White Paper

Antibiotic Use in Food Animals

Information synthesized from an Oct. 26-27, 2011, symposium in Chicago, IL: "Antibiotic Use in Food Animals: A Dialogue for a Common Purpose"

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EXECUTIVE SUMMARY

Broad concern and confusion about antibiotic use on farms have been expressed by the general public and policymakers. Key reasons for this concern and confusion can be traced to numerous factors including:

- Antibiotic use in food animals is not a black-and-white issue. It is a complex issue that is all too frequently over simplified by both critics and proponents.
- Misunderstanding that a concern is not equivalent to risk.
- The disconnect between consumers and agriculture (and those in agriculture), with most consumers being at least three generations removed from the farm.
- Activist messaging, the media and the Internet are often inaccurate and misleading regarding antibiotic use, and in particular antibiotic resistance and its relationship to use, in food-animal production.

Antibiotic use in food animals is highly regulated by the U.S. Food and Drug Administration Center for Veterinary Medicine (FDA CVM). Regulatory oversight provides assurance in the development of safe products. Education and training encourages producers to have a strong relationship with their veterinarians and provides guidance on the responsible use of antibiotics. Government surveillance and testing ensures that no harmful residues, as established by the FDA, enter the food supply.

The use of antibiotics in food-animal production has elicited concern about antimicrobial resistance (AMR). The development and dissemination of antibiotic resistance is a highly complex, multi-faceted issue *(see Figure 1 on page 12)*.

Resistance to antimicrobials continues to evolve, with many types of resistance mechanisms. As such, it is imperative that antibiotics be used appropriately not only in animal agriculture but also in the human population.

The issue of AMR is not strictly an issue of science-based decision-making. Like many other aspects of food production, the issue of AMR inherently invokes differing opinions, and, given the intricacies and size of the modern food production system, it’s a foregone conclusion that any policy issue will invoke many different perspectives. The symposium was intentionally designed to be respectful of all opinions, including the varying politics and values related to modern food production practices. Therefore, it is essential to initiate broad dialogue around the role of antibiotics in animal agriculture and the issue of antibiotic resistance.

Ultimately, key questions concerning antimicrobial use in human and animal populations revolve around:

- Who should benefit and by how much?
- What is “over” or “unacceptable” use?
- What is acceptable risk?

Given these questions, concern about AMR bacteria is not equivalent to risk. Risk to humans exists only if there is a causal pathway from the AMR bacteria in food-producing animals and humans. Risk is not a result of the hazard alone, but also in conjunction with the exposure (or dose).

Estimated farm-to-fork risk from on-farm antibiotic use is extremely low. In fact, the alternative risk of sub-optimal animal health may be higher than the risk of on-farm antibiotic use.

Although activists often claim that antibiotics used in livestock and poultry are the cause of human antibiotic resistance, the attributable risk of human disease outcomes, e.g., additional illness days due to resistance, associated with the use of antibiotics in food-producing animals is unknown, and studies show it is extremely low.

Livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) is a new and potential health concern for persons in the swine/livestock industries, but current evidence indicates it is not a concern for the broader community as it has not been shown to be a significant cause of the overall MRSA burden in humans. Since LA-MRSA is not a food-borne pathogen, it is not a food safety or public health concern.

Common on-farm practices that consumers should know about regarding food-animal production include:

1) Modern livestock farms increasingly involve licensed veterinarians who advise on health management decisions.
2) Vaccines are used to protect animals from various illnesses.
3) Sick animals are treated with medicines, such as antibiotics, to restore their health, and protections are in place to ensure that their meat or milk is safe for people.
4) The FDA approves the use of all new animal drugs after testing and confirming animal safety and human food safety.
5) If antibiotics are administered to cure a sick animal, the animal itself — in the case of meat production — or animal products — such as milk — are not allowed to enter the food supply until the withdrawal period has passed and the medicine has sufficiently cleared the animal's system. The required periods for withdrawing medication are specific for each drug and species and are approved by the FDA based on research studies of residues in edible tissues.

Animal agriculture stands on the belief that healthy animals make safe food. Those who produce food animals agree with the veterinarian's oath: *"Being admitted to the profession of veterinary medicine, I solemnly swear to use my scientific knowledge and skills for the benefit of society through the protection of animal health and welfare, the prevention and relief of animal suffering, the conservation of animal resources, the promotion of public health, and the advancement of medical knowledge."* Today, however, consumer concerns may cause two phrases in the oath to collide: "prevention and relief of animal suffering," and "promotion of public health."

Individuals dedicated to food-animal production recognize that proper production practices, such as maintaining flock and herd health by preventing disease through biosecurity and the use of vaccines, help minimize the need for antimicrobial use. Medically important antibiotics used in food-animal agriculture should be used under the supervision of a veterinarian to combat disease on a case by case basis. Access to antibiotics to prevent and treat animal disease is essential for the health of food animals as well as to ensure a safe food supply.

