White Paper

Antibiotic Use and Resistance: Moving Forward Through Shared Stewardship

Information synthesized from Nov. 12-14, 2014, symposium in Atlanta, Ga.: "Antibiotic Use and Resistance: Moving Forward Through Shared Stewardship"

DISCLAIMER: The information provided in this White Paper is strictly the perspectives and opinions of individual speakers and results of discussions at the 2014 "Antibiotic Use and Resistance: Moving Forward Through Shared Stewardship" symposium.

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BACKGROUND

The symposium *Antibiotic Use and Resistance: Moving Forward through Shared Stewardship* was developed by the National Institute for Animal Agriculture (NIAA) and was conducted Nov. 12-14, 2014, in Atlanta, Ga. The symposium was a continuation of discussion and sharing of information that commenced with the Oct. 26-27, 2011, *Antibiotic Use in Food Animals: A Dialogue for a Common Purpose* symposium conducted in Chicago, Ill.; the Nov. 13-15, 2012, *A One Health Approach to Antimicrobial Use & Resistance: A Dialogue for a Common Purpose* symposium conducted in Columbus, Ohio; and the Nov. 12-14, 2013, symposium *Bridging the Gap Between Animal Health and Human Health* conducted in Kansas City, Mo.

NIAA is a non-profit, membership-driven organization that unites and advances animal agriculture: the aquatic, beef, dairy, equine, goat, poultry, sheep and swine industries. NIAA is dedicated to 1) furthering programs working toward the eradication of diseases that pose risk to the health of animals, wildlife and humans; 2) promoting the efficient production of a safe and wholesome food supply for our nation and abroad; and 3) promoting best practices in environmental stewardship, and animal health and well-being.

The 2014 symposium was funded in part by the Beef Checkoff®, U.S. Department of Agriculture Animal and Plant Health Inspection Service – Veterinary Services, United Soybean Board, Indiana Soybean Alliance®, *Drovers CattleNetwork, Dairy Herd Management, Bovine Veterinarian, PorkNetwork, Brownfield Ag News* – A Division of Learfield, *DairyBusiness,* Merck Animal Health, Pork Checkoff®, Zoetis™, Farm Bureau Georgia®, American Farm Bureau®, Elanco™, Auburn University – Food Systems Institute, Qiagen®, Vetericyn® and the American Veterinary Medical Association®.

PURPOSE AND DESIGN OF THE SYMPOSIUM

The symposium provided a platform where academia, government, and other stakeholders within animal agriculture, human health and consumers interacted, and shared the most current science-based information as well as their professional insights in order to identify potential solutions to the often misunderstood issues of antimicrobial use and resistance. An integral part of the annual NIAA antibiotics symposium are large group sessions with presentations by experts as well as participant discussions via small breakout groups where individuals learn from each other, engage in productive discussion and create successful strategies to address antibiotic resistance and preserve antibiotic efficacy.

The goals of the 2014 symposium were the same as for past symposiums:

- To build relationships among participants from different disciplines with diverse backgrounds and expertise in animal, human and environmental health, and gain a better understanding of other's perspectives.
- To lead and engage participants in an open dialogue.
- To find common ground and formulate a path forward.
- To focus on continuous improvement and commitment to long-term health (animals, people and the environment).

Symposium Planning Committee Co-Chairs

David Dargatz, DVM, U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Centers for Epidemiology and Animal Health, Ft. Collins, Colo.
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Eric Moore, DVM, Technical Services Manager, Ruminant Business Unit, Norbrook, Inc.

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Nevil Speer, Ph.D., Consultant
Susan Vaughn Grooters, , MPH, Policy Analyst, Keep Antibiotics Working

SYMPOSIUM TOPICS AND SPEAKERS (in order given at the symposium)
Symposium Moderator: Daniel Thompson, DVM, Jones Professor of Production Medicine, Director, Beef Cattle Institute, Kansas State University

"Welcome and Opening Comments," Dr. Chris Braden, MD, Director, Division of Foodborne, Waterborne and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention

"Antibiotic Use and Resistance: Moving Forward Through Shared Stewardship," Lonnie King, DVM, MS, MPA, DACVPM, Dean, College of Veterinary Medicine, Executive Dean, Health Science Colleges, Ruth Stanton Chair in Veterinary Medicine, The Ohio State University

"Antimicrobial Resistance and the Human-Animal Interface: The Public Health Concerns," Robert Tauxe, MD, MPH, Deputy Director, Division of Foodborne, Waterborne and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention

"Animal Agriculture and Antibiotic Resistance: What Should (and Should Not) be on the Table," Brian Lubbers, DVM, Ph.D., DACVCP, Director, Clinical Microbiology, Kansas State University Veterinary Diagnostic Laboratory

"Steward is the Right Word," Jim Hutchinson, MD, Consultant Medical Microbiologist, Medical Director – Antimicrobial Stewardship, Vancouver Island Health Authority

"Antimicrobial Use and Stewardship in the Pediatric Outpatient Setting," Theoklis Zaoutis, MD, MSCE, Frederick McNair Scott Professor of Pediatrics, University of Pennsylvania School of Medicine, Chief, Division of Infectious Diseases, The Children's Hospital of Philadelphia

"Antimicrobial Stewardship for Companion Animal Practice," Jeff Bender, DVM, MS, DACVPM, Hospital Epidemiologist, University of Minnesota, College of Veterinary Medicine

"Antibiotic Stewardship: Quality Assurance Programs," Timothy J. Goldsmith, DVM, MPH, DACVPM, University of Minnesota, College of Veterinary Medicine

"Gathering Antimicrobial Use Data in Animals," Craig Lewis, VMO, Center for Veterinary Medicine, U.S. Food and Drug Administration; William T. Flynn, DVM, MS, Center for Veterinary Medicine, U.S. Food and Drug Administration

"Metrics and Decision-Making for Antibiotic Stewardship in Human Medicine," Steve Solomon, MD, Director, Office of Antimicrobial Resistance, Centers for Disease Control and Prevention

"The Canadian Integrated Program for Antimicrobial Resistance Surveillance: Building a Voluntary Farm Surveillance Framework," David Léger, DVM, MSC, Veterinary Epidemiologist, Laboratory for Food-borne Zoonoses, Public Health Agency of Canada

“Building Consumer Trust,” Susan Vaughn Grooters, MPH, Policy Analyst, Keep Antibiotics Working

“Combating Antibiotic Resistance Bacteria,” L.M. Granger, DVM, Surveillance, Preparedness, Response Services, U.S. Department of Agriculture Animal and Plant Health Inspection Service – Veterinary Services

