products important to the health of food animals is antibiotics. Antibiotics are used by livestock producers, poultry producers, and the veterinarians who work with them to prevent, control and treat often fatal bacterial infections. There are many benefits to animals, producers and consumers that come from the use of antibiotics in animal agriculture:

- Healthy animals reduce the need for greater, more involved disease interventions, and limit the spread of disease and illness that can impact the people that care for animals.
- Animal welfare is improved as a result of veterinarians and producers having the tools to be able to maintain the animal's health.
- Producers are more efficient because they can produce more food from fewer animals. Without antibiotics to treat, prevent, and control diseases, more animals get sick and die with producers losing not only the animal but all the input costs, including feed, that have gone into the animal.
- There are ecologic benefits. Young animals that have their diseases controlled through the use of antibiotics grow faster and more efficiently, thereby using less land and feed to maintain the same herd and flock sizes. Moreover, some studies have shown that certain antimicrobials used in cattle feeds reduce levels of methane emissions.
- Benefits to global food markets. With the concern over food costs and availability in today's economic climate, antimicrobials and other animal drugs that improve animal health and productivity are critical to American agriculture's ability to feed the world's growing population. The Food and Agriculture Organization (FAO) of the United Nations estimates that more than 1 billion people worldwide do not have enough to eat. They propose that one solution is to help producers to raise their output.
- Consumers benefit because healthy animals are needed to produce safe food. Over the past five years, published, peer-reviewed studies have indicated that carcasses from chickens without subclinical diseases are more likely to be free of human foodborne pathogens.^{1,2,3,4} Research shows this is due in part to more standardized carcass size, reducing the potential for intestinal breakage during mechanical evisceration.

The FDA approves antibiotics to treat specific diseases or conditions at specific dosages rates. There are four specific efficacy claims that FDA approves antibiotics for use in food animals: disease treatment, disease prevention, disease control and growth promotion - as measured by the amount of feed needed to produce a pound of animal weight or increased rate of weight gain.

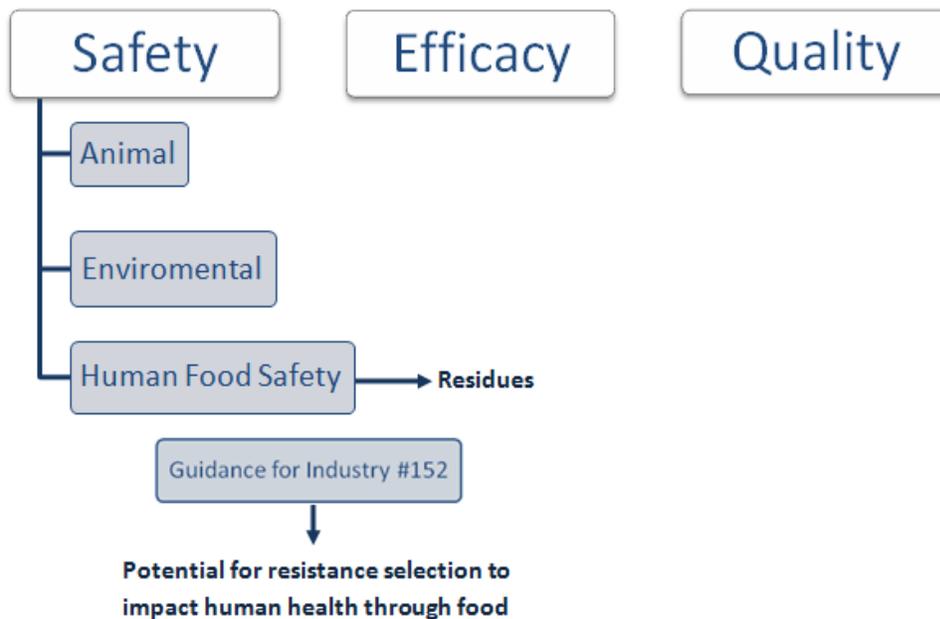
The first three uses – disease treatment, prevention and control – are considered to be therapeutic uses by FDA, the American Veterinary Medical Association (AVMA) and such international bodies as Codex Alimentarius and the World Health Organization (OIE). While critics of antibiotic use like to use the term “nontherapeutic” to refer to disease prevention, disease control and growth promotion, this term is not used nor recognized in national or international regulation.