It is critical that policy actions regarding the use, limited use, or non-use of antibiotics in food-animal production be based on science with a commitment to carefully weighing the benefits and costs as well as the desired — and potentially undesired — consequences of any specific course of action.

In final analysis, the ultimate priority about antibiotic use going forward is the development of well-established, science-based criterion in the regulatory decision-making process. Simultaneously, the livestock industry should remain focused on continual improvement of good animal husbandry practices and disease prevention.

There should be an achievable, unified goal of "One Health: Healthy People, Healthy Animals, Healthy Food."

Background

The symposium *Antibiotic Use in Food Animals: A Dialogue for a Common Purpose* was developed by the National Institute for Animal Agriculture and conducted October 26-27, 2011, in Chicago, Illinois.

The National Institute for Animal Agriculture (NIAA) is a non-profit, membership-driven organization that unites and advances animal agriculture: the beef, dairy, equine, goat, poultry, sheep and swine industries. NIAA is dedicated to programs that work toward the eradication of diseases that pose risk to the health of animals, wildlife and humans; promote the efficient production of a safe and wholesome food supply for our nation and abroad; and promote best practices in environmental stewardship, animal health and well-being.

The symposium was funded in part by the Beef Checkoff, Pfizer Animal Health, the Pork Checkoff, the American Veterinary Medical Association, Elanco Animal Health and the *National Hog Farmer*.

Purpose and Design of the Symposium

The use of antibiotics in the production of food animals elicits polarized opinions today as consumers seek information regarding how their food is produced. While livestock producers know that various animal illnesses can be prevented and controlled by the use of antibiotics, many consumers are hearing from popular media, media campaigns or urban legends — or may have concluded on their own — that any use of antibiotics in animals is ill-advised and leads to a lower effectiveness of antibiotics used in humans.

Proponents and critics of the use of antibiotics in livestock have conflicting views on the correct interpretation of the body of evidence related to agricultural use of antibiotics and the development of resistant organisms. That said, some individuals taking a stand or speaking out either do not have access to, or know where to turn, for accurate, scientifically credible information. In addition, modern consumers are three generations or more removed from the farm and are not well informed about farm practices in general, including methods to prevent and treat disease.

The 13 animal health and human health scientists and other experts speaking at the *Antibiotic Use in Food Animals: A Dialogue for a Common Purpose* symposium were asked to address four main topic areas:

- Antibiotics in food-animal production and human health
- Antibiotics in food-animal production
- Human health implications relative to antibiotic use
- Livestock methicillin-resistant *Staphylococcus aureus*: Understanding and communicating the risks

The end goal of the symposium was for animal health and human health experts to share science-based information so an honest dialogue can ensue. Three questions need to be addressed in order for that to occur:

- What are the key components of agreement/disagreement about the science of antibiotic resistance?
- What role does agreement/disagreement about values regarding food production play into the discussion?
- Where do we find aspects of consensus across science and values?

To that end, information shared by food-animal health experts and human health experts should establish a new benchmark of valuable scientific information that may be used to further communicate valid and essential facts to food-animal producers and consumers on the use of antibiotics in food-animal production.

The Symposium Planning Committee consisted of representatives of livestock producers, veterinarians, academia, government and agribusiness concerned with the use of antibiotics in food animals and their effects on human health.

Planning Committee Chair:
Dr. Leonard Bull, NIAA Past Chair

Planning Committee Members:
Dr. Rodney "Butch" Baker, Iowa State University
Mr. Mike Bumgarner, Ohio Farm Bureau Federation
Dr. Tom Field, National Cattlemen's Beef Association
Mr. Glenn Fischer, Allflex USA, Inc.
Dr. Tony Forshey, Ohio Department of Agriculture
Mr. Ray Hilburn, Alabama Poultry & Egg Association
Dr. Christine Hoang, American Veterinary Medical Association
Mr. Travis Justice, Arkansas Farm Bureau Federation
Dr. Hailu Kinde, University of California-Davis
Dr. Jennifer Koeman, National Pork Board
Mr. Stan Mannschreck, National Livestock Producers Association
Dr. Harry Snelson, American Association of Swine Veterinarians
Dr. Annette Whiteford, California Department of Food & Agriculture

Symposium Topics and Speakers

Symposium Moderator: Dr. Scott Hurd**,** Associate Professor, *Iowa State University College of Veterinary Medicine, Department of Veterinary Diagnostic and Production Animal Medicine* and former Deputy Undersecretary for Food Safety, *USDA/Food Safety Inspection Service*

- **"Antibiotics in Food Animal Production and Human Health: A Clinical Pharmacologist's View of the Interaction of Antimicrobials and Bacteria in Food Animals"** – **Dr. Mike Apley**, Professor, *Kansas State University College of Veterinary Medicine, Department of Production Medicine/Clinical Pharmacology*