“FDA Antibiotic Resistance Strategy,” William T. Flynn, DVM, MS, Center for Veterinary Medicine, U.S. Food and Drug Administration

“International Activities in Antimicrobial Resistance,” Tom M. Chiller, MD, MPHTM, Associate Director for Epidemiologic Science, Division of Foodborne, Waterborne and Environmental Diseases, Centers for Disease Control and Prevention

“Combating Antimicrobial Resistance: The Way Forward,” James M. Hughes, MD, Professor of Medicine and Public Health, Emory University

EXECUTIVE SUMMARY

The 15 presentations delivered by antibiotic use and resistance experts representing animal health, human health and public health resulted in a robust dialogue and exchange of information. The following points were among those brought forth during the symposium by the speakers and participants:

1) In order to address antibiotic stewardship in human and animal practice, we must assure the careful and accountable, use of antibiotics in all settings, decrease the need for antibiotics through prevention, including the development and use of vaccines, increased veterinary oversight, optimum management practices, development and use of rapid diagnostics, development of patient/client stewardship programs with A One Health perspective, and educational programs for doctors, patients, veterinarians and clients.[1]
2) *Campylobacter* and *Salmonella* continue to be the largest issues in antibiotic resistance in the U.S. at the human-agriculture interface, and specific antibiotics of most concern are the cephalosporins , fluoroquinolones and macrolides. Resistant *Salmonella* can reside in the patient with no clinical signs until they are placed on an antibiotic for an infection – that's when the resistant bacteria can flourish and cause major secondary illness, just as happens with *C. difficile.*[2]
3) Focus should be on decreasing antibiotic *use* where possible*,* not resistance, with measures for the following metrics: use, resistance (antibiogram), inflammation and outcome (morbidity, retreatments, deaths and case outcomes).[3]
4) Physicians and veterinarians, who are responsible for writing antibiotic prescriptions, have a principal role in addressing bacterial resistance. For example, in pediatric medicine, there has been a decrease in narrow-spectrum antibiotic prescribing and an increase in broad-spectrum antibiotic prescribing practices.[4]
5) Unlike the human medical community, veterinarians also manage as their own pharmacies. This practice has been incorporated into their business plan. It is time to reassess this practice and its potential affect on prescribing practices.[5]
6) A positive step has been the evolution of quality assurance programs in animal agriculture from concentrating on eliminating drug residue to including enhanced antibiotic stewardship.[6]
7) Metrics of success in the effort to minimize the development of antibiotic resistance include assessing the effectiveness of antibiotic stewardship programs, increasing veterinary oversight in animal agriculture, more careful monitoring of antibiotic usage and resistance in human and animal health, ongoing evaluation of individual and aggregate case outcomes, population health indicators and measuring the economic impact of resistance on health costs and society.[7]
8) The key to assuring good public policy is access to complete and accurate information on population health, assessments based on scientific methods that can be peer-reviewed and reproducible, and the ability to evolve conclusions and interpretations based on new evidence.[8]
9) The national strategy for combating antibiotic resistance includes implementing interventions to slow the spread of antibiotic resistant bacteria, improving One Health surveillance, development and application of rapid diagnostics for accurate treatments, new research and development for

therapies and other tools (e.g., new antibiotics, vaccines, etc.), and international collaboration to achieve near real-time information sharing.[9]

10) Guidance for Industry #213 provides recommendations for drug sponsors to voluntarily change product use conditions to eliminate production uses of medically important antimicrobials and require veterinary oversight of the remaining therapeutic uses in the feed and water of food-producing animals.[10]
11) Game changers for antibiotic resistant bacteria include culture independent diagnostic testing, whole genome sequencing, bioinformatics, electronic health records, use of social media, taking a One Health approach and acknowledging wildlife as vectors for animal-to-human transmission.[11]
12) Moving forward, we need to reduce and refine the use of antibiotics; establish shared commitment, increase communication and education, and encourage a One Health approach; collect better data about antibiotic use in humans and animals; develop patient management alternatives through research and development; move beyond “the blame game”; identify priorities and develop metrics; and develop and implement stewardship programs.[12]
13) There is a need for more rigorous research and development to understand human-to-human antimicrobial resistance transmission, companion animal-to-human antimicrobial resistance transmission and foodborne pathogen transmission of antimicrobial resistance to humans. Another area of research interest is the antimicrobial resistance transmission in foodborne pathogens that are live or those that have been killed by prevention methods but still reside in the meat. This would be important for understanding the role of irradiation of food products for preventing foodborne pathogen infections but also for antimicrobial resistance from foodborne pathogens to humans.[13]

PRESENTATION HIGHLIGHTS

ESTABLISHING STATISTICS

Past NIAA-hosted antibiotic symposiums have established that antimicrobial resistance (AMR) is a complex issue and, over the past decade, has become a growing global issue which global public health authorities have characterized as a crisis. The evolution of antibiotic resistance is occurring at an alarming rate that is now outpacing the development of new counter measures for treating bacterial infections in humans – this situation threatens patient care, economic growth, public health, agriculture, economic security and national security.[14] While antibiotics have been used for 70 years, if cooperation can't be fostered among all key stakeholders, a post-antibiotic era is inevitable.

It's estimated that antibiotic resistance costs the US economy $20 to $35 billion a year, including as many as 8 million extra patient days spent in the hospital and another $35 billion in indirect cost including lost productivity; some bacterial diseases are becoming untreatable and have led to 2 million illnesses and 23,000 deaths annually.[15] Unfortunately, the investment to combat this issue isn't commensurate with the threat: fiscal year (FY) 2014 federal spending on antibiotic resistance was approximately $450 million in direct funding ($1.40 per American per year).[16] New investments, both private and public, are necessary to create change.

That change needs to take place through stewardship: A commitment to always use antibiotics only when necessary to prevent or treat disease, to choose the right antibiotics, and to administer them with the right dose, for the right period of time and using the right route of administration in every case. Antibiotics represent a limited, finite, valuable resource and all need to be used judiciously.[17] Challenges are spawned by our growing interconnectivity and accelerated scale of human activity – individual actions and accountability are key to the ultimate solution and collective response.

IDENTIFYING AND PRIORITIZING KEY RESISTANCE ISSUES AT THE HUMAN AND ANIMAL INTERFACE

Antibiotic treatments have been critical in human and veterinary medicine for more than 70 years, and the resistance they evoke has been a challenge for almost as long. Resistance occurs in settings wherever antimicrobials are used, and can be associated with infections caused by bacteria, viruses, fungi and parasites. Bacteria, however, are particularly adept at sharing genetic material and can rather easily spread resistance genes from one bacterial strain to another.

