The Infectious Diseases Society of America's (IDSA) Statement on

Antibiotic Resistance: Promoting Judicious Use of Medically Important Antibiotics in Animal Agriculture

Before the House Committee on Energy and Commerce Subcommittee on Health

July 14, 2010

The Infectious Diseases Society of America (IDSA) appreciates this opportunity to speak in support of the House Energy and Commerce Committee Health Subcommittee's efforts to promote the appropriate ("judicious") use of medically important antibacterial drugs ("antibiotics") in animal agriculture. My name is James R. Johnson, MD, FIDSA, FACP. I am an infectious diseases specialist and a Professor of Medicine at the University of Minnesota School of Medicine. I also am a member of IDSA's Antimicrobial Resistance Work Group.

IDSA represents more than 9,000 physicians and scientists devoted to patient care, prevention, public health, education, and research in the area of infectious diseases. Our members care for patients of all ages with serious infections, including meningitis, pneumonia, tuberculosis (TB) and HIV/AIDS, emerging infections like the 2009 H1N1 influenza virus, food-borne diseases caused by *Salmonella*, *Campylobacter*, and *Escherichia coli* (*E. coli*), and diverse infections caused by antibiotic-resistant bacteria. Among the most concerning antibiotic-resistant organisms are methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus*, *E. coli*, *Salmonella*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Acinetobacter baumannii*.

To better protect our patients and the general public against antibiotic-resistant bacterial infections, IDSA strongly supports efforts to eliminate all non-judicious uses of antibiotics in human medicine and animal agriculture (e.g., cattle, swine, and poultry production and aquaculture), including H.R. 1549, the Preservation of Antibiotics for Medical Treatment Act (PAMTA) and the Food and Drug Administration's (FDA's) recently announced public health approach to address antibiotic use in animal agriculture. IDSA also supports the elimination of non-judicious uses of antibiotics in plant agriculture. Antibiotics currently are used inappropriately on fruit and vegetables (e.g., use of gentamicin as a pesticide in apple orchards[1]). However, we have been asked to limit our comments today to animal agriculture.

In the animal agriculture context, the elimination of non-judicious uses will mean the end of antibiotic use for purposes of growth promotion, feed efficiency, and routine disease prevention. We also support requiring all remaining uses of antibiotics to be carried out under the supervision of a veterinarian and within the boundaries of a valid veterinarian-client-patient relationship. Finally, we urge Congress to enact legislation requiring the collection of antibiotic consumption data in the United States in a manner that parallels data collection advances achieved within the European Union.

Today, many of us in the United States take antibiotics for granted—we do not realize how fortunate we are to have them. Many of our parents, grandparents, and great-grandparents were not so lucky. Prior to the discovery of antibiotics, many injuries and illnesses became death

sentences as there was no way to treat the common infections that were often associated with them. Antibiotics often are referred to as "miracle drugs," because patients traditionally only needed to take them for a number of days for most infections to be cured.

The development of antibiotics to treat serious and life-threatening infections has indeed been one of the most notable medical achievements of the past century. However, there is growing concern among infectious diseases specialists that the effectiveness of antibiotics in treating infections is being increasingly compromised by the ever-growing presence of drug-resistant bacteria. Drug-resistant organisms are plaguing Americans, and others around the world, including otherwise healthy individuals, in the community and healthcare settings alike. Antibiotic resistance is a serious threat to public health, to patient care and safety, and to national security. Antibiotic-resistant infections are extremely difficult to treat and frequently recur. These infections often result in tremendous pain, suffering, and disfigurement in adults, children and infants, have caused millions of deaths worldwide, and have been estimated to cost the U.S. health care system between $21 billion and $34 billion annually.