- **"Antibiotics in Food Animal Production and Human Health: The Challenge of Antimicrobial Resistance in Human Health"** – **Dr. Robert Flamm**, Director of Antimicrobial Development, *JMI Laboratories*

- **"Antibiotics in Food Animal Production"** (Panel)
  Moderator: Mr. Ron Phillips, Vice President of Legislative and Public Affairs, *Animal Health Institute*
  Beef Cattle Panelist: Dr. Mike Apley, Professor, *Kansas State University College of Veterinary Medicine, Department of Production Medicine/Clinical Pharmacology*
  Dairy Cattle Panelist: Dr. Mike Lormore, Director of Dairy Veterinary Operations, *Pfizer Animal Health*
  Poultry Panelist: Dr. Hector Cervantes, Senior Manager of Poultry Technical Services - North American Region, *Phibro Animal Health*
  Swine Panelist: Dr. Paul Ruen, practicing swine veterinarian, *Fairmont Veterinary Clinic*

- **"Human Health Implications Relative to Antibiotic Use: Initiatives to Ensure Public Health, Food Safety, Animal Health and Welfare of Antibiotic Use in Food Animals"** – **Dr. Tom Shryock**, Senior Research Advisor of Microbiology, *Elanco Animal Health*

- **"Human Health Implications Relative to Antibiotic Use: Challenges in Antibiotic Product Development in a Rapidly Changing Global Landscape"** – **Dr. Scott Brown**, Senior Director of Metabolism and Safety, *Pfizer Animal Health*

- **"Human Health Implications Relative to Antibiotic Use: Risk Management Approaches to Antimicrobial Resistance in the U.S. and Abroad: Expectations, Results and Conundrums"** – **Dr. H. Morgan Scott**, Professor, *Kansas State University, College of Veterinary Medicine, Department of Diagnostic Medicine/Pathobiology*

- **"Human Health Implications Relative to Antibiotic Use: U.S. FDA Initiatives Regarding the Judicious Use of Antibiotics in Food-Producing Animals"** – **Dr. William T. Flynn**, Deputy Director for Science Policy, *Food and Drug Administration Center for Veterinary Medicine*

- **"Understanding and Communicating the Risks of Livestock MRSA: An Overview of Livestock-Associated *Staphylococcus aureus*"** – **Dr. Tara Smith**, Assistant Professor, *University of Iowa College of Public Health, Department of Epidemiology*

- **"Livestock Associated MRSA: What is the Appropriate Level of Concern? "** – **Dr. Peter Davies**, Professor, *University of Minnesota College of Veterinary Medicine, Department of Veterinary Population Medicine*

- **"Reaching Out to Consumers"** – **Dr. Mike Lormore**, Director of Dairy Veterinary Operations, *Pfizer Animal Health*

PRESENTATION HIGHLIGHTS[1]

Antibiotics in Food Animal Production

Antibiotics are regulated by the U.S. Department of Health and Human Services' Food and Drug Administration (FDA). Additional research, surveillance and monitoring activities are conducted by the U.S. Department of Agriculture (USDA) and the Centers for Disease Control (CDC).

The FDA Center for Veterinary Medicine (CVM) utilizes the same regulatory approaches for antibiotics used in food-animal production as those intended for human use. The FDA CVM also determines withdrawal times, i.e., the time required to elapse between the last dose administered and when food animals can enter the food chain. The National Antimicrobial Resistance Monitoring System (NARMS) tracks antimicrobial resistant (AMR) bacteria in food animals, retail meats and humans. The USDA Food Safety & Inspection Service (FSIS) ensures withdrawal time compliance and helps track AMR bacteria. FSIS's Hazard Analysis Critical Control Program (HACCP) helps reduce the possibility of bacterial transfer from animals to humans via food of animal origin. The CDC also helps track AMR bacteria.

Antibiotics are employed carefully and responsibly to optimize animal health and well-being, especially for those classes that are shared. The following principles are important:

1) Advancing science helps improve antimicrobial use protocols.
2) Collaboration between the American Veterinary Medical Association (AVMA) and the FDA CVM has produced judicious use guidelines designed to minimize the need for antibiotic use and maximize their effectiveness when needed.
3) Producers and veterinarians work closely together to ensure judicious antimicrobial use on the farm.

Major classes of antimicrobials shared by animals and humans include:

β-lactams	Penicillin, amoxicillin; ceftiofur
Macrolides & lincosamides	Tylosin; tilmicosin; tulathromycin, lincomycin
Aminoglycosides	Gentamicin; neomycin
Fluroquinolones	Enrofloxacin, danofloxacin
Tetracyclines	Tetracycline; oxytetracycline, chlortetracycline
Sulfonamides	Various
Streptogramins	Virginiamycin
Polypeptides	Bacitracin
Phenicols	Florfenicol
Pleuromultilin	Tiamulin

The poultry industry has received significant criticism for its use of antibiotics as feed additives with ionophore use being proportionally higher in poultry production for coccidiosis prevention purposes in mainstream production chains. Ionophores are a non-medically important antimicrobial agent, are not used in human medicine, and play no role in the antimicrobial-resistance debate.