Many assume in-feed uses equate to growth promotion, but this confuses the use with the route of administration. In fact, any of the four uses, including therapeutic, can be administered via feed or water, as that is under certain circumstances the only practical way to administer medication to large flocks or herds. In most cases, a veterinarian is involved in this process, recommending feed that is specifically formulated for the health management system used for the flock or herd.

How Antibiotics are Regulated

Veterinarians, Producers, and Animal health companies rely on a rigorous, efficient, predictable and science-based review process at the Food and Drug Administration’s Center for Veterinary Medicine (CVM) to provide these products. The standard for the approval of antibiotics used in animals is the same as that for antibiotics used in human medicine: they must be shown to be safe and effective.

FDA Approval Process



The rigorous review process and post approval monitoring systems in place are at the heart of a broad system of protections that ensure that all medicines, including antibiotics, are safe for animals and humans. Antibiotics for use in animals must meet all the same requirements as antibiotics used in humans, with two additional requirements: first, sponsors must show the meat, edible tissues, milk and or eggs from animals in which the medicine is used is safe for human consumption. Product sponsors have the burden of proof upon them to demonstrate the safety to the Agency. Second, beginning in 2003, CVM instituted Guidance for Industry (GFI) # 152, which

outlines a qualitative risk assessment process that is applied to all antibiotics approved for use in animals. This guidance process is designed to measure the risk of antibiotic resistant bacteria being transferred from animals to humans if the product is approved. Based on this risk, FDA makes decisions to either deny or approve the drug with certain restrictions to significantly reduce risk. Restrictions can include requiring a veterinary prescription, prohibiting extra-label use in certain species or restricting the antibiotic to individual animals. In most cases antimicrobial resistance monitoring is required post approval. The methodology is very conservative – meaning it is very difficult to get an antibiotic approved. Further, the guidance is sufficiently broad so that if new, previously unidentified or undescribed, resistant organisms or genes were to become of concern, the Agency can act swiftly to take this information into account. The existing guidance allows the Agency sufficient flexibility to allocate resources appropriately to changing issues of safety related to resistance emergence.

In response to concerns raised in the 1970's, FDA required sponsors to conduct tests to determine the potential for resistance to be selected in the animals and to be transferred to bacteria that could cause human disease. While the standards and science may have changed over the years, the safety of these products has been continually demonstrated as an ongoing exercise at FDA. Since there has been a greater availability of susceptibility data on marketed products, we believe that quantitative risk assessment is now the proper tool for making policy decisions about the safety of currently approved antimicrobials and is more appropriate than simply applying the tenets contained in Guidance 152. Published quantitative risk assessments, performed by both the Agency and individual product sponsors, have affirmed that the risks to human health from these antibiotics in animal feed under approved conditions of use are very low.

Recent FDA Actions

The FDA has proposed two initiatives to ensure the judicious use of animal antibiotics. In March, the Agency issued an Advance Notice of Proposed Rulemaking regarding the modernization of the Veterinary Feed Directive, which requires veterinarian involvement when antibiotics are administered in animal feed. And on June 28, the FDA issued draft guidance on the use of medically-important antibiotics in food-producing animals. Draft Guidance 209, *The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*, had two specific recommendations: 1) the use of medically-important antibiotics in food-producing animals should be limited to uses necessary for assuring animal health, and the use for growth promotion are not judicious uses and 2) that the use of medically-important antibiotics in food-producing animals should be limited to uses that include veterinary oversight.

We look forward to collaborating with the Agency to help ensure that the process envisioned by these new initiatives will result in animal producers and veterinarians having access to the tools they need to protect the health of food producing animals. We appreciate that FDA has reached out to stakeholders for input on how to achieve their objectives. It is critical that stakeholders are involved to ensure that changes to the judicious use guidelines and the regulatory framework are carefully considered.

These recent initiatives further illustrate that FDA already has a great deal of authority to regulate the labeling and use of antimicrobials, and that it is willing to use it to ensure safe and judicious use of antibiotics in food producing animals.

In addition to the rigorous review process and the additional public and private risk assessments that have been conducted, there are other post-approval layers of protection to ensure the safe use of antibiotics.