Chairman Pallone, Ranking Member Shimkus, and Subcommittee members, at the same time that the numbers of drug-resistant infections are increasing, we have seen a steep decline in the number of new antibiotics in development. This Subcommittee has conducted a series of hearings to gain a better understanding of the many factors that are contributing to the current antibiotic resistance crisis. These hearings are critically important, and IDSA applauds your efforts. IDSA was pleased to testify before the Subcommittee on June 9, 2010 about antibiotic resistance and the dire antibiotic pipeline problem.[2] As you may recall, IDSA's testimony explored several key themes:

- Antibiotics are a vital resource and a precious gift from prior generations, and we have a moral obligation to ensure this resource is available for future generations.
- Safe and effective antibiotics are urgently needed to treat serious and life-threatening infections caused by a growing list of drug-resistant bacteria.
- As with other diminishing resources (energy, forests, clean water, etc.), Congress and the Administration must establish policy to nurture both the conservation and restoration of antibiotics through the development of innovative antibiotics and other relevant tools (e.g., rapid diagnostics, vaccines, and other biologicals).
- We must adopt, promote, and continue to refine effective strategies to prevent both the emergence and transmission of resistant organisms, which undercut the effectiveness of our current antibiotic arsenal. Transmission of resistant organisms can be prevented by good infection control practices, effective immunization policies, and (for food-borne organisms) hygienic food production, processing, distribution, and preparation. Emergence of drug-resistant bacteria can be reduced by ensuring that antibiotics are used judiciously in all settings. Antibiotic stewardship strategies are the best way to achieve this goal.

Our statement today will examine in greater detail this last principle and specifically the need to eliminate all non-judicious uses of antibiotics in animal agriculture and to ensure that all antibiotic uses in animals be carried out under the supervision of a veterinarian within a valid

veterinarian-client-patient relationship.[i] Considerable efforts have been taken in human medicine to eliminate non-judicious antibiotic use. As described in our prior testimony, antibiotic stewardship programs and practices are being established in health care settings across the country. Stewardship can take the form of restricting which antibiotics are included in the health facility formulary or requiring preauthorization to prescribe a specific therapy. Additional mechanisms can include antibiotic order forms, formal prospective audit and feedback, de-escalation of therapy based upon microbiological data of what specifically is causing an infection, and dose optimization. Educational efforts focused on appropriate uses have targeted both providers and patients. Of critical importance, antibiotics used in human medicine require a prescription. In contrast to human medicine, although animal agriculture uses of antibiotics also contribute significantly to the development of drug-resistant pathogens, only limited measures have been taken in this setting to eliminate non-judicious uses. Also, appropriate marketing and distribution safeguards have not been implemented in the agricultural setting as tons of antibiotics are purchased over-the-counter without a prescription each year for use in animal agriculture.

ANTIBIOTIC RESISTANCE: THE COSTS ARE GREAT

The U.S. Centers for Disease Control and Prevention (CDC) has described antibiotic resistance as "one of the world's most pressing health problems", because "the number of bacteria resistant to antibiotics has increased in the last decade [and] … many bacterial infections are becoming resistant to the most commonly prescribed antibiotic treatments." The World Health Organization (WHO) has identified antibiotic resistance as "one of the three greatest threats to human health." Infectious diseases physicians agree. The costs due to antibiotic resistance, both in the numbers of lives lost or devastated and in economic terms, are exceedingly high.

Drug-resistant bacteria, such as MRSA and resistant enterococci and *E. coli*, affect many hospitalized patients, and resistant bacteria likewise are impacting a growing number of people in the community, including healthy athletes, parents, working people, and children. A 2007 study published in the *Journal of the American Medical Association*[3] demonstrates that annually in the U.S. more than 94,000 people are infected with invasive MRSA, and nearly 19,000 die from MRSA alone – which is more deaths than are caused by emphysema, HIV/AIDS, Parkinson's disease, and homicide. CDC reports that nearly 2 million health care-associated infections (HAIs) and 90,000 HAI-related deaths occur annually in the U.S.[4] Most of these infections and deaths involve antibiotic-resistant bacteria. A February 2010 study published in

[i] The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA; Public Law 103-396) defines a valid veterinarian-client-patient relationship as one in which:

1. A veterinarian has assumed the responsibility for making medical judgments regarding the health of an animal and the need for medical treatment, and the client (the owner of the animal or other caretaker) has agreed to follow the instructions of the veterinarian;
2. There is sufficient knowledge of the animal by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal; and
3. The practicing veterinarian is readily available for follow-up in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal by virtue of examination of the animal, and/or by medically appropriate and timely visits to the premises where the animal are kept.