[1] Full presentations are available at: http://www.animalagriculture.org/Solutions/Proceedings/Symposia/2011%20Antibiotics.html.

According to FDA's most recent data, ionophore sales in 2010 comprise the second largest category of sales for food-animal production purposes – nearly five times larger than the next specific category reported by FDA.[1] In fact, animal drug makers are surveyed annually to determine the amount of antibiotics sold for use in animals. In 2007, only 13 percent of the total was used to enhance productivity while the remaining 87 percent was used to target an identified pathogen – uses considered therapeutic by the FDA, AVMA and the Office of International Epizoonotics and Codex Alimentarius.[2]

The livestock and poultry industries are working to make strides in animal genetics to understand the heritability of disease resistance. In addition, food-animal production has evolved to include multiple advisors: veterinarians, nutritionists, geneticists, academicians, farm managers and animal caretakers.

Individuals dedicated to food animal production recognize that proper production practices, such as maintaining flock and herd health by preventing disease through biosecurity and the use of vaccines, help minimize the need for antimicrobial use. Air filtration is an example of one of the newest aspects of biosecurity. Good animal husbandry, preventive health care, use of proper rations and providing quality care are the keys to raising healthy animals.

Animal agriculture stands on the belief that healthy animals make safe food. However, when disease strikes, livestock and poultry producers should work with their veterinarian to appropriately treat the animals and better ensure food safety. Medically important antibiotics used in food-animal agriculture should be used under the supervision of a veterinarian to combat disease on a case by case basis. Access to antibiotics to prevent and treat animal disease is essential for the health of food animals as well as to ensure a safe food supply.

Veterinarians are bound by oath to prevent and relieve animal suffering while promoting public health: "*Being admitted to the profession of veterinary medicine, I solemnly swear to use my scientific knowledge and skills for the benefit of society through the protection of animal health and welfare, the prevention and relief of animal suffering, the conservation of animal resources, the promotion of public health, and the advancement of medical knowledge. I will practice my profession conscientiously, with dignity, and in keeping with the principles of veterinary medical ethics. I accept as a lifelong obligation the continual improvement of my professional knowledge and competence.*"[3]

A continuing media focus on plausible, yet largely unestablished, negative public health outcomes linked to antimicrobial use in food animals may place conflicting pressures on veterinarians to sacrifice their core principle of prevention and relief of animal suffering to address these theorized negative public health concerns.

To prevent unsafe antibiotic residue foods of animal origin, the various sectors of the livestock industry employ "best" practices in disease prevention and treatment. For example, the dairy industry is highly vigilant about managing mastitis and has rigorous guidelines to encourage and manage withdrawal times so residues don't find their way into dairy products.[4] The swine industry has implemented multi-phase, all-in, all-out management that coupled with advanced diagnostics and responsible antibiotic use practices, as part of the industry's Pork Quality Assurance® Plus Program,[5] has improved strategic disease prevention.

Because the primary health challenge in beef cattle is bovine respiratory disease (BRD), especially prevalent among newly weaned and/or received calves, the beef industry encourages preconditioning - vaccination, nutrition and management strategies designed to prepare immunologically naive cattle to withstand the stress and pathogen exposure associated with marketing and shipment to a backgrounding yard or feedlot. Management inputs associated with prevention, like preconditioning, aid in reducing the incidence of the disease and subsequent need for antibiotic treatment among new arrivals. To provide a safe, wholesome and healthy beef supply, the beef industry also encourages responsible antibiotic use practices, among other proper management techniques, through its Beef Quality Assurance (BQA) program.[6]