Antibiotic use in animals is of concern to human health because resistant bacteria can be transmitted from food-producing animals to humans through the food supply and cause human illness. Resistance complicates empiric therapy by limiting choices and prompting the use of broad-spectrum drugs that are more likely to lead to resistance. Infection with resistant strains, often leads to a more complicated course of illness and is associated with increased morbidity and mortality.[18]

Our approach to AMR in foodborne infections in the 21st century will be constantly tested by substantial and changing challenges to human and animal health caused by the emergence of antibiotic resistance. In the long term, resistance among foodborne bacteria will not necessarily be reversible. We need to accept that foodborne pathogens are becoming resistant to antibacterial drugs important in human medicine as a result of both agricultural and human uses. This understanding of the role that human medicine, veterinary medicine and agricultural uses of antibiotics play in resistance is vital to assuring implementation of initiative for stewardship, for better tracking and monitoring of human and agricultural uses of antibiotics, for sharing of information that can be directly applied to limiting the emergence of resistance and prolonging the utility of current antibiotics.[19] Expertise in animal health and management will need to rapidly evolve in the same way that medical practices must evolve, bolstered by cutting edge research. Important areas of research include optimally effective ways of reducing the introduction of resistant strains or genes, techniques to reduce selection for resistance and spread of resistant genes and strains, and strategies to implement successful and sustainable antibiotic stewardship and prevention measures.[20]

Foodborne Pathogens with Animal Reservoirs

The Centers for Disease Control and Prevention (CDC) report released Sept. 17, 2013, "Antibiotic Resistance Threats in the United States, 2013" identified 18 pathogens, four of which are foodborne; two of those four have human reservoirs (*Salmonella* Typhi and *Shigella*), and the other two have animal reservoirs (Non-typhoidal *Salmonella* and *Campylobacter*). All four are resistant to important drugs used for treatment.[21]

According to the World Health Organization (WHO) publication "Critically Important Antimicrobials for Human Medicine, 3rd Rev." from 2011, from the human perspective, the bacterial diseases of concern and antimicrobials of importance are non-typhoidal *Salmonella,* resistant to ceftriaxone, ciprofloxacin and/or multidrug resistant (resistant to three or more classes of antimicrobials); and *Campylobacter,* resistant to azithromycin and ciprofloxacin.[22]

In the US, the proprtion of *Campylobacter jejuni* found to be resistant to specific antibiotics is now 25 percent resistance to fluoroquinolone, 2 percent resistance to azithromycin and 48 percent resistance to tetracycline; *Campylobacter coli* shows a 34 percent resistance to fluoroquinolone, 9 percent resistance to azithromycin and 45 percent resistance to tetracycline.[23]

Drug resistance in *Salmonella* Typhi (typhoid fever) has jumped from about 20 percent in 1999 to more than 70 percent in 2011; typhoid fever is almost always related to foreign travel and resistance reflects human use patterns in developing countries.[24]

Non-typhoidal *Salmonella* causes about 1.2 million illnesses per year, but National Antimicrobial Resistance Monitoring System (NARMS) surveillance shows improvements in multi-drug resistance: Frequency in all reported *Salmonella* infections are down 3 percent from 2003 to 2012; in *Salmonella* Typhimurium infections are down 9 percent; and in *Salmonella* Newport infections are also down 9 percent.[25]

However, NARMS surveillance from 2012 also shows trends of concern, including resistance to ceftriaxone in all *Salmonella* at 2.9 percent and in *Salmonella* Heidelberg at 22 percent; there is also decreased susceptibility to ciprofloxacin in all *Salmonella* at 2.5 percent and in *Salmonella* Enteritidis at 7.7 percent.[26]

Multidrug resistant *Salmonella* Newport (*S.* Newport MDR CMY2) first appeared in 1999 and affected cattle and humans; it was resistant to seven agents, sometimes more, including ceftriaxone. When resistance is located on a mobile genetic element like a plasmid, it may be transferred to other bacteria (also known as jumping genes); CMY resistance genes in *Salmonella* are on plasmids, and the CMY2 gene was carried on one large plasmid and only affected persons in North America.[27]

Recent multistate outbreaks of resistant *Salmonella* infections have been caused by the NT Salmonella serotypes Typhimurium and Heidelberg contaminating ground beef, ground turkey and chicken.[28] A prolonged outbreak of resistant *Salmonella* Heidelberg in 2013-2014 was associated with a single poultry producer. The complex challenge presented seven different Pulsed-field Gel Electrophoresis patterns in patients, poultry meat and processors; multiple resistance patterns, including pan-susceptible; one sub-cluster from broilers cooked at a retail outlet; and trace back that led to three different slaughter facilities. An important finding in this outbreak was that contamination occurred not at a single isolated point in the production process at a single plant but instead included many different products (breasts, wings and whole birds), traced back to three different facilities and at least four of the outbreak strains were found at all three facilities. The outbreak was controlled after major efforts were taken to reduce contamination of chicken parts in plants and on farms. Control measures at several levels were put into place, including the live bird side (*Salmonella* can spread vertically through the poultry breeding pyramid), processing plants (parts as well as carcasses), and retail safety and consumer education.[29]

AMR Concerns for Animal Agriculture

From the animal perspective, the bacterial diseases of concern and antimicrobials of importance are respiratory disease (treatable with macrolides, fluoroquinolones and 3rd generation cephalosporins); digestive diseases (treatable with cephalosporins and macrolides); and other diseases, including mastitis and foot rot (treatable with macrolides and cephalosporins). Macrolides/lincosamides treat a broad range of these diseases amongst various species; fluoroquinolones are only approved for bovine and swine respiratory disease and federal law currently prohibits their extra-label use in food animals; and 3rd generation cephalosporins also cover a broad range of species and diseases, but federal law currently limits their extra-label use in food animals.[30]

Still, the benefits of agricultural use of antimicrobials are improved animal health; improved food safety; and economic benefits for the producer, the nation through Gross Domestic Product and consumers through decreased food prices.