the *Archives of Internal Medicine* showed that two common types of HAI—sepsis and pneumonia—killed 48,000 people and increased health care costs by $8.1 billion in 2006 alone.[5]

The direct and indirect economic costs associated with antibiotic-resistant infections are also enormous in terms of dollars spent, length of hospital stay, and loss of productivity. A recent analysis of antibiotic-resistant infections at Chicago Cook County Hospital[6] , when extrapolated nationwide, indicated that annually in the U.S. antibiotic-resistant infections are responsible for more than $20 billion in excess health care costs, more than $35 billion in societal costs, and more than 8 million additional hospital days.[7]

ANTIBIOTICS ARE UNIQUE

In addition to their extremely high level of effectiveness and the value they provide to society, antibiotics are unique among medicines in one critically important way. Unlike other drugs, over time antibiotics lose their ability to treat the diseases for which they were developed—due to the ability of bacteria to develop resistance to the antibiotic. Therefore, in an effort to prolong antibiotics' effectiveness for as long as possible, infectious diseases physicians and professional societies urge that antibiotics be used appropriately and sparingly and seek ways to limit unnecessary use of these drugs.

A CLEAR LINK BETWEEN ANTIBIOTIC USE IN ANIMAL AGRICULTURE AND ANTIBIOTIC-RESISTANT INFECTIONS IN HUMANS

Physicians, health care professionals, and public health and food safety advocates are greatly concerned about non-judicious uses of antibiotics in animal agriculture. The relationship between antibiotic-resistant infections in humans and antibiotic use in animal agriculture is complex, but well-documented. A large and compelling body of scientific evidence demonstrates that antibiotic use in animal agriculture contributes to the emergence of resistant bacteria and their spread to humans. For example, it is well documented that fluoroquinolone use in poultry was a major source of fluoroquinolone-resistant *Campylobacter* infections in humans, leading to treatment failures and an increased risk of death. Likewise, cephalosporin and fluoroquinolone use in food animals has led to cephalosporin and fluoroquinolone-resistant *Salmonella* infections in humans, also with adverse health consequences. A livestock-associated strain of MRSA, which was first encountered in the Netherlands in 2003 and now accounts for one fifth of human MRSA infections there,[8] was recently found also in swine in Iowa, and Illinois.[9] This food animal-derived MRSA strain has caused various human infections, including hospital outbreaks; serious skin, wound, lung, and heart infections; and, in a dairy worker, necrotizing fasciitis – also known as flesh-eating bacterial infection.[10] Many of the antimicrobial-resistant *E. coli* strains that cause urinary tract and bloodstream infection in humans appear likely to derive from food animals, having become resistant on the farm.

The evidence of a cause-and-effect link between food animal antibiotic use and drug-resistant infections in humans is broad-ranging and derives from numerous epidemiological, molecular epidemiological, ecological, and experimental studies. The threat to humans due to antibiotic use in animal agriculture includes both acquisition of resistant pathogens by humans (whether from the food supply, direct contact with animals, or environmental sources) and transfer of

resistance genes from animal to human bacterial populations. A broad consensus exists among relevant experts that, based on the available evidence, it is reasonable and prudent to conclude that the use of antibiotics in animal agriculture poses an important threat to human health that warrants urgent action.

That antibiotic use in animal agriculture can give rise to resistance in humans has long been recognized by the infectious diseases and public health communities. A 1995 report by the Office of Technology Assessment[11] listed at least a dozen earlier expert committee reviews of the health effects of antibiotic use in animal husbandry, dating to the 1969 Swann Report, a report by the Joint Committee on the use of Antibiotics in Animal Husbandry and Veterinary Medicine, chaired by Professor M. M. Swann.