Human Health Implications Relative to Antibiotic Use

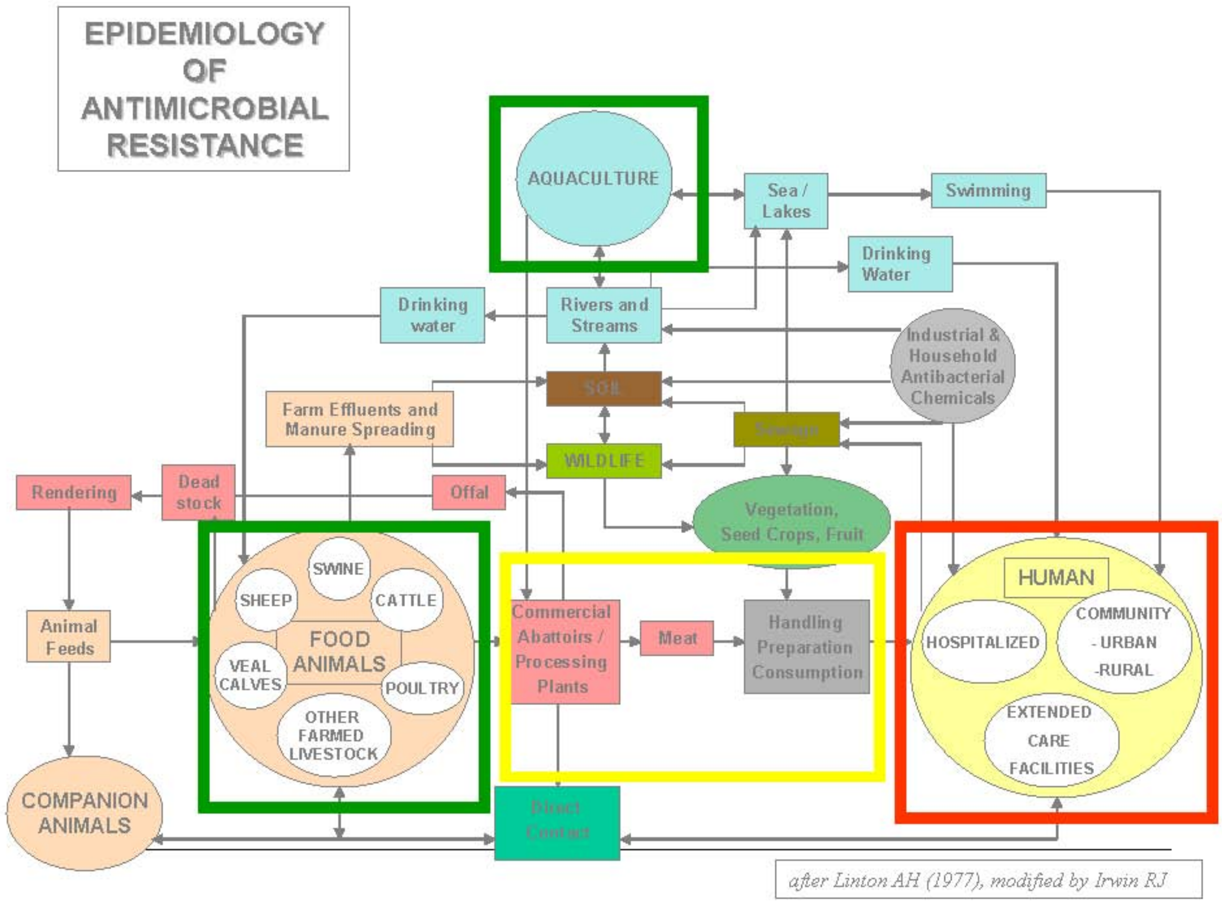
Antibiotic resistance is a natural biological phenomenon that predates the era of antimicrobial therapy by millennia. Resistance to penicillin in some strains of staphylococci was recognized almost immediately after introduction of the drug in 1946. Likewise, very soon after their introduction in the late 1940s, resistance to streptomycin, chloramphenicol and tetracycline was noted. By 1953, a strain of the dysentery bacillus (*Shigella dysenteriae*) was isolated and exhibited resistance to chloramphenicol, tetracycline, streptomycin and the sulfonamides.[7]

AMR bacteria are found in many places besides the farm: ground water,[8] ocean trenches,[9] wild animals,[10,11] and even in 30,000-year-old permafrost.[12] Additionally, there is no known connection between several drug-resistant human pathogens and food-producing and/or companion animals. Some drug-resistant infections in humans are a result of extensive use in humans since the antibiotics in question have never been approved for use in food-producing animals.[13]

Antimicrobial resistance is not an all-encompassing, across-the-board phenomenon. Rather, it results from complex interactions among three factors: 1) antibiotic class; 2) specific pathogen; and 3) potential host population. Alternatively, managing the biology around antimicrobial resistance has been described as volatile, uncertain, complex and ambiguous. As a result, resistance is difficult, if not impossible, to predict. Blanket approaches to minimize resistance development and dissemination are simply unable to effectively solve each and every antibiotic/pathogen/host combination.

Development and dissemination of antibiotic resistance is a highly complex issue *(see Figure 1 on the following page)*.

Figure 1



The medical community has stressed that the speed of change of the regulatory and political landscapes is faster than product development can move. "…the drug pipeline and resistance problems have only grown worse as more companies have withdrawn from antibiotic research and development (R&D) and ever-more resistant 'bad bugs' have spread across the United States…"[14]

Some might argue that the regulatory environment, coupled with the influence of well-intentioned activists and political opportunists, has unfortunately created a situation that discourages research and development of new and novel antimicrobials. The long-term consequence of this could well be increasing risk to the lives and health of countless numbers of people and animals.