Monitoring programs

USDA's Food Safety and Inspection Service monitor meat samples for the presence of antibiotic residues as a check on the observance of the withdrawal times set by FDA. It is very uncommon for FSIS to find an unsafe residue, an indication that products are being used according to label directions.

The National Antibiotic Resistance Monitoring System (NARMS) is a multi-agency program coordinated by FDA to monitor antibiotic resistant bacteria and allow for implementation of management and control measures if needed. The three agencies involved are:

- The USDA Agricultural Research Service (ARS), which analyzes *Salmonella* and *Campylobacter* isolates collected from carcasses and meat samples in the USDA FSIS HACCP/Pathogen Reduction Program for antibiotic resistance;
- The FDA, which monitors for resistant bacteria in retail meats;
- The Centers for Disease Control and Prevention (CDC), which collects isolates from public health laboratories to monitor for the emergence of antibiotic resistant enteric pathogens in humans.

To date, the animal and human arms of the program have produced eleven years of data representing over 19,000 *Salmonella* isolates from livestock and poultry carcasses and meats and 12,000 human *Salmonella* isolates, while retail meat testing was added later. Most bacterial species isolated from humans and tested for resistance against drug classes potentially related to animal usage have shown stable or declining resistance to most antimicrobials. Most of the multiple-drug resistance types, such as *Salmonella typhimurium* DT104 show stable or declining prevalence in both food animals and humans since 1996, according to an expert report issued in 2006 by the Institute of Food Technologists entitled "Antibiotic Resistance: Implications for the Food System."

While AHI strongly supports continued funding of the NARMS program, we would point out that there are inherent weaknesses in the sampling strategies that prevent the data from estimating a true national prevalence of resistance and yearly trends. The FDA Science Board has identified these weaknesses as well and has encouraged the agencies involved in NARMS to work to improve the data.⁵

Judicious Use Guidelines

Responsible or judicious use programs that are specific to different livestock species give veterinarians and producers specific guidelines to help them safely and properly use of antibiotics in their health management systems. Generally, these guidelines have been prepared collaboratively by FDA, CDC and veterinary groups. These guidelines help ensure there is no unnecessary use of antibiotics in animal agriculture. Others testifying today will provide additional detail on how these principles are used by veterinarians and producers.