The Swann Report concluded:

> *"the administration of antibiotics to farm livestock, particularly at sub-therapeutic levels, poses certain hazards to human and animal health; in particular it has led to resistance in enteric* [food-borne] *bacteria of animal origin. This resistance was transmissible to other bacteria, and enteric bacteria were transferable from animals to man."*

The United Kingdom banned the use of penicillin and tetracycline for growth promotion in 1971.[12]

In a 2000 report from a new expert review panel,[13] the World Health Organization (WHO) stated:

> *"Another source of resistance lies in our food supply. Since the discovery of the growth-promoting and disease-fighting capabilities of antibiotics, farmers, fish-farmers and livestock producers have used antimicrobials in everything from apples to aquaculture. Currently, only half of all antibiotics produced are slated for human consumption. Ongoing and often low-level dosing for growth promotion and prophylaxis [disease prevention] inevitably results in the development of resistance in bacteria in or near livestock, and also heightens fears of new resistant strains between species.*
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> *"Vancomycin-resistant Enterococcus faecium (VRE) is one particularly ominous example of a resistant bacterium appearing in animals that may have 'jumped' into more vulnerable segments of the human population. The emergence of VRE in food can be traced to the widespread use of avoparcin (the animal equivalent of the human antibiotic vancomycin) in livestock. Moreover, with livestock production increasing in developing countries, reliance on antimicrobials is likewise expanding – often without guidelines in those nations where antibiotics are sold without prescription.*
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> *"Often bacteria that are harmless to livestock are fatal to humans. This is true of a number of outbreaks that have taken the medical community by surprise. One example occurred in Denmark in 1998, when strains of multi drug-resistant Salmonella typhimurium struck 25 people, killing two. Cultures confirmed that the organisms were resistant to seven different antibiotics. Epidemiologists eventually traced the micro-*

organism to pork and to the pig herd where it originated. In 1998, 5,000 people in the United States learned the hard way about antimicrobial resistance when they fell ill with multi drug-resistant campylobacteriosis caused by contaminated chicken. The same drugs that eventually failed them had also been used in the poultry that turned up on their plates."

In 2002, the journal *Clinical Infectious Diseases* published a special supplement,[14] based on a two-year review by experts in human and veterinary medicine, public health, microbiology, biostatistics, and risk analysis of more than 500 scientific studies on the human health impacts of antibiotic use in agriculture, which concluded the "*[u]se of antimicrobials in food animals contributes to the growing problem of antimicrobial resistance in animal and human infection."*

In 2003, a National Academy of Sciences report[15] stated, "*Immediate action must be taken to preserve the effectiveness of available drugs by reducing the inappropriate use of antimicrobials in human and animal medicine.*" The authors recommended a ban on the use of antibiotics as growth promoters in animal agriculture if those antibiotics also are used in human medicine.

A December 2003 report[16] of the proceedings of an expert workshop on the Scientific Assessment of Non-Human Antimicrobial Usage and Antimicrobial Resistance, sponsored by the United Nations Food and Agriculture Organization, WHO, and the World Animal Health Organization concluded:

"There is clear evidence of adverse human health consequences due to resistant organisms resulting from non-human usage of antimicrobials. These consequences include infections that would not have otherwise occurred, increased frequency of treatment failures (in some cases death) and increased severity of infections, as documented for instance by fluoroquinolone resistant human Salmonella infections. Evidence shows that the amount and pattern of non-human usage of antimicrobials impact on the occurrence of resistant bacteria in animals and on food commodities and thereby human exposure to these resistant bacteria."

In 2004, the U.S. Government Accountability Office issued a report[17] to Congress stating, *"Scientific evidence has shown that certain bacteria that are resistant to antibiotics are transferred from animals to humans through the consumption or handling of meat that contains antibiotic-resistant bacteria. Many studies have found that the use of antibiotics in animals poses significant risks for human health."*

A 2006 study[18] by a noted expert on aquaculture stated: "*The accelerated growth of aquaculture has resulted in developments detrimental to the environment and human health, such as the widespread and unrestricted use of prophylactic antibiotics in this industry. The use of a wide variety of antibiotics in large amounts, including antibiotics useful in human medicine, has resulted in the emergence of antibiotic-resistant bacteria in aquaculture environments, in the increase of antibiotic resistance in fish pathogens, and in the transfer of these resistance determinants to bacteria of land animals and to human pathogens. It appears that global efforts are needed to promote more judicious use of prophylactic antibiotics in aquaculture as*

accumulating evidence indicates that unrestricted use is detrimental to fish, terrestrial animals, and human health and the environment."