Conflicting pressures are brought to bear when attempting to conserve "critically important" antimicrobials for human medicine while simultaneously restricting access to less important but widely used antimicrobial options in animal agriculture:

- Shared perspective — Antibiotics are essential for humans and animals; overuse/misuse is recognized in both fields; and protecting the efficacy of antibiotics is considered a desirable objective.
- Risk-averse perspective — Humans take precedence over animals. Therefore drugs deemed critically important to human medicine should not be used at all in animals.

- Risk-tolerant perspective — The judicious use of antibiotics in animals is sometimes required to provide safe, nutritious food at a reasonable price, and prevention of infectious diseases improves animal and human health and well-being.

Resistance to antimicrobials is an evolving process, with many types of resistance mechanisms, that occurs both in the presence and absence of antimicrobial use in both human and animal populations. However, the use of antimicrobial drugs is known to contribute to antimicrobial resistance development.[15] As such, it is imperative that antibiotics be used appropriately in all sectors, including public health and livestock production.

Managing antimicrobial resistance doesn't have a simple answer. Instead it requires a multi-disciplinary approach including:

- Formulary controls
- Infection control
- Microbiology laboratory resistance detection systems and epidemiologic typing methods
- Interested medical staff with institutional commitment of resources
- Local and global surveillance systems
- Further research on antimicrobial resistance
- Increased drug development
- More public education

While the human health community has shown increased interest in addressing antibiotic use and antibiotic resistance, no conclusive evidence exists as to primary causal factors of antibiotic resistance.

The ecology of microorganisms is not a static state with all in perfect harmony but is an intensely competitive biosphere filled with change, competition and adaption.

Robust research and development investment is needed to commercialize new antimicrobials and to better understand the effects of dose, duration and timing of antimicrobial use in both human and animal populations.

Regulatory Oversight and Risk Mitigation

FDA CVM Guidance (GFI #152) formalized a process to assess resistance risks and provide a pathway for approving new animal drugs. Products that predate GFI #152 remain a public health concern. Draft GFI #209[16] recommends to limit use of medically important antimicrobial drugs to those uses that 1) are considered necessary for assuring animal health, i.e., to treat, control or prevent disease, and 2) include veterinary involvement/consultation. Draft GFI #209 doesn't affect all antimicrobial drugs. Rather it is intended to apply to those drugs that are considered medically important, i.e., important for treating disease in humans. The proposed strategy outlined in the draft guidance recommends that steps be taken to phase out the growth promotion use of medically important drugs. In response to the concern that eliminating growth promotion use of certain drugs may lead to an increase in animal disease, FDA proposes that changes be phased in over time to minimize impacts and to assure that animal health needs continue to be met. The draft guidance also acknowledges the critical role that veterinarians play as diagnosticians and consultants for assuring judicious use and recommends that the marketing status of medically important drugs be changed from OTC (Over-The-Counter) to Rx (medically prescribed) or VFD (Veterinary Feed Directive).

The focus of FDA's proposed strategy is to implement the recommended changes through a voluntary approach over a number of years to provide for an adequate transition period to minimize adverse impacts on animal health and industry disruption.

Numerous global reports[17] on antibiotic use have been published since 1997 and include risk management strategies such as responsible use, resistance monitoring, antibiotic sales monitoring, regulatory controls and research. Concern and risk are two very different concepts, however. Concern can arise over any number of issues and can occur independent of any real, substantiated, measurable existence of risk. Risk, on the other hand, can be present independent of concern and represents a threat to humans only if there is a causal pathway from the AMR bacteria in food-producing animals such that resistance is transferable to humans.

The estimated risk of farm-to-fork AMR transfer has been estimated to be extremely low.[18] In addition, the alternative risk of sub-optimal animal health may actually exceed the risk of on-farm antibiotic use — thereby invoking concern about unintended animal health and food safety consequences if certain antibiotic uses in livestock are banned. One recent study looked at the swine health impact on carcass contamination and human food-borne risk. In this study, individual carcass swabs were cultured for *Salmonella*, and logistic regression analysis showed the probability of *Salmonella* contamination in lesioned carcasses was 90 percent higher than in non-lesioned carcasses.[19]

Although activists often claim that antibiotics used in livestock and poultry are the cause of human antibiotic resistance, the attributable risk of human disease outcomes, e.g., additional illness days due to resistance, associated with the use of antibiotics in food-producing animals is unknown.

Using an antibiotic, or using more of it, will not necessarily cause resistance to that antibiotic to appear, or to increase from current levels. Likewise, ceasing to use an antibiotic, or using less of it, will never completely eliminate resistance, or necessarily even decrease it from current levels. That's especially true given the large number of interacting factors on the human side including the dynamics surrounding medical and socialized care.