The CDC is addressing the challenge of resistant foodborne infections by working with partners to prevent foodborne infections; tracking resistance through NARMS collaboration; making information more available more quickly; refining estimates of the health impact of resistance; refining understanding of sources, the spread of resistance genes and plasmids, and resistant bacterial strains; and making real-time resistance data part of outbreak investigations. The goal is to reduce resistant *Salmonella* infections by 25 percent by 2020.[31]

New for 2015 is a proposal to increase surveillance for resistance by testing all human *Salmonella* isolates for resistance in real-time, identifying the resistance patterns involved when surveillance detects a cluster of similar isolates, prioritizing resistant clusters for investigation and trace back, controlling them faster and attributing resistance to specific sources.[32] Collective progress will be tracked with outcome measures, including reductions in multidrug resistance in general and specific resistance to advanced cephalosporins and fluoroquinolones; and by process measures, including ending use for growth promotion, increasing use under veterinary supervision and measuring changes in use.[33]

STEWARDSHIP PROGRAMS TO MINIMIZE RESISTANCE

Stewardship Programs in Human Health

Antibiotic stewardship is the commitment to always use antibiotics appropriately and safely – only when they are needed to treat disease – and to choose the right antibiotics and to administer them in the right way in every case. It's doing right by patients whether they're humans or animals.[34]

Commonly used stewardship tactics in human hospitals include clinician education, formulary optimization, antibiotic use restrictions, prospective audit with intervention and feedback, optimization of dose administration, streamlining (de-escalation and elimination of redundant therapy), early switch from intravenous therapy to oral antibiotics, appropriate duration of antibiotic therapy and clinical guidelines with site specific treatment pathways. Additional general recommendations include treating the infection (not colonization); ideally, culturing before antibiotic treatment, but providing antibiotics as soon as possible; and evaluating the patient daily, especially within 48-72 hours (taking routine antibiotic "time outs").[35]

With all antibiotics, it's been recommended to focus on use, not resistance. The use of antibiotics is the single most important factor leading to antibiotic resistance, and the single most important action needed to greatly slow the development and spread of resistance.[36] Where use is concerned, the "right amount" is the smallest amount that does the job. Getting to the right amount is a minimization act: the right amount that keeps antibiotics from being less scarce and helps to figure out the best distribution. Data needed for quality management of infections include measures of antibiotic use, resistance, inflammation and outcome.[37]

The CDC estimates that up to 50 percent of all antibiotics prescribed by physicians aren't needed or aren't optimally prescribed; this misuse or overuse of antibiotics is a major contributor to AMR.[38]

For example, there is extreme variability in pediatric antibiotic use in the U.S. and worldwide that includes antibiotic prescribing, broad-spectrum antibiotic prescribing, rate of diagnosis and adherence to prescribing guidelines. Antibiotic prescribing in ambulatory pediatrics in the U.S. from a National Ambulatory Medical Care Survey, 2006-2008, reported that antibiotics were prescribed during 21 percent of pediatric ambulatory visits: 50 percent were broad-spectrum (mostly macrolides), and respiratory infections accounted for 70 percent of use. One in three prescriptions are for an acute respiratory tract infection for which antibiotics aren't indicated. While the rate of prescriptions has remained steady, but the rate for broad-spectrum antibiotics has increased.[39]

The impact of antibiotic resistance includes patients with resistant infections who are at higher risk for disability or death due to loss of effective antibiotics; an increase in the number of immunosuppressed patients; and insufficient drug development to deal with this threat.[40]

A randomized trial was conducted in the Philadelphia area on the effect of outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians by Gerber JS, Prasad PA, Fiks AG, Localio AR, Grundmeier RW, Bell LM, Wasserman RC, Keren R and Zaoutis TE. For one year, an antibiotic stewardship program focused on guideline development, education and prescription audits, and feedback, resulting in decreased antibiotic prescribing. However, within six months of the conclusion of the program, prescribing practices went back to pre-program levels. Perceptions of the intervention revealed skepticism of the audit and feedback reports; respondents ignoring reports or expressing distrust about them; one respondent admitting to gaming behavior; recognizing AMR is a problem, but believing it was driven by the behaviors of non-pediatric physicians; identifying pressure to prescribe antibiotics from parents by all respondents as a major barrier to the more judicious use of antibiotics; and respondents reporting they sometimes "caved" to parental pressure for social reasons.[41]

Core actions to combat resistance included preventing infections and the spread of resistance through immunization, infection control, hand washing and safe food preparation; tracking; improving antibiotic use and stewardship; and the development of drugs and diagnostic tests.

Stewardship Programs in Companion Animal Health

Companion animals, especially cats and dogs, are potential sources of spread of AMR due to common use of antimicrobials, such as cephalosporins or fluoroquinolones, and their close contact with humans. In 2002, companion animals accounted for 37 percent of pharmaceutical product sales in the EU.[42]

Drug resistant infections in companion animals include methicillin-resistant *Staphylococcus pseudintermedius* and *Schlieferi;* methicillin-resistant *Staphylococcus aureus;* and multidrug resistant *Klebsiella* and E. *coli.* A dog park study conducted by the University of Minnesota showed that 27 percent of samples were positive for *E. coli* and many were multidrug resistant.[43]

Antibiotics are inappropriately prescribed because of an absence of bacterial infection or an indication for prophylaxis; or violation of the right dose, right drug, best route of delivery, attention to de-escalation or appropriate duration of administration. Unfortunately, the selective pressure of antibiotics underscores the importance of prudent use to slow the development of resistance. The most influential reasons for choosing a specific antimicrobial are owner finances, AMR concerns, side effects and client expectations.

In response, the American Veterinary Medical Association (AVMA) task force for antimicrobial stewardship in companion animal practice seeks to understand practitioner prescribing behaviors and laboratory practices; encourage development of practice guidelines; and promote educational programs, including the CDCs "Get Smart" program, state-sponsored programs, web-based training modules and client focus.[44]

The primary purpose of stewardship in companion animal health is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms and the emergence of resistance. "On Target" antimicrobial therapy general considerations for judicious use include considering and ruling out non-bacterial causes; considering other therapeutic options; utilizing culture and sensitivity results; referring to published treatment guidelines; monitoring treatment response and client compliance; and taking a "time out" before adding, switching or changing antibiotic treatments.[45]

Stewardship Programs in Food Animal Health

There are multiple quality assurance programs in food animal production that offer state-implemented, nationally coordinated training and certification for producers (now with an online option), site assessments, audits and industry surveys. For the purpose of this paper, Beef Quality Assurance (BQA) will be used as an example.

BQA is a voluntary program supported by Beef Checkoff funds that involves producers, veterinarians, nutritionists and industry professionals. Historically, quality assurance programs have primarily focused on the pre-harvest segment of the industry (farm and ranch level), and use of Hazard Analysis and Critical Control Points (HACCP)-based approaches to implement science-based management practices. Initially, they focused on safety concerns (volatile chemical residues), but have evolved to include animal well-being, and information to help producers implement best management practices that improve both Quality Grades and Yield Grades of beef carcasses.

BQA objectives are to set production standards for quality and safety that are appropriate to an operation (that can be met or exceeded), including biosecurity, animal health and well-being, production performance and environmental stewardship; establish data retention and recordkeeping systems which satisfy federal guidelines; provide hands-on training and education; and provide technical assistance through qualified individuals working with the BQA program.