Finally, a 2009 report[19] by the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance states, *"A large number of studies have shown that the use of antimicrobial agents in food animals favors antimicrobial resistance among non-typhoid Salmonella and Campylobacter; later, these can transmit to and cause infections in people. This can then result in failure of antimicrobial treatment in people with resistant infections."*

THE DANISH AND BROADER EUROPEAN EXPERIENCE

Denmark banned the prophylactic (i.e., routine disease prevention) use of antibiotics in animal agriculture; it halted the growth promotion use of antibiotics in broiler chickens and adult swine (finishers) in 1998 and in all swine in 2000. Today in Denmark, all uses of antibiotics in animal agriculture must be accompanied by a prescription in a valid veterinarian-client-patient relationship. In addition, farmers, veterinarians and pharmacies must report the use and sale of antibiotics, and farm inspections are conducted regularly. In 2006, the entire European Union banned non-therapeutic use of antibiotics in animal agriculture due to the threat to human health.

Contrary to claims made by some in the U.S. agricultural sector, experiences in Denmark and other parts of Europe have shown that reductions in antibiotic use do not lead to increased pathogen loads in animals or on carcasses, more food-borne illness in humans, greater total antibiotic use in animals, or impaired animal health or farm productivity. The WHO determined that Denmark's ban achieved its stated public health goal of reducing resistant organisms in food animals in order to prevent related human resistance from emerging.

The ban on growth promoters has been shown to be beneficial to both animal and human health. As one example of Danish and European actions, Danish scientists determined that the use of avoparcin as a growth promoter led to a strain of VRE in food animals. Vancomycin and avoparcin are related drugs, and vancomycin is important to combating serious antibiotic-resistant human infections. In Europe, this strain of VRE spread to humans through the food supply, particularly contaminated meat and poultry. Before the European ban on avoparcin use in animals, Europeans commonly carried VRE in their intestinal tract. Following the avoparcin and related bans, studies showed a drop in related resistance patterns in animals, as well as reductions in humans (both colonization and disease).

The WHO also found that the Danish ban reduced human health risk without significantly harming animal health or farmers' incomes.[20] In fact, Danish government and industry data show that livestock and poultry production has increased since the ban, while antibiotic resistance has declined in animal agriculture, in meat, and in healthy and infected humans (in the case of VRE, and with similar trends for *Campylobacter*). The growth promoter ban implemented throughout Europe in 2006 was followed in subsequent years by sustained decreases in food-borne illness in Europe.[21]

A 2004 Swiss study[22] analyzed prescription patterns for medicated feedstuffs in the Swiss canton of St. Gall to determine whether Switzerland's ban on antibiotics for growth promotion,

introduced in 1999, had caused an increase in the therapeutic use of antibiotics given orally to piglets and fattening pigs. The study found that the ban on growth promoters did not lead to an increase in therapeutic uses in swine.

In Denmark, the only detectable impact of the growth promoter ban in animal agriculture was a short-term effect among weaning-age pigs.[23] Specifically, while there was some reduction in weaner productivity and a small increase in weaner mortality associated with the ban, these effects lasted only one year. Weaner productivity is currently higher and mortality lower than before the growth promoter ban took effect.[24] Danish pork production has increased by 40 percent since the ban.

A July 2010 study,[25] conducted by notable experts in the field, led to the conclusion that:

> *"From 1992 to 2008, a reduction of greater than 50 percent in antimicrobial consumption per kilogram of pig produced was observed in Denmark. This change was associated with the implementation of policies to discontinue the use of antibiotics as antimicrobial growth promoters. During the same period, overall swine productivity improved markedly, which suggests that the change in antimicrobial consumption has not had a negative impact on long-term swine productivity."*

U.S. POLICY APPEARS TO BE MOVING IN THE RIGHT DIRECTION

IDSA is encouraged by the growing support within Congress for the PAMTA legislation, which would phase out the use of the seven classes of medically significant antibiotics that are currently approved for non-therapeutic use in animal agriculture. IDSA also views favorably FDA's new draft Guidance to Industry 209,[26] issued on June 28, which establishes a policy framework regarding the judicious use of medically important antibiotics in animal agriculture. We believe FDA's guidance is a step in the right direction. However, Congressional action is necessary to quickly and fully implement this new policy. Embedded within FDA's guidance are two key principles:

1. The use of antibiotics important in human medicine should be limited in food-producing animals to those uses that are considered necessary for assuring animal health; and

2. The use of antibiotics important in human medicine should be limited in food-producing animals to those uses that include veterinary oversight or consultation.

IDSA strongly supports banning the use of antibiotics for growth promotion and feed efficiency, and requiring that all remaining uses of these drugs be carried out under the supervision of a veterinarian and within the boundaries of a valid veterinarian-client-patient relationship—which would effectively end over-the-counter sales of thousands of tons of antibiotics annually. The sale of antibiotics for use in human medicine requires a prescription; there is no sound reason to permit a lower standard for agricultural purposes, where considerably more antibiotics are used, and in much larger numbers of recipients. We also support clearly defining the limited instances in which antibiotics may be used judiciously in animal agriculture for purposes of disease prevention, as well as more closely monitoring, through enhanced data collection, all remaining

uses (targeted disease prevention, control, and treatment) to prevent non-judicious use. Implementing these changes will better protect our patients and the U.S. public against resistant infections and will help preserve the curative power of existing antibiotics. Both PAMTA and the principles articulated in FDA's new guidance offer elements of the complete framework Congress should consider as it moves forward to develop and enact legislation.

A concern with the FDA's guidance is the agency's apparent decision to rely on drug companies to voluntarily agree to remove growth promotion and feed efficiency claims from their drug labeling. Based on past experience, we believe this process will take years, if not decades, and that many companies are unlikely to comply. Therefore, we urge Congress to expedite this process by eliminating these uses through legislation.

We are concerned that FDA's guidance does not provide sufficient detail about how it plans to address non-judicious uses of antibiotics of importance to human medicine related to disease prevention and therapeutic uses. Therefore, in addition to limiting the marketing status of these drugs to prescription only, we believe FDA and Congress must work together to:

- Establish specific indications for antibiotic use and narrowly limit off-label uses of new and existing antibiotics;
- Define procedures for antibiotic administration that will expose only those animals that have a current need;
- Expand post-approval surveillance under the National Antimicrobial Resistance Monitoring System (NARMS)[ii] to include all drugs of importance to human medicine.

As drafted, FDA's guidance will permit consultation with a veterinarian rather than the veterinarian's direct oversight of the treated animal before an antibiotic can be prescribed. Obviously, FDA took into account logistical issues (the vast rural expanses and limited number of veterinarians within the U.S.) when it considered this principle. However, the consultation allowance, if included in FDA's final guidance/regulation, provides opportunity for abuse as it does not require a veterinarian's direct oversight of the treated animal within the context of a valid veterinarian-client-patient relationship as defined by AMDUCA. Accordingly, legislation or regulation, depending on which option is chosen, must be carefully crafted.

IDSA also urges a reassessment of existing FDA Guidance #152, which is the framework by which the agency approves new antibiotic products for use in animals. FDA must reevaluate the current ranking of drugs according to their importance to human medicine. In particular, the

[ii] NARMS was established in 1996 as a collaborative effort between FDA's Center for Veterinary Medicine (CVM), U.S. Department of Agriculture (USDA), and the Centers for Disease Control and Prevention (CDC). NARMS monitors changes in antibiotic susceptibilities of selected enteric bacterial organisms in humans, animals, and retail meats to a panel of antibiotics important in human and animal medicine. Animal specimens for NARMS are collected from federally inspected slaughter and processing facilities, from healthy animals on farms, and from Veterinary Diagnostic Laboratories, including USDA's National Veterinary Services Laboratories. Animal and human isolates currently monitored in NARMS are non-typhoid *Salmonella*, *Campylobacter*, *E. coli*, and Enterococci. CDC also tests additional human isolates including *Salmonella* typhi, *Listeria* and *Shigella*. Retail meats collected from grocery stores were recently added to NARMS sampling. Accessed online at: http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/default.htm.

agency should reconsider the criteria used to categorize antibiotics as "critically important" and "highly important" to human health. For example, IDSA believes fourth-generation cephalosporins should be considered "critically important," the same ranking currently given to third-generation cephalosporins. Third- and fourth generation cephalosporins are used to treat complicated, high-severity intra-abdominal infections, as well as invasive *Salmonella* infections in humans. WHO agrees with the categorization of fourth-generation cephalosporins as critically important.[27] We also support broadening the scope of Guidance 152 criteria beyond enteric pathogens. The current focus on enteric-only pathogens fails to consider the human risk posed by horizontal gene transfer or clonal spread of resistant strains of bacteria, including such species as *Enterococcus* and *E. coli*, which are intestinal commensals in food animals but extraintestinal pathogens in humans.

Additional investments into new vaccines for animals that would prevent infections and result in decreased antibiotic use in animals, as well as rapid diagnostics to more quickly identify bacterial infections, also would be helpful. These new tools would help to prevent the emergence and transmission of infections and help to protect both animal and human health.

ELIMINATING NON-JUDICIOUS USES WILL NOT HARM U.S. FARMERS

IDSA recognizes that eliminating non-judicious uses of antibiotics in animals will require changes in the agriculture industry's current practices. Ultimately, protection of the public's health must be our highest priority, and we believe terminating these uses can be accomplished in a way that minimizes costs to the agricultural sector. As previously noted, studies have shown that food animal producers in Denmark have adapted to such policy shifts without disruption to farm productivity or a negative impact on animal health.

In addition, a USDA analysis of U.S. finishing pigs found that, "*farms that use non-therapeutic antibiotics have costs of production that differed little from those that do not. Any productivity improvement from use of antibiotics has not been large enough to offset the additional expenses, suggesting the viability of alternative practices or technologies to reduce disease or improve feed efficiency at finishing stages.*"[28] For U.S. poultry producers, the benefits of non-therapeutic antibiotics have been shown to be very limited and less than the cost of the drugs.[29]

U.S. ANTIBIOTIC CONSUMPTION AND RESISTANCE DATA COLLECTION MUST BE STRENGTHENED

To control the antibiotic resistance epidemic, U.S. experts (government and non-government) need ongoing access to reliable, standardized data regarding the scope of antibiotic consumption in humans and animals. "Consumption" data includes drug use data (i.e., prescribing data) as well as manufacturers' distribution and sales data. The lack of adequate U.S. antibiotic consumption data impedes our understanding of geographic and temporal trends in antibiotic resistance. Greater understanding of these factors will contribute to more effective and targeted interventions to reduce unnecessary antibiotic use and resistant infections. These include: 1) targeting appropriate antibiotic use interventions to the geographic areas and drugs of greatest importance, and 2) predicting and responding to new resistance problems based on changes in antibiotic utilization.

In the agricultural context, the collection of accurate antibiotic consumption data will make information currently collected under the NARMS program of greater relevance, because it could be used to show possible correlations between antibiotic use and the development of resistance. The United States is far behind other countries in collecting, and benefiting from, antibiotic consumption data. The Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP) performs continuous monitoring of both consumption data and resistance data in humans, animals, and food. Human consumption data is collected from the pharmaceutical industry and the Danish Medicines Agency, while DANMAP's "VetStat" system collects food animal data by species from pharmacies, farms, feed mills, and veterinary practitioners. On a Europe-wide level, the European Surveillance of Antimicrobial Consumption (ESAC) system collects human and more limited animal consumption data from 34 countries, while the European Antimicrobial Resistance Surveillance System (EARSS) collects resistance data. The inputs are largely standardized since countries must adhere to WHO standards regarding measurement ("defined daily doses") and classification of antibiotics.

Better understanding of the correlation between antibiotic consumption and the development of resistance holds potential benefits for U.S. public health efforts. In the earlier example of the avoparcin ban in Europe, it was the DANMAP and other surveillance efforts that helped the Danes and other Europeans see the benefit that elimination of avoparcin as a growth promoter in animal agriculture had on the reduction of VRE in humans.