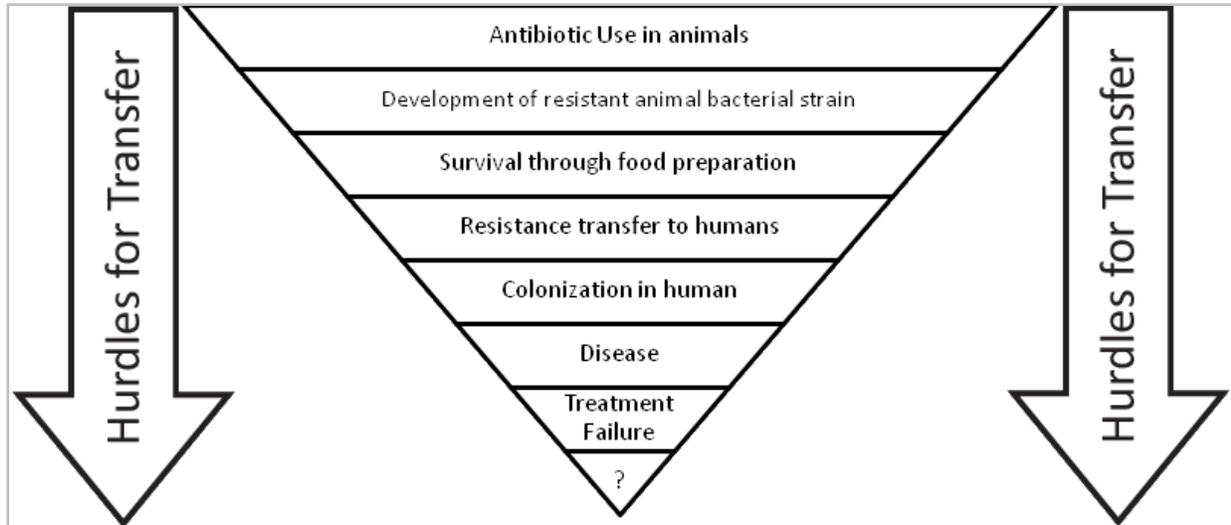
International Guidelines

Codex Alimentarius is responsible for protecting the health of consumers and ensuring fair practices in food trade. In 2007, Codex established an ad hoc Intergovernmental Task Force on Antimicrobial Resistance to develop guidelines for food safety risk analysis of antibiotics used in animals. The Codex Commission just last week, advanced draft guidelines to Step 5, meaning that the Task Force will likely be finalizing guidance in October 2010 for adoption as a Codex standard in 2011. International standards are important, because bacteria knows no borders and actions taken within the U.S. may not be as effective if there is not concerted international action. It is also important that the international community establishes a sound scientific basis for countries to assess the risk of antibiotic use. Otherwise, government regulators are left open to outside pressure to take overly zealous precautionary measures that may be unjustified and in the long term harmful to animal health and food safety.

Correlation Between Use of Antibiotics in Animals and Human Antibiotic Resistance

There is no question that antibiotic resistance is a serious public health threat. But resistance is not a single problem: it is a problem comprised of several different bacteria-drug combinations that must be examined individually to ascertain risk. For instance, some of the most widely recognized antibiotic resistance problems in humans are in respiratory tract infections and venereal diseases like gonorrhea. In neither of these cases is there any evidence that antibiotics used in animals are associated with these problems. In fact, in a survey published in 2000 a group of medical experts estimated the animal contribution to the overall human resistance problem is less than 4 percent.⁶

That small contribution was attributed to the potential for antibiotics used in food animals to contribute to resistance in certain bacteria which can be transferred from animal food products to humans. However, there is a chain of events from the “farm to the fork” that must be traversed by bacteria that develop resistance in animals as outlined in the accompanying chart:

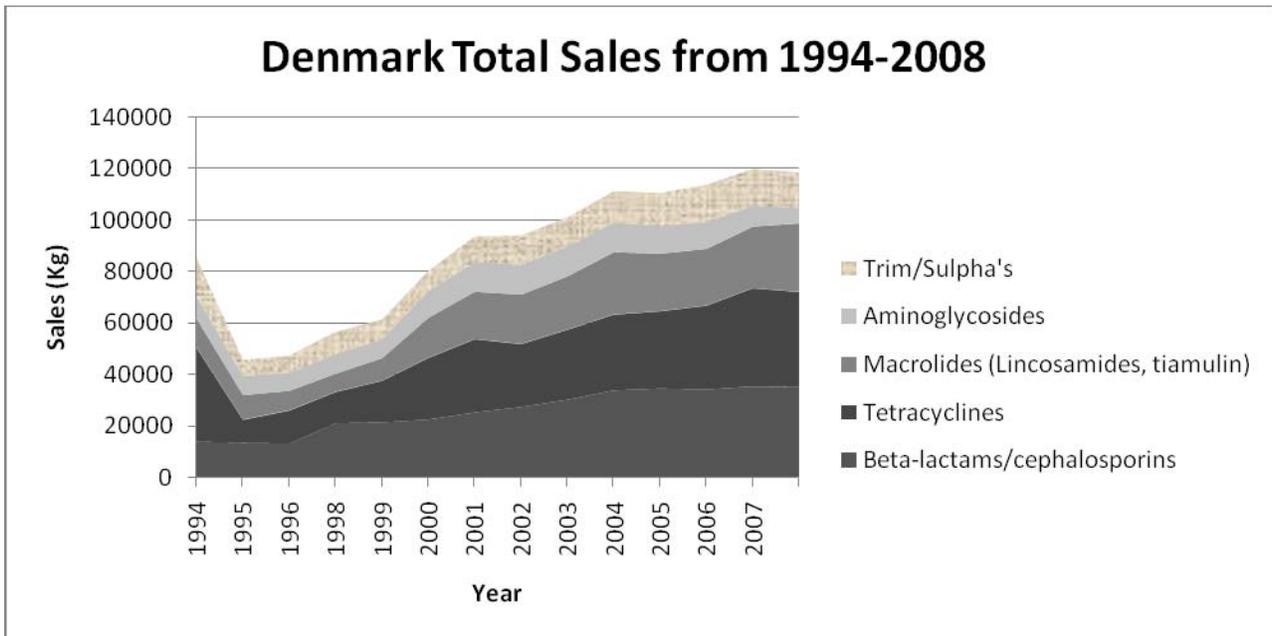


In order for resistance to happen, the antibiotic must be used in the animal, resulting in the selection of resistant bacteria in the animal. Those bacteria then must survive the slaughtering and processing of the animal. Remember, we have successfully reduced the number of bacteria -- both resistant and not resistant -- that survive this process through the implementation of controls like HACCP. The bacteria must then survive the normal cooking process. If enough resistant bacteria survive to this point and are ingested in a large enough quantity, they can make an individual sick with a common foodborne illness. As you know, most foodborne illnesses are self-limiting -- they resolve themselves in most cases without antibiotics being necessary. In the event that an antibiotic is necessary, the illness could be treated with the antibiotic that the bacteria is resistant to, and the treatment could fail, prolonging the illness.

While we know this can happen, the question becomes, how often does this happen and how severe are the consequences? The answer to this much-studied question is that it does not happen enough that we can find it and measure it. So, scientifically, we cannot say it does not happen, but we can say it is uncommon.

Danish Experience

The Danish experience provides a real world example of what happens when producers lose access to antibiotics. In the late 1990s, the European Union phased out one particular use --the use of antibiotics for growth promotion. Data from the Danish government, which you see on the accompanying chart, shows that use of antibiotics to treat disease has doubled since the ban.



This data, along with the discussion in the Danish report, clearly indicates the ban led to additional animal disease and death. The important question is: what impact did it have on public health? There is some evidence to indicate resistance declined in the animals and humans in certain bacteria. However, there is no evidence that this has resulted in reducing the public health burden of resistant bacterial infections in humans. The list of references at the end of my testimony includes published papers on the results of the ban.

Antibiotics Data

Critics have charged that we don't know how big the problem is because we don't have reliable data about the use of antibiotics in animal agriculture. However, it is important to note, that levels of antibiotic resistance are not correlated to the amount of use. Nonetheless, Congress has addressed the lack of data issue by requiring antimicrobial sales and distribution data to be reported to FDA under the Animal Drug User Fee Amendments of 2008. The ADUFA data collection requirements commenced this year, and our companies have complied. The FDA has indicated they will publish a report later this year.

Furthermore, Congress acted on this issue in the 2008 Farm Bill. That legislation contained an authorization for USDA's Agriculture Research Service to conduct additional research to study the development of antibiotic resistant bacteria in livestock on how judicious use principles can help producers use these products to protect both human and animal health.

Summary

In conclusion, antibiotics are vitally important to the health of our nation's livestock and poultry herds and flocks. Antibiotics are highly regulated and are used carefully by veterinarians and livestock and poultry producers. The many regulatory layers of protection that have been put in place allow us to safely use antibiotics to protect both animal and human health. The FDA regulatory process and risk assessment are the proper tools for making decisions about the use of these products. FDA has recently expressed concerns with antibiotic use in food animals; the industry is committed to working collaboratively with the Agency to address these concerns while assuring the availability of important animal health products to prevent, control, and treat animal disease.

Notes

¹Russell SM. The effect of airsacculitis on bird weights, uniformity, fecal contamination, processing errors and populations of *Campylobacter* spp. And *Escherichia coli*. Poult. Sci 2003; 82:1326-31.

²Cox Jr LA. Potential human health benefits of antibiotics used in food animals: a case study of virginiamycin. Environ Int 2005;31:549-63.

³Hurd HS, et al. Swine Health Impact on Carcass Contamination and Human Foodborne Risk. Public Health Reports, May-June 2008; 123: 343-351.

⁴Berrang ME, et al. Subtherapeutic Tylosin Phosphate in Broiler Feed Affects *Campylobacter* on Carcasses During Processing. Poult. Sci. 2007;86:1229-1233.

⁵<http://www.fda.gov/cvm/Documents/NARMSExecSum03.pdf>.

⁶Bywater, RJ and Casewell M. An assessment of the impact of antibiotic resistance in different bacterial species and of the contribution of animal sources to resistance in human infections. J Antimicrob Chemother 2000;46:643-635.

ADDITIONAL REFERENCES

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