Changes in regulatory oversight will re-shape producers' access to antibiotics and the practice of veterinary medicine, creating intended and unintended consequences, potentially negative, with regard to animal health, public health and food safety. A Danish experience underscores unintended consequences that can occur. After certain antibiotic uses were banned in Denmark, more livestock became sick and required greater use of therapeutic antibiotics. Furthermore, the elimination of antibiotics at the health maintenance level in Denmark has not led to a substantial impact on the incidence of antibiotic-resistant food-borne illness in humans.[20,21]

An American Academy of Microbiology Colloquium Report (c. 2009), "An Ecological Approach to an Old Problem," poses the question: If science and medicine cannot win a war against antibiotic resistance, what can be done? The Report's answer: Find a way to co-exist with resistance. To minimize the loss of life, strategies must be developed to prevent new resistance from spreading and, where resistance already exists, identify the strains we need to protect against, find ways to treat resistant infections effectively in patients, and manage reservoirs of antibiotic resistant strains in the environment.

Livestock MRSA: Understanding and Communicating the Risks

Methicillin-resistant *Staphylococcus aureus* is a leading cause of hospital-associated infections.[22] But MRSA is no longer just a hospital problem as it has been documented to exist among other public populations as well as among food-producing animals and companion animals.[23,24]

It is important to recognize the differences between contamination, colonization, and infection of *S. aureus*. Surfaces or objects are considered contaminated if presence of the bacteria is found. Colonization means that the presence of the bacteria is detected in humans or animals, but there are no signs of illness or infection, thus treatment is not needed. Infection occurs when invasion by the bacteria results in clinical signs of illness or inflammation. Infection requires treatment; however, various treatment options exist and do not always require the use of an antibiotic.

ST398 is the livestock-associated MRSA, and it, as well as ST398 human infections, has been recognized in several countries, including the United States. In one multi-state study,[25] ST398 was found in Iowa swine herds only. In this same study, although MRSA was not found on any antibiotic-free farms, it was detected in confinement operations, and nasal swabs from humans working in the confinement facilities were found to be colonized by MRSA. Pigs have also been found to be colonized with "human" types of MRSA.

Working with live pigs is the most important factor for testing positive for colonization of LA-MRSA. The risk, however, for potential for transmission of LA-MRSA to the community via farmers, air, meat products, and water/manure is uncertain. Studies show that while MRSA ST398 has been identified on some pig farms and in those in direct contact with the live animal, LA-MRSA has not been found to spread into the wider community.[26]

ST398 MRSA has caused a small number of serious infections, with not all human ST398 infections known to have contact with livestock/poultry. Other MRSA clinical isolates are more common causes of human infection. ST 398 – spa type t571 can be a MRSA or a methicillin-susceptible *S. aureus* (MSSA) strain and is uncommon in animal isolates. This MSSA strain has been found in several cases of human infection where there was no apparent contact with livestock or contact was unlikely. While *Staphylococcal* food-borne disease is common, there are only rare reports of MRSA involvement.

LA-MRSA is a new and potential health concern for persons in the swine/livestock industries, but current evidence[27,28,29,30,31,32,33] indicates it is not a concern for the broader community as it has not been shown to be a significant cause of the overall MRSA burden in humans. Since LA-MRSA is not a food-borne pathogen, it is not a food safety or public health concern.

Connecting with Consumers

The use of antibiotics in food-animal production is a complex issue that is often simplified, thus misleading the public and adversely affecting perceptions.

Research shows that consumers mostly support farm antibiotic use for the treatment of sick animals.[34,35] But some consumers are not certain that treated animals should go into the food supply, and some even contend that antibiotics used to promote growth are unacceptable. Perceptions, misperceptions, and beliefs among some consumers or consumer groups that have been heard by the animal agriculture industry and require addressing include:

- "Antibiotics are used indiscriminately on the farm, with minimal oversight of either veterinarians or FDA."
- "Antibiotics given to animals will end up in the food and possibly jeopardize my family's health."
- "Using antibiotics on the farm contributes to the creation of resistant pathogens that threaten health."

Common on-farm practices that consumers should know about regarding food-animal production include:

1) Modern livestock farms increasingly involve licensed veterinarians to advise on health management decisions.
2) Vaccines are used to protect animals from various illnesses.
3) Sick animals are treated with medicines, such as antibiotics, to restore their health, and protections are in place to ensure that their meat or milk is safe for people.
4) The FDA approves the use of all new animal drugs after testing and confirming animal safety and human food safety.
5) If antibiotics are administered to cure a sick animal, the animal itself — in the case of meat production — or animal products — such as milk — are not allowed to enter the food supply until the withdrawal period has passed and the medicine has sufficiently cleared the animal's system. The required periods for withdrawing medication are specific for each drug and species and are approved by the FDA based on research studies of residues in edible tissues.

Since antibiotics will always be needed to ensure animal and human health, the animal agriculture industry together with various regulatory agencies must consistently and effectively communicate and demonstrate its food safety commitment to the food chain and consumers in order to build long-term trust. Messages must come from a position of shared values as producers of food animals have many shared values with consumers. After all, producers are consumers too.

Additional Points/ Need for Dialogue Going Forward

- Reported sales of antibiotics are NOT equivalent to use. Moreover, a very sizeable portion of reported antibiotic sales by FDA — upwards of 40 percent — include the sales of ionophores — which are not used in human medicine and play no role in the antimicrobial-resistance debate and possess no implications around the issue of resistance. Collecting information about antibiotic use must be carefully analyzed; specifically, production and/or sales data should not be considered in an aggregate manner (total sales) — such data can be largely misleading as it provides no context of actual use. Rather, antibiotic sales should be clearly delineated by species and respective class in relation to total production over time.

- Consolidation is ongoing in the production sector of animal agriculture. Increasing economies of scale have allowed for improved engineering of facilities, management systems and labor specialization with the outcome being improved health, productivity and quality of livestock production and resulting food products. The livestock and poultry industries, though, allow room and capacity for different farm sizes and production practices across all species, and consumers should be allowed to exercise purchasing options to reflect individual values.

- Better and broader detection methods and surveillance are finding providing more timely data. Thus, the perception that more food safety issues exist than ever before may not be accurate. Potential health concerns are simply being discovered before they might become a more serious problem, e.g., food recalls.

- Aspects of modern life that potentially exacerbate resistance include: Large hospitals, the concentration of the very young and very old in socialized care, and increasing travel. In short, more research is needed in order to find the root cause of the upward trends. Another avenue to explore more closely is the overuse and improper use of antibiotics in humans.

- The relative contribution that dose and duration have on resistance selection is ill-defined. For example, the effect of duration of therapy on therapeutic outcome is ill-defined in both human and veterinary medicine.

- Antimicrobial resistance management has no absolute answers — active, objective, fact-based dialogue must continue to ensure continued safe and efficacious use of antibiotics in both humans and animals.

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[1] 2010 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals, Department of Health and Human Services, Food and Drug Administration Center for Veterinary Medicine, October 2011
[2] SafeFoodInc.com, http://www.safefoodinc.org/index.php?option=com_content&view=article&id=3&Itemid=11
[3] American Veterinary Medical Association's Veterinarian's Oath, Approved by the HOD, 1954; Revision approved by the HOD, 1969; Revision approved by the Executive Board 1999, 2010
[4] American Association of Bovine Practitioners "Guidelines for Therapy of Clinical Mastitis in Lactating Dairy Cows"
[5] Pork Quality Assurance Plus Program, www.pork.org/Certification/11/pqaPlus.aspx
[6] Beef Quality Assurance, www.bqa.org
[7] History of Antimicrobial Agents and Resistant Bacteria, JMAJ 52(2): 103-108, 2009, Saga and Yamiguchi
[8] Kümmerer 2004

[9] Sizemore and Colwell 1977
[10] Rolland et al 1985
[11] Williams et al 2011
[12] D'Costa et al 2011
[13] The Infectious Diseases Society of America, http://www.idsociety.org/Content.aspx?id=5650
[14] The Infectious Diseases Society of America's (IDSA) Statement on Antibiotic Resistance: Promoting Critically Needed Antibiotic Research and Development and the Appropriate Use ("Stewardship") of these Precious Drugs before the House Committee on Energy and Commerce Subcommittee on Health, June 9, 2010
[15] FDA "Battle of the Bugs: Fighting Antibiotic Resistance" http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143568.htm
[16] Draft GFI #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals, U.S. Department of Health and Human Services, Food and Drug Administration Center for Veterinary Medicine, June 28, 2010
[17] Shryock 2011, Slides 25-28, http://www.animalagriculture.org/Solutions/Proceedings/Symposia/2011%20Antibiotics/Shryock,%20Tom.pdf
[18] Hurd 2011, Slide 19, http://www.animalagriculture.org/Solutions/Proceedings/Symposia/2011%20Antibiotics/Hurd,%20Scott.pdf
[19] In press American Journal of Veterinary Medical Research, S. Hurd
[20] GAO-11-801 Antibiotic Resistance: Agencies Have Made Limited Progress Addressing Antibiotic Use in Animals, p. 41
[21] The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP), www.danmap.org
[22] Klein et al 2009
[23] The New England Journal of Medicine 2005 352(5), p. 468-75
[24] NEJM 2008 358(11), p. 1200-01
[25] Smith, T. et al, in preparation
[26] Cuny et al 2009
[27] Van Cleef et al 2010
[28] Van Cleef et al 2011
[29] Graveland et al 2011
[30] Bootsma 2010
[31] Wassenberg 2011
[32] Golding et al 2010
[33] Leedom Larson et al 2010
[34] Pfizer Animal Health 2008
[35] PEW 2011