BQA guidelines include care and husbandry practices, feedstuffs, feed additives and medication, processing and treatment records, and use of injectable animal health products. BQA best management practices include feedstuffs and sources, feed additives and medications, animal treatments and health maintenance, prevention and processing, pesticides, recordkeeping and inventory control, action in case of violation, cattle handling, culling management, carcass quality, husbandry and other considerations, and contamination/adulteration.

Great strides were made in the National Beef Quality Audit Fed Cattle sector from 1991 to 2000 as injection-sites went from the No. 2 concern to no longer being in the Top 10 quality issues at all.[46] Beef cattle producers follow BQA guidelines because it’s the right thing to do, they’re committed to improvement.

METRICS OF SUCCESS TO MINIMIZE RESISTANCE

The ultimate metric of success is seeing a reduction in human illnesses. A reduction in human illnesses occurs from a better understanding of the whole problem of resistance – the pathways and the risks. Antibiotics routinely given to farm animals kill susceptible bacteria, but resistant bacteria survive in these animals and can be transmitted to the general population, in whom antibiotic resistant infections may develop.[47]

To address this issue, a number of metric programs have been implemented to combat AMR.

Actions in Animal Agriculture: PCAST

The President’s Council of Advisors on Science and Technology (PCAST) is an advisory group of the nation’s leading scientists and engineers appointed by the President to augment the science and technology advice available to him. This group offered an integrated framework for collective action through eight recommendations to combat antibiotic resistance: international cooperation, federal investment and leadership, surveillance and response capacity, stewardship in human health care and animal agriculture, commercial development, new antibiotics and fundamental research.[48]

A report to the President on combating antibiotic resistance from PCAST in Sept. 2014 stated, “While it is clear that agricultural use of antibiotics can affect human health, what is less clear is its relative contribution to antibiotic resistance in humans compared to inappropriate or overuse in health care settings. This uncertainty is largely due to difficulties in tracing precisely the origins and spread of specific resistant microbes and, more fundamentally, the transmission and spread of specific resistance genes in microbial communities. It also reflects a gap in our understanding of the complexity of resistance across different species and the environment." This report also notes the diversity of livestock operations, assesses the impact of changes, and calls for national capability for microbial surveillance in humans and agriculture. The report says about animal agriculture, "… [the] extent to which antibiotic resistance in animal agriculture contributes to human infection is not known [and] risks to human health posed by the agricultural use of antibiotics are, appropriately, a matter of serious concern."[49]

Specific to animal agriculture, the PCAST recommendations aim to:

- Support U.S. Food and Drug Administration (FDA) guidelines and Veterinary Feed Directive (VFD) changes
- Develop and implement effective stewardship programs for both food and companion animals
- Create and deliver educational programs
- Establish a research portfolio and integrated agenda
- Improve surveillance, response and prevention strategies as part of the national plan
- Develop public-private partnerships and innovation centers
- Coordinate government agency's plans
- Help lead global antimicrobial plans and programs through collaboration with the World Organization for Animal Health (OIE), WHO and the Food and Agriculture Organization of the United Nations (FAO)
- Emphasize sanitation, hygiene and disease prevention
- Incorporate an animal health diagnostic network with a public health network
- Improve animal health and infrastructure at the state and local level
- Advocate for new antibiotic development, re-purpose human antibiotics and develop non-antibiotic interventions to combat bacterial diseases
- Create actions and plans that measure metrics to define success
- Actively participate as a strategic partner developing and implementing a national plan of action[50]

New strategies for animal agriculture include:

- Breaking the impasse with consensual approaches
- Recognizing the need for execution through people, processes and strategies
- Using NIAA as a "community practice" (i.e., a group of people who share a concern or a passion for something they do and learn how to do it better as they interact regularly)
- Accepting stewardship as a means of accountability and action
- Embracing a national plan and accepting responsibility for action and change
- Using One Health as a frame work for collaboration (One Health is a multidisciplinary collaborative effort that focuses on the interconnectedness of a large ecosystem to achieve optimal health of humans, animals and environments across the world).[51]
- Developing a common ground
- Not accepting inaction as a viable solution in the face of a worsening crisis
- Taking action with imperfect or incomplete data – doing, learning and adapting concurrently
- Leveraging the unique attributes of NIAA through their mission, membership and as a forum to define common interests and catalyze action

- Reconciling the “knowing-doing gap” (i.e., when knowledge of what needs to be done fails to result in appropriate action or behavior change) of complex and difficult problems and resolving them by turning knowledge into action.[52]

Actions in Animal Agriculture: FDA Judicious Use of Antimicrobials

Useful baseline information is currently available on antimicrobial drug sales and AMR, but limited data are available regarding actual use. Collecting additional information to link shifts in on-farm antimicrobial use practices with AMR data is a high priority and meaningful metrics are needed to assess the impacts of different antimicrobial use practices on AMR, particularly related to stewardship and policy initiatives.[53] A National Institute for Mathematical and Biological Synthesis (NIMBioS) working group is developing an analytic approach for associating population-level changes in antimicrobial use in livestock with population level changes in AMR.

Appropriate refinement of principles and regulatory policies for promoting antimicrobial stewardship in animal agriculture requires improved understanding of the associations between on-farm use and resistance, which in turn requires long-term studies capturing the range of antimicrobial use patterns and resistance across different production classes.[54]

In the past, there has been extensive use of antibiotics in animal agriculture to prevent disease and promote growth; these practices may contribute to antibiotic resistance in animals which, through a variety of mechanisms, can spread to people. Now, the landscape in animal agriculture is changing. The FDA’s “Judicious Use of Antimicrobials” policy seeks to ensure judicious use of therapeutic antimicrobials is an integral part of good veterinary practice in order to maximize therapeutic efficacy and minimize selection of resistant microorganisms. Policy objectives include eliminating the use of medically important antimicrobials for production indications (such as weight gain or improved feed efficiency); and requiring veterinary oversight of the remaining therapeutic uses of these drugs in the feed and water of food-producing animals. These label changes are scheduled to be completed by Dec. 12, 2016, and represent significant steps forward in addressing concerns about the use of antimicrobials in food-producing animals.[55]

Components of this strategy include implementing changes to labels (removing production claims) and requiring veterinary oversight and finalizing the VFD rule (currently set to be finalized in Spring 2015); producing progress reports every six months and performing an evaluation at the end of the 3-year implementation period; assessing impacts by continuing to collect data on sales and resistance, and by collecting additional data from on-farm use and resistance; and reinforcing stewardship by performing training and outreach to support the new VFD rule and promoting judicious use principles.[56]

A government interagency group was formed to explore possible approaches for obtaining antimicrobial use data. The ongoing work of this group includes mapping the distribution of antimicrobials (medicated feeds vs. other products), reviewing literature for analytic approaches that associate antimicrobial use and resistance, surveying the work other international programs have done to relate antimicrobial use and resistance, submitting a NIMBioS Working Group proposal to develop analytic method to evaluate the association between shifts in antimicrobial use practices and AMR, and continuing to develop possible approaches for collecting on-farm data.[57]

The next steps include seeking public input on proposed approaches in the near future, potentially through public meeting. Their goal is to start collecting new data in 2016, before the end of the 3-year implementation period.[58]

Actions in Animal Agriculture: CIPARS

In 1997, calls for surveillance of AMR and antimicrobial use in Canada were published, with the recommendation to establish a national farm surveillance system to monitor AMR and use in the agri-food and aquaculture sectors. As a result, the Canadian Integrated Program for AMR Surveillance (CIPARS) was established, and is coordinated by the Public Health Agency of Canada (with staffing that includes veterinary epidemiologists and species/commodity specialists) in partnership from Veterinary Drugs Directorate, Health Canada; Canadian Food Inspection Agency; Agriculture and Agri-foods Canada; Provincial agriculture and public health academia; and private industry.[59]

The objectives of the CIPARS Farm Program include establishing an infrastructure to support a national farm surveillance program that collects AMR and use data, describes trends in farm use and AMR, investigates the association between farm antimicrobial use and resistance, and provides sound data for human health risk assessments.

Recommendations from species-specific expert panels/advisory committees included the approval of these objectives, the creation of inclusion/exclusion criteria for herd selection/recruitment, and identification of herd veterinarians as the most trusted group to perform field work (i.e., to collect composite pen fecal samples and administer a questionnaire about antimicrobial use and animal health), and the establishment of a communication process that provides the industry with timely prepublication notification.

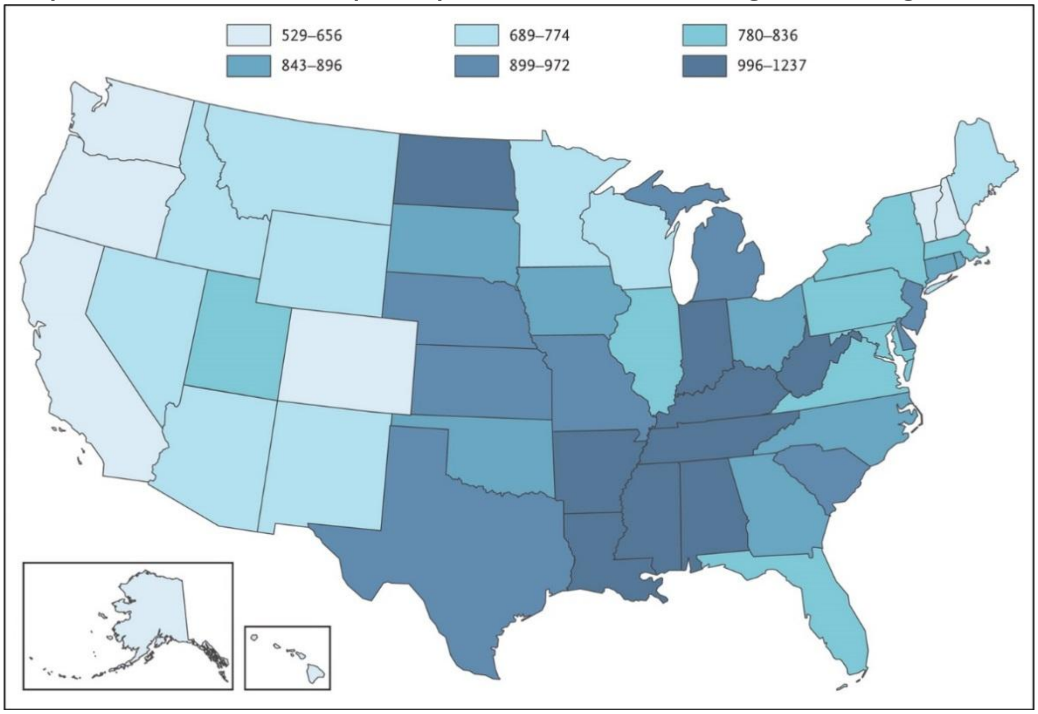
The CIPARS Farm Program was developed through a transparent, consultative process. It established a national framework for farm-level antimicrobial use and resistance surveillance. Today, there is on-going surveillance in the grower-finisher swine and broiler poultry industries, with expansion planned for the beef (cow-calf and feedlot), dairy cattle, turkey and layer industries. The outputs from this program are integrated with data across CIPARS components and agricultural commodity sectors to provide information on trends in antimicrobial use and resistance (temporal/years and spatial/regional) for evidence/risk-based policy development.[60]

Actions in Human Medicine: Optimal Prescribing

Improving the use of antibiotics in human medicine will require careful attention to employing the right metrics to measure how antibiotics are used and how that use relates to patient outcomes. The ultimate goals of antibiotic stewardship include improved population health, optimal prescribing of antibiotics for all patients and sustainable changes in how physicians use antibiotics in clinical practice.[61]

Poor prescribing harms patients—not just by contributing to AMR but by exposing patients to avoidable risks of drug side effects, allergic reactions and drug-drug interactions. Despite years of efforts to improve prescribing, practices vary greatly in both the inpatient and outpatient settings, with doctors in some hospitals prescribing three times as many antibiotics as doctors in other hospitals and significant state-to-state variation in outpatient prescribing (see figure).[62]

Outpatient Antibiotic Prescriptions per 1,000 Persons of All Ages According to State



Hicks LA et al. N Engl J Med 2013;368:1461-1462.

Evaluating progress toward the goals of improved use of antibiotics in human medicine will require a combination of outcome and process measures along with specific objectives targeting those measures. Information for these measures may come from proprietary data, hospital and healthcare medical records, pharmacy data bases both of purchases and dispensing, laboratory data, and insurance information including Medicare and Medicaid.[63]

Outcome measures include better clinical results (decreased morbidity, mortality overall and fewer adverse events), reduction in antibiotic resistance (fewer resistant infections and less spread of resistant bacteria) and economic benefits (lower health care costs for infections and complications, and reduced pharmacy and consumer costs for antibiotics).

Process measures can draw on standards developed by the CDC defining the necessary components of a hospital antibiotic stewardship program. Successful programs will need leadership commitment, personnel accountability, professionals with drug expertise, a menu of specific actions, a system for tracking, and ongoing reporting or results and education. [64]

Similarly, the steps in optimal prescribing have been established and these include identifying a correct indication for the prescription, the appropriate choice of an antibiotic, timing and route of administration consistent with guidelines/best practices, appropriate laboratory confirmation/review and an opportunity for de-escalation of therapy--an antibiotic "time out" allowing for a change of therapy.[65]

As is true for successful programs in animal agriculture, antibiotic stewardship in human health requires an environment of trust, openness, two-way communication and transparency to assure that prescribers, regulators, decision makers and consumers accept a shared commitment to achievable goals. Reduction in antimicrobial use isn't an end in itself, but a natural outcome of better prescribing practices; continuous quality improvement within each setting is the process objective. Optimal prescribing is a key goal to complement appropriateness of use. Process measures include facility stewardship programs, optimal prescribing and rates of use.[66]

STRATEGIES TO MOVE FORWARD: REAL-WORLD SOLUTIONS

Antibiotic use in animal agriculture has been the subject of scientific and policy debate for decades; consumers, public health advocates, Congress and others continue to be concerned about public health impacts. While the debate continues, we must continue to identify measures that address public health concerns and assure animal health needs are met.[67]

The current understanding of AMR is that it's complex, multi-factorial and points to use as a driver of acquired resistance. While gaps in our understanding of the issue remain and the science continues to evolve, these complexities and uncertainties don't mean steps can't be identified to mitigate risk.[68]

While previous measures to address AMR risks have been taken, concerns remain. In 2010, Guidance for Industry #209, "The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals" was implemented, two of its key principles are: 1) Limit use of medically important antimicrobial drugs to those uses considered necessary for assuring animal health, and 2) Increase veterinary involvement, consultation and oversight. The goal of the judicious use strategy is to focus on initiating steps to assure that medically important antimicrobial drugs are used as judiciously as possible while maintaining their availability to combat disease in animals, including treatment, control and prevention. It is also a goal to preserve availability of effective drugs for both humans and animals.[69]

The judicious use strategy components include:

- Implementing changes: Guidance for Industry #213 established a three-year timeline and FDA identified 283 affected applications – all 26 affected sponsors confirmed their intent to voluntarily engage in Guidance for Industry #213; once changes are complete, it will be illegal to use medically important antimicrobials in the feed or water of food animals for production purposes or without veterinary oversight
- Reporting progress: Establish a list of affected products, write progress reports every six months, evaluation at the end of the three-year period and continuing assessment reports
- Assessing impacts: Continue collecting, reporting and enhancing existing data; collect additional data
- Reinforcing stewardship (perform training/outreach to support new VFD rules and promote judicious use principles[70]

National Strategy for Combating Antibiotic Resistant Bacteria (CARB)

The national strategy for CARB is being led by a task force consisting of the secretaries of Defense, Agriculture and Health and Human Services; they plan to have a five-year national action plan in place by Feb. 15, 2015. The key message is action/implementation; themes are preventing the spread of resistant bacteria; strengthening national efforts to identify instances of antibiotic resistance; working to develop new antibiotics, therapies and vaccines; and improving international collaboration on this issue.[71]

The U.S. Department of Agriculture (USDA) agencies involved with the national action plan for CARB include the Foreign Agricultural Service, Agricultural Research Service, Animal and Plant Health Inspection Service (APHIS), National Institute of Food and Agriculture, National Agriculture Statistics Service, Food Safety and Inspection Service, and Economic Research Service.

The vision of CARB is that, "The United States will work domestically and internationally to prevent, detect and control illness and death related to infections caused by antibiotic resistant bacteria by implementing measures to mitigate the emergence and spread of antibiotic resistance, ensuring the continued availability of therapeutics for the treatment of bacterial infections[,]" and includes the following goals:

- GOAL 1: Slow the development of resistant bacteria and prevent the spread of resistant infections
- GOAL 2: Strengthen national One Health surveillance efforts to combat resistance
- GOAL 3: Advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria
- GOAL 4: Accelerate basic and applied research and development for new antibiotics, other therapeutics and vaccines
- GOAL 5: Improve international collaboration and capacities for antibiotic resistance[72]

CARB also recommends developing, expanding and maintaining capacity in state and federal veterinary and food safety laboratories to conduct standardized antibiotic susceptibility testing, and characterizing select zoonotic and animal pathogens. Data should be stored in a centralized repository that can be linked with relevant public health databases, as appropriate, while maintaining source confidentiality. Further, they recommend enhancing monitoring of antibiotic resistance patterns as well as antibiotic sales, usage and management practices at multiple points in the production chain of food-animals from on-farm use, through processing to retail.[73]

Over the next six months, CARB plans to develop and implement a national action plan; address recommendations made in the recent PCAST report; ensure the national action plan establishes clear milestones and metrics for success; ensure activities will be coordinated by the White House National Security Council, and Office of Science and Technology Policy; regularly report to the President on progress made; encourage departments and agencies to take steps to combat antibiotic resistance that are not explicitly included; encourage industry and other non-governmental organizations as well as international partners to play a key role in accelerating progress in combating antibiotic resistance; and work to make sure this national strategy will solidify an ongoing partnership among these entities that will ensure resources are leveraged effectively to address this urgent threat to public health and national security.[74]

To meet the challenge, USDA proposes to obtain and disseminate science-based, actionable, quantitative antibiotic drug use information, coupled with the development of resistance in food producing animals, and to relate this to livestock management practices. (The FDA approves and regulates the use of all antibiotics in both humans and animals, relies on this information to form its policy and regulatory decisions, and taps into USDA's extensive network of collaborative relationships for outreach.) USDA roles in the plan include surveillance, research and development, education, extension and outreach, and the development of metrics to gauge progress. In general, they are seeking more complete data on antimicrobial use in animals; better surveillance information regarding associations between antibiotic use and resistance patterns for bacteria in food animals; and needed data, which includes information from on the farm, at the time of slaughter, and at retail for meat and poultry products. This will assist with evaluating linkages and determining how and when antimicrobial drug use causes adverse human health impacts.[75]

Objectives of the plan are to determine or model purposes and impacts of antibiotic use in food producing animals, monitor antibiotic drug susceptibilities and monitor for drug use in food animals presented at slaughter, and identify feasible management practices and new technology applications.[76]

Common Ground for Human and Animal Health

The problem, as defined by the Institute of Medicine (IOM) in 1992, is new, reemerging or drug-resistant infections whose incidence in humans has increased within the past two decades or whose incidence threatens to increase in the near future. Factors contributing to the emergence of infectious diseases include human demographics and behavior, technology and industry, economic development and land use, international travel and commerce, microbial adaptation and change, and breakdown of public health measures. The 2003 IOM report added human susceptibility to infection, climate and weather, changing ecosystems, poverty and social inequality, war and famine, lack of political will and intent to harm as factors contributing to the emergence of infectious diseases. In that report, they state, "A robust public health system – in its science, capacity, practice and through it collaborations with clinical and veterinary medicine, academia, industry and other public and private partners – is the best defense against any microbial threat."

The challenges in facing this issue include public health surveillance (ongoing, systematic collection analysis and interpretation of outcome-specific data); it needs to be closely integrated with the timely dissemination of these data to those responsible for taking public health action to prevent and control disease or injury (i.e. information for action).[77]

The No. 1 priority for the Infectious Diseases Society of America (IDSA) is AMR. They put emphasis on increased support for basic and translational research, development of rapid point of case diagnostics, surveillance of use and resistance, antimicrobial stewardship, and regulatory reform for clinical trial design and new antibacterial drug approval. The October 15, 2014, IDSA "Clinical Infectious Diseases" report identifies the core elements of AMR as leadership commitment, accountability (single leader), drug expertise (pharmacist), action (recommendation implementation), surveillance (usage and resistance), education (prescribers) and data sharing.[78]

AMR game changers include culture independent diagnostic testing, whole genome sequencing, bioinformatics, health care reform, electronic health records, social media and One Health.[79] Common ground for medical and veterinary communities include AMR and usage; avian, animal and pandemic influenza; other zoonotic diseases, including those associated with exotic pet and wildlife trade; foodborne disease; health care-associated infections; blood, organ and tissue safety; pathogen discovery/new diagnostics; drug and vaccine development; disease eradication; biosafety/biosecurity; and bioterrorism/biodefense.[80]

Ways forward for shared stewardship include replacing, reducing and/or refining the use of antibiotics when possible in human medicine and animal medicine/agriculture. Needs for moving forward through shared stewardship include shared commitment, better data on use for humans and animals, communication and research.[81]

Conclusions are to move beyond "the blame game;" respond to and leverage the President's Executive Order, CARB national strategy and PCAST recommendations; identify priorities and develop metrics; establish shared commitment to antimicrobial stewardship, and the development of better data on usage and resistance in various settings; development of a collaborative research agenda to improve the evidence base; and shared commitment to communication and collaboration with professional societies, public-private sector partners and the public.[82]

Real-World Solutions Internationally

"We are all connected by the food we eat, the water we drink and the air we breathe."
–Dr. Thomas Frieden, CDC director

Globally, there is a lack of basic health care and infrastructure, low rates of vaccination, inadequate clean water, indiscriminate access to over-the-counter drugs, sub-standard quality and counterfeit, limited availability of newer drugs, and a shortage of trained health care providers.[82] AMR is a complex global problem that will require a multi-sectoral and global approach. To better understand the problem and effectively address it, we need global surveillance to detect the emergence and spread of AMR, international data sharing and harmonization, and international cooperation to limit global spread.[84]

WHO and other international organizations have prioritized AMR, and the U.S. is working closely with international partners to build international capacity for monitoring foodborne diseases and resistance in the food chain through various initiatives to identify and investigate emerging resistance, and to harmonize resistance testing and reporting to facilitate data sharing. In 2008, the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) was formed. The group provides expert advice to WHO on containing food-related AMR and promoting integrated surveillance of AMR and usage. Key AGISAR activities include supporting WHO capacity-building activities, maintaining and updating the list of critically important antimicrobials, and developing guidance on integrated surveillance of AMR.[85]

AGISAR[86] published Guidance on Integrated Surveillance of AMR; the publication is an important output of the 5-year strategic framework for AGISAR, provides basic information that countries need to establish programs for integrated surveillance of resistance, and makes recommendations that facilitate global harmonization and data comparability. NARMS scientists from CDC, FDA and USDA helped draft the guidance.

To aid in globally addressing this issue, in 2005, a WHO expert working group developed a list of critically important antimicrobials intended to help preserve the effectiveness of antimicrobials, and act as a reference to help formulate and prioritize risk assessment and management strategies for containing resistance due to antimicrobial use in humans and animals. Antimicrobial agents were ranked as critically important, highly important and important. The highest priority agents are fluoroquinolones, 3rd and 4th generation cephalosporins, macrolides and glycopeptides. This publication recommends that classes not currently used in food animals (such as carbapenems) and any new class developed for human therapy not be used in animals or plants.[87] Likewise, OIE published a list of antimicrobial agents of veterinary importance, standards on prudent use of antimicrobials in terrestrial and aquatic animals, standards on monitoring antimicrobial use and resistance, and held the first global conference on prudent use of antimicrobials in veterinary medicine in 2013.[88]

Further, *Tackling Antibiotic Resistance from a Food Safety Perspective in Europe* was published by the WHO regional office for Europe in 2011, and explains the problem and options for prevention and containment of antibiotic resistance in the food chain. It was primarily intended for policy-makers and people working in the public health, agriculture, food production and veterinary sectors.

Finally, the Transatlantic Taskforce on AMR (TATFAR) was constituted in 2009 with the goal of improving cooperation between the U.S. and EU on AMR in 3 areas: 1) appropriate therapeutic use of antimicrobial drugs in medical and veterinary communities, 2) prevention of health care and community-associated drug resistant infections and 3) strategies for improving the pipeline of new antimicrobial drugs. They identified and adopted 17 recommendations, and implemented the plan through increased communication, regular meetings, joint workshops, and exchange of information and approaches on best practices and methodologies.[89] Activity #18 of TATFAR is to establish a joint working group of international subject matter experts to identify key knowledge gaps in understanding the transmission of AMR to humans arising as a result of the use of antimicrobial drugs in animals, and on the development of effective intervention measures to prevent this transmission, including the development of alternatives to antimicrobial drugs.[90]

NEXT STEPS

While the symposium was key in bringing together experts from human medicine and veterinary medicine and public health to discuss Antibiotic Use and Resistance: Moving Forward Through Shared Stewardship, the seriousness of antibiotic resistance calls for further dialogue and cooperative efforts to be sustained going forward. Resistance needs to be carefully monitored and better understood, and incentives are needed to hasten the development of new antibiotics and non-antibiotic treatments.

Animal agriculture takes its role in this matter seriously, and NIAA will continue to provide leadership within animal agriculture and establish a platform to develop further collaboration whereby antibiotic resistance solutions can be developed from the perspective of science and not reflect a political divide between the human and animal health communities.

Antibiotic resistance is a complex issue and doesn't derive from any single source. As such, it is best addressed by a systems-based approach that strives to close gaps of misunderstanding and avoid implementing impetuous remedies that may produce ineffective solutions.

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FOOTNOTES

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