The U.S. Animal Drug User Fee Amendments (ADUFA; Public Law 110-316) enacted in 2008 contained a provision to begin to strengthen FDA's authority to collect animal antibiotic sales and distribution data from the manufacturer by requiring data based on a calendar year, as opposed to the anniversary date of the product's approval. However, the ADUFA data do not include retail-level use data and are at the national level only. To really understand how antibiotics are being used on U.S. farms, the ADUFA requirements must be strengthened to mandate collection of antibiotic use data at the local level as well. Consumption data also must be collected by species (swine, chicken, turkey, cattle) and in a unit of measure that can be compared across species and localities. European countries collect such data at the farm and feed mill level; so should the United States. Collection of such data, along with strengthened surveillance, will enable us to understand how and where antibiotics are being used, including non-judiciously. The urgency for better data will not be reduced once the FDA's new principles for growth promotion and veterinary supervision of antibiotics become operational. To the contrary, comparable and reliable data will become even more important as a way to monitor whether the agricultural sector (e.g., farms, feed mills, and others) are complying with these new principles.

While IDSA supports further strengthening the ADUFA data collection provisions, we also believe there are steps that federal agencies can take under current authority to assist in surveillance and monitoring of antibiotic use in animal agriculture. The U.S. Department of Agriculture (USDA) could use the National Animal Health Monitoring and Surveillance System to monitor trends in the volume and type of antibiotics used in animal agriculture by adding targeted questions that would help determine the total volume and type of animal antibiotics used. They also could enhance the Agricultural Resource Management Survey to include

information about the volume and efficiency of antibiotic usage to help producers make better decisions about optimal use of antibiotics and to allow public health officials a better understanding of a potential source of resistance. Additionally, NARMS could be expanded to gather information about additional pathogens to provide public health officials a wider array of information to determine the magnitude of the antibiotic resistance problem.

IMPACT STATEMENT AND MANAGEMENT PLAN

IDSA supports requiring manufacturers of new antibiotics intended for use in animal agriculture to first evaluate the potential impact that approval of the drug would have on the development of antibiotic resistance and, subsequently, to develop a management plan to limit potential antibiotic resistance from occurring. New drug sponsors also should be required to submit updates to the impact statement and management plan within three years after the initial approval of the antibiotic.

These impact statements and management plans should be made public so that researchers can use each to study and strengthen our understanding of the science of predicting, preventing, and controlling resistance development. However, IDSA believes that neither the impact statement nor the management plan should be used for enforcement purposes.

CONCLUSION

The problem of antibiotic resistance is complex and multi-factorial. In contrast to efforts by the medical community to begin to curtail human overuse and misuse of antibiotics, the U.S. is among the last developed countries to implement similar control polices for antibiotic use in animal agriculture. It is inescapable that non-judicious uses of antibiotics in animals' feed and water over prolonged periods for purposes of growth promotion, increased feed efficiency, and routine disease prevention contribute to antibiotic resistance and create health dangers for humans.

No single strategy can solve the antibiotic resistance problem—a multi-pronged approach is required. We must promote the development of new priority antibiotics to treat serious and life-threatening infections. We must prevent the emergence and transmission of resistant infections through research into new vaccines and diagnostics and implementation of other effective infection prevention and control initiatives. And we must eliminate all non-judicious uses of antibiotics, in human medicine and animal agriculture alike.

The Subcommittee on Health has a long history of leadership in addressing our nation's most pressing public health issues. Today, we call on you to adopt strong measures to end non-judicious uses of antibiotics in animal agriculture and to require that all other uses of these drugs in animals be carried out under the supervision of a veterinarian and within the boundaries of a valid veterinarian-client-patient relationship. Such measures have been advocated repeatedly by the World Health Organization, the National Academy of Sciences, and many medical and public health organizations, and successfully implemented by multiple European nations in the past one to two decades. We also urge the Committee to move with haste to enact PAMTA, as well as the Strategies to Address Antimicrobial Resistance Act (H.R. 2400), which we believe

will significantly strengthen U.S. antibiotic resistance data collection, surveillance, research, and prevention and control efforts.

Any new policy on antibiotic use in animal agriculture should be mandatory, retroactive to already-approved drugs, and enforceable. This will help reduce antibiotic resistance in order to save lives and protect public health.

Thank you again for the opportunity to testify on this important issue. IDSA stands ready to assist the Subcommittee in any way that we can.

REFERENCES/ATTACHMENTS

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