

# ANTIBIOTICS SYMPOSIUM

NOVEMBER 7-9, 2023 | ATLANTA, GA

## WHITE PAPER





## Table of Contents

Background 2
Contact Information2
Symposium Purpose and Design3
Symposium Topics and Speakers4
Executive Summary6
The current state of antibiotic stewardship from producer to processor to restaurant
The multi-dimensional aspects of antibiotic stewardship and AMR – animal welfare, human health, food security, veterinary-client relationships, and more 12
One Health lessons on antibiotic stewardship and AMR to celebrate and build
upon14
Agency Partner Updates16
Breakout Sessions
Public Health's focus for antibiotic stewardship and AMR
Why is it important for a One Health conversation to continue?
Antibiotic Stewardship, emerging fungal pathogens in livestock, and AMR on the Horizon what should we be watching/engaging in?
References

## Background

The 13<sup>th</sup> Annual Antibiotic Symposium, "Thriving in a Changing Landscape," hosted by the National Institute for Animal Agriculture (NIAA), was held in person in Atlanta, GA, on November 7-9, 2022. In attendance were participants representing a broad range of stakeholder groups, including state and federal government, academia, veterinarians, producers, producer organizations and cooperatives, food retailers, animal health manufacturers and retailers, trade organizations, agricultural marketing, and non-profit organizations.

The NIAA is a non-profit, membership-driven organization that unites and advances animal agriculture for the challenges facing animal agriculture industries (aquatic, beef, dairy, equine, goat, poultry, sheep, and swine). NIAA is dedicated to furthering programs to eradicate diseases that pose risks to the health of animals, wildlife, and humans, promoting the efficient production of a safe and wholesome food supply for our nation and abroad, and promoting best practices in environmental stewardship and animal health and well-being.

The 2023 13<sup>th</sup> Annual Antibiotic Symposium was funded in part by the Cattlemen's Beef Board.

## **Contact Information**

## National Institute for Animal Agriculture

435 Nichols Road STE 200 Kansas City, MO 64112 Phone: (844) 589-3944 Communications@AnimalAgriculture.org

## Symposium Purpose and Design

The 2023 Antibiotic Symposium, "Thriving in a Changing Landscape," continues a conversation that began in 2011. Though animal agriculture is a common theme, this symposium connects leaders across all aspects of animal production, food processing, animal health, human health, and environmental health to provide an opportunity for collaboration to improve the future of antimicrobial resistance research, education, and communication.

## Symposium Planning Committee:

## **Co-Chairs**

Dr. Megin Nichols - Centers for Disease Control and Prevention

Dr. Justin Welsh – Merck Animal Health

## Symposium Planning Committee Members

Dr. Chelsey Shivley - USDA, APHIS

Dr. Michael Costin - American Veterinary Medical Association

Dr. Heather Fowler - National Pork Board

Dr. Paul Plummer – National Institute for Antimicrobial Resistance Research and Education (NIAMRRE)

Bradon Burks - Kentucky Beef Council

Dr. Michelle Kromm - Food Forward

Dr. Alexandra Medley - The Centers for Disease Control & Prevention

Courtney Youngbar - Association of State & Territorial Health Officials

Dr. Patrick McDermott – Food and Drug Administration

Dr. Hayley Springer- Penn State University

## **Symposium Topics and Speakers**

#### Welcome and Introductions

Dr. Eric Moore – Norbrook, Inc. Dr. Megin Nichols – The Centers for Disease Control and Prevention Dr. Justin Welsh – Merck Animal Health

## Opening Conversation: The current state of antibiotic stewardship from producer to processor to restaurant

Dr. Ken Opengart - Tyson Foods Ryan Goodman - Certified Angus Beef Dr. Chris Gambino - The Breakthrough Institute Dr. Michelle Kromm (moderator) - Food Forward

### Panel Discussion: The multi-dimensional aspects of antibiotic stewardship and AMR – animal welfare, human health, food security, veterinary-client relationships, and more

Dr. Mike Murphy - American Veterinary Medical Association Collette Kaster - Professional Animal Auditor Certification Organization (PAACO) Dr. Terry Lehenbauer – University of California - Davis Dr. Jomana Musmar - Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) Dr. Chelsey Shivley (moderator) - USDA- APHIS

# Panel Discussion: One Health lessons on antibiotic stewardship and AMR to celebrate and build upon

Leah Dorman – Health for Animals Dr. Dawn Sievert – Centers for Disease Control & Prevention Dr. Heather Fowler – National Pork Board Bradon Burks (moderator) – Kentucky Cattlemen's

#### **Agency Partner Updates**

Dr. Amber McCoig - Food & Drug Administration Dr. Alexandra Medley - Centers for Disease Control & Prevention Dr. Chelsey Shivley - USDA - APHIS Dr. Catherine Rockwell - USDA - FSIS Susan Jennings - Environmental Protection Agency Dr. Paul Plummer (moderator) – NIAMRRE

#### **Breakout Sessions**

Communication – led by Certified Angus Beef Research – led by the NIAMRRE Education – led by Relevant Classroom, A Division of Vivayic

#### Opening Keynote Public Health's focus on antibiotic stewardship and AMR

Karen Smith, MD, MPH Founding Partner Healthy Community Partners, Inc

## Panel Discussion: Why is it important for a One Health conversation to continue?

Dr. Benjamin O'Kelley - Blue Pearl Vet Hospitals Jim Lanier - HEB Dr. Paul Morley - Texas A&M Dr. Alex Tasker – Bristol University Dr. Heather Fowler (moderator) - National Pork Board

## Panel Discussion: Antibiotic Stewardship, emerging fungal pathogens in livestock, and AMR on the Horizon ... what should we be watching/engaging in?

Dr. Paul Plummer – NIAMRRE

Dr. Patricia S. Gaunt - Mississippi State University CVM Fish Diagnostic Laboratory Dr. Tom Chiller - Centers for Disease Control & Prevention

Dr. Alexandra Medley (moderator) - Centers for Disease Control & Prevention

## **Executive Summary**

The 13<sup>th</sup> annual NIAA Antibiotics symposium convened in Atlanta, Georgia, steps from the Centers for Disease Control and Prevention (CDC). Early arrivals had the opportunity to tour CDC facilities and explore the history of U.S. public health efforts at the CDC museum. The official program began with an evening of Conversations & Collaborations among symposium attendees and speakers. As presentations and panel discussions progressed, several common themes of change within the antibiotic resistance landscape emerged. Perhaps most prominent was the need for engagement with and integration of social science within the antibiotic stewardship discussion. The natural sciences have provided much of the current antimicrobial resistance (AMR) research. This research has provided valuable insight into the scale of the AMR problem, risk factors associated with AMR, and interventions to slow the development and spread of AMR. Implementation of most stewardship interventions requires human behavioral change. Eliciting behavioral change in people is complex. Without social science experts with an intimate knowledge of human behavior, we can never achieve optimal implementation of stewardship programs.

Though antibiotic stewardship in human and livestock medicine will continue to play an important role, other focus areas emerged throughout the symposium. The intimate relationship between people and their pets presents an ideal opportunity to transfer AMR between animals and humans. These intimate relationships also build strong bonds, often resulting in the pursuit of medical interventions that mirror human medicine, including the use of high-powered antibiotics. With cases of zoonotic transmission of resistant pathogens from companion animals and circulation of carbapenem-resistant bacteria in canine populations, antibiotic stewardship in companion animal medicine has become a focus within the industry and among regulatory bodies. Antibiotic stewardship efforts are also looking toward aquaculture, a complex industry with few antibiotic choices, limited diagnostic options, and an ever-shrinking margin as U.S. growers face pressure from imported fish often raised under less-regulated systems. Another focus of antibiotic stewardship goes beyond animal agriculture. A recently recognized antifungal-resistant human pathogen appears to have emerged from environmental sources. The class of drugs this pathogen is resistant to is commonly used in crop production, bringing another area of agriculture into the antimicrobial stewardship discussion.

The final, and perhaps the most important, theme is the need for U.S. engagement in the global AMR discussion, particularly as the United Nations prepares to discuss the Muscat Manifesto. This agreement, signed by several countries, requires a massive reduction in antibiotic use in food and agriculture. The United States does not look to arbitrary antibiotic use reductions as a viable solution to AMR due to the numerous concerns with kilogram usage as a measure of stewardship. Though not accepted as a viable means of stewardship by U.S. regulatory officials, these drastic antibiotic use cuts could still impact U.S. agriculture if trading partners bar the import of agricultural products raised under less restrictive standards. The United States and animal agriculture must engage on this global stage and bring policy ideas to ensure a strong future. Absence from this conversation will not halt decision-making; it will only ensure decisions are made without U.S. input. It is critical for voices from across the One Health spectrum, including animal agriculture, to continue to be at the table as the landscape of stewardship changes and new issues emerge on the horizon.

The 13<sup>th</sup> Annual NIAA Antibiotic Symposium brought together a broad array of speakers and a diverse audience to engage in discussion. With so much expertise on stage addressing the theme of "Thriving in a Changing Landscape" of antimicrobial stewardship, many profound statements were made. A small collection of these adages, either quoted or paraphrased from speakers and audience discussion, follows:

## We must promote a paradigm shift away from "how it's always been done." **Dr. Ken Opengart**

We must build "One Future", where environmental sustainability, antibiotic stewardship, animal welfare, and farm productivity can all thrive.

## Dr. Chris Gambino

The best and most effective policies are built through collaboration with those who will be most affected by the policy.

## Dr. Karen Smith

When one word can make a huge difference, perhaps even ruin a conversation, having social science experts who understand human behavior becomes critical.

When we show up, we counter the perception that we have something to hide.

*If we want to understand antimicrobial resistance, we cannot look directly at it; we must understand the entire ecological context from which it emerges.* 

Dr. Alexandra Medley

# The current state of antibiotic stewardship from producer to processor to restaurant

As the symposium began exploring the continually changing landscape of antimicrobial resistance (AMR), it opened with a reflection on the current state of antibiotic stewardship across the food system. Dr. Ken Opengart started by sharing not only the current antibiotic stewardship efforts at Tyson Foods but also how the program evolved to meet the needs of consumers while still emphasizing animal welfare. In the early days of Tyson Foods' antibiotic stewardship journey, the organization relied on broad, industry-led programs like Beef Quality Assurance (BQA), Pork Quality Assurance (PQA), and stewardship statements from veterinary groups such as the American Association of Avian Pathologists (AAAP). However, the company realized that these industry-wide stewardship efforts did not reflect all aspects of how Tyson Foods wanted to practice stewardship, so the organization began crafting its own antibiotic position statement. In building this statement, they sought advice from industry experts, the World Health Organization, and the World Organization for Animal Health. They also strived for a balanced approach that recognized Tyson Foods as not only stewards of antibiotics but also the animals they raised.

To achieve this balance, Tyson Foods focused on reducing the need for antibiotics through improving disease prevention practices. They avoided antibiotic use reduction targets or antibiotic class restrictions to ensure sick animals could receive needed treatment. Through engaging in international efforts, funding research, and educating the supply chain on the importance of antibiotic stewardship, they continued to refine and strengthen their role in antimicrobial stewardship. In addition to the Tyson Foods position statement, the organization developed an antibiotic stewardship framework and assessment. This was built off earlier work with the Farm Journal Foundation and the Pew Charitable Trust, and the final product was evaluated by NIAA to provide third-party perspective and credibility.

Despite the challenges of implementing antibiotic stewardship as a global company facing widely varying supply chains and geographies, Tyson Foods understands the importance of a continually evolving stewardship program. One example of how they accomplish this is through promoting a paradigm shift away from the "how it's always been done" attitude. When overuse of antibiotics is suspected, rather than mandating reduced use, Tyson Foods strives to understand the "why" behind antibiotic use, build a process to solve the underlying issues and map out a process to reduce antibiotic use. In the U.S., Tyson Foods' "no antibiotics ever" (NAE) program in poultry production exemplifies its continual reassessment of programs. Upon reflection on the NAE program, Tyson Foods recognized that, although it was an effort towards antibiotic stewardship, it did not meet the animal welfare ideals set forth by their stewardship statement due to a lack of access to critical medications for animal health. This led Tyson Foods to shift towards a program eliminating antibiotics essential for human health, allowing producers to use antibiotics such as ionophores that can control common animal diseases but are not used in human medicine. Though this change may push back against consumer desire for NAE, Tyson Foods chose to find balance in this changing world, allowing products that support animal welfare and improve sustainability while limiting the antibiotics that pose the most significant risk to public health.

In contrast to the perspective of an integrated producer like Tyson Foods, Ryan Goodman shared his antibiotic stewardship perspectives as both a lifelong beef producer and through the lens of Certified Angus Beef. Raising cattle requires a toolbox complete with all the tools to care for cattle properly. These tools help producers raise high-quality beef and cattle that "have no bad days." Certified Angus Beef recognizes the production of top-quality beef by rewarding producers for their efforts.

Though antibiotics are one of the tools of cattle care, Certified Angus Beef recognizes the importance of looking beyond just a single tool when building a cattle care program. Producers are encouraged to be good stewards of all their resources, which builds a culture of optimal animal care, sustainable practices, and antibiotic stewardship. This culture and the changes needed to achieve it require people involved and engaged in moving the industry forward. In addition to building an organization of producers dedicated to producing top-quality beef, sharing the work of producers with stakeholders across the food supply chain is another critical role of Certified Angus Beef. In addition to utilizing packaging labels to communicate with consumers, Certified Angus Beef also elevates stories of beef farmers and ranchers. Although social media is a common way to share these stories, many producers also open their farm gates to on-site visitors. These visits allow producers to share the story of quality cattle care with chefs, nutritionists, and other professionals in the food industry who may not have exposure to animal agriculture. Building the toolbox and continually improving how they utilize these tools to produce high-quality beef is a lifelong endeavor for beef producers. Though these efforts are critical to animal welfare, environmental sustainability, and antibiotic stewardship, animal agriculture also needs to communicate this story so that the work of producers is recognized across the supply chain.

In addition to spreading the story of producers, Dr. Chris Gambino of the Breakthrough Institute emphasized the importance of sharing the value of innovation with the consumer. Many consumers skeptically view technology, particularly technology that increases production efficiency, yet these consumers also value environmentally sustainable practices. Consumers often do not understand that improving production efficiency is an excellent tool for improving environmental sustainability. When efficiency increases, the inputs needed to produce each pound of product decline, as do greenhouse gas (GHG) emissions. Genetic engineering is one of the most promising tools to improve efficiency in animal agriculture, a technology that again faces consumer skepticism.

One of the challenges of talking about genetic engineering is terminology. The scientific community refers to genetically engineered (GE) products, while Congress defines the same technology as bioengineered, and the public uses the term genetically modified organism (GMO). When the public thinks of GMOs, they often think of the science of transgenesis, the transfer of genetic material from one species to another, but modern genetic engineering in animals is typically not transgenesis. Instead, it is more often gene editing, where genetic material is altered, often by deletion, but no genetic material from a different organism is inserted. If they understand the difference, Consumers are likely to be more accepting of gene editing than transgenesis.

A recent European study reported that consumers were more willing to purchase GE animal products if the genetic changes improved animal welfare and reduced environmental impact rather than just increasing the bottom line at the farm (Dupré et al., 2021). The Breakthrough Institute advocates for the acceptance of gene editing in food animals, sharing with consumers the many benefits of this technology. As demand for high-quality protein increases, particularly across lowand middle-income countries that may lack adequate and adaptive tools to improve production efficiency, GHG emissions from animal agriculture will continue to climb. One opportunity to increase production efficiency in animal agriculture is to concentrate livestock; however, this also makes spreading disease easier. Genetic engineering could provide a solution to this issue.

Disease-resistant GE livestock could greatly benefit the environment, animal welfare, and antibiotic stewardship. Bovine respiratory disease (BRD) sickens over 20% of cattle placed in U.S. feedlots. Nearly 90% of cattle with BRD are treated with antibiotics, and about 10% die or become chronically ill. Modeling predicts that a 75% uptake of GE BRD-resistant cattle could reduce GHG emissions by 3.5 million metric tons (MMT) while reducing antibiotic use by nearly 5 million doses (Shanthalingam et al., 2016). Much like BRD plagues the beef industry, mastitis is the most prominent disease concern in the dairy industry. Modeling predicts that a 75% uptake of GE cattle resistant to *Staphylococcus aureus*, one of many mastitis pathogens, could reduce GHG emissions by 0.5 MMT and antibiotic use by nearly 6 million doses (Wall et al., 2005). These data provide an excellent case for adopting GE livestock from the industry and consumer perspectives.

As animal agriculture moves towards "One Future", where environmental sustainability, antibiotic stewardship, animal welfare, and farm productivity can all thrive, we need to help consumers understand the value of technology. Moving away from absence labeling, where "non-GMO" is seen as a benefit by consumers, and towards descriptive labeling that tells the story of technology may help us get there. Rather than just labeling the product as bioengineered, as required by law, perhaps a label that states "bioengineered for reduced GHG emissions and improved animal health and welfare" could help consumers understand the reality of modern technology in animal agriculture.

Labeling was discussed further as the audience joined in the conversation. An audience member expressed concern that using anti-labeling could thwart the adoption of GE and other technologies. The panel's responses pointed to the incredible power of communication, with comments about bringing people to the table, framing the conversation, educating across the supply chain, and listening to know the value to others. Although building consumer acceptance is an essential aspect of changes in animal agriculture, new technologies, like GE livestock, face challenges even before getting to market. The panel suggested advocating for more research dollars and well-defined policies and regulations. GE livestock still faces uncertainty about what government organization has jurisdiction, which led GE salmon into an 18-year approval process. Even if approved, these technologies must have industry uptake, a process that will look very different across different industry sectors. Adoption could be rapid in the chicken industry, where two companies control most of the genetics. At the same time, it will be much slower across other industries where farms individually adopt new technologies. Bringing GE food animal products to market will require strategic partners to improve

communication not only of the benefits of the technology from the consumer perspective but also of the value to the producer who will raise these animals.

## The multi-dimensional aspects of antibiotic stewardship and AMR – animal welfare, human health, food security, veterinary-client relationships, and more

Antibiotic stewardship is viewed as a One Health issue, necessitating crossdiscipline collaboration and communication. This panel discussion examines stewardship from multiple perspectives inside and outside of animal agriculture. Dr. Mike Murphy of the American Veterinary Medical Association (AVMA) led the discussion with a reminder of how food security plays into antibiotic stewardship in animal agriculture. As the population grows and food prices rise, expanding our ability to produce high-quality protein will be critical. However, we need to do this in a way that does not compromise antibiotic efficacy. Though the Veterinarian, Client, Patient Relationship (VCPR) is a critical aspect of proper antibiotic use, it is vital that veterinarians truly understand what stewardship is and how to implement it.

The world of antibiotic stewardship has evolved, with one of those changes being a shift from focusing on judicious use towards a broader view of stewardship that includes disease prevention. During a meeting of the AVMA Committee on Antimicrobials (COA), a group of veterinarians interested in antibiotic use and stewardship, members were asked to define judicious use and antibiotic stewardship. Each person gave a different definition. This conversation brought about the AVMA definition and core principles of antibiotic stewardship. This clear definition of stewardship and how to achieve it has become an invaluable resource. The species-specific veterinary groups under AVMA have tailored these principles for their respective niche within veterinary medicine, providing clear guidance for practicing veterinarians.

Another area where definitions can vary wildly between individuals is animal welfare. Collette Kaster of the Professional Animal Auditor Certification Organization (PAACO) shared how the organization strives to provide consistent, science-based, measurable outcomes that can define the level of animal welfare in an operation. Despite these well-researched measures, human inconsistencies remain since not all auditors are created equal. Though many come from a strong livestock background, others come from other areas of the food chain, such as food safety, where livestock interaction may not occur. The learning curve for these individuals can be steep, but PAACO builds in-depth training programs to ensure all auditors can effectively apply their standards.

A PAACO audit will evaluate animal-based measures, on-farm documentation, and resources and facilities. Part of the facility's evaluation includes essential aspects of antibiotic stewardship, particularly drug use and timely *National Institute for Animal Agriculture*  treatment of sick animals. This evaluation does not assess the type of drug used but whether it is appropriately stored, handled properly, disposed of once expired, and given to animals promptly once diagnosed as sick. All of these are essential parts of stewardship. Another critical aspect of PAACO audits is their separation of animal welfare from production or marketing claims. For example, there is a clear recognition within the organization that restrictive programs, like raised without antibiotics (RWA) claims, are not welfare claims and do not predict animal welfare. PAACO helps to define what antibiotic stewardship is and is not for the entire animal agriculture community. They do it in a way that allows farms to assess and improve animal welfare.

The American Association of Bovine Practitioners (AABP) has also brought forward clear definitions for their members. They have a stewardship statement that builds upon the AVMA stewardship definition and core principles and a position statement that differentiates between RWA claims and animal welfare, emphasizing the importance of welfare over marketing claims. In addition, Dr. Terry Lehenbauer of the University of California shared the changing role of the veterinarian in antibiotic use. Recent antibiotic-related regulations have focused on bringing medically important antibiotics under veterinary oversight. This has applied to both in-feed and other forms of medically important antibiotics. These all feed into a multi-dimensional approach to antibiotic stewardship, including animal disease prevention and zoonotic disease control. Despite these advancements in veterinary stewardship, we still need more data, particularly antimicrobial use data. Data allows veterinarians to make more informed decisions regarding antibiotic use, but collecting data anonymously is challenging.

Antibiotic use data is not only an interest of bovine veterinarians. It is also recognized as vital in antimicrobial stewardship across the One Health spectrum. Dr. Jomana Musmar of the Presidential Advisory Council on Combatting Antibiotic-Resistant Bacteria (PACCARB) shared the role of PAACARB in identifying gaps in knowledge, with antibiotic use data being one of the persistent gaps across all of One Health. The role of PAACARB is not regulatory, but rather, it provides advice to policymakers and resources to the public. One of the most significant resources that PAACARB provides is a wealth of reports that cover a wide range of topics related to antibiotic stewardship. One of their most recent reports looks at preparation for the next pandemic. This includes many recommendations for human health but also many that benefit animal health, such as building diagnostic labs, increasing surveillance, and finding solutions to assure data privacy. This broad array of presenters helped attendees view antimicrobial stewardship from many angles.

This discussion continued as the audience joined in. The first question reminded us that despite all we know about stewardship, it is still hard to change

human behavior. This led to a discussion of the value of social sciences and the importance of including this aspect of science in stewardship efforts. When one word can make a huge difference, perhaps even ruin a conversation, having experts who understand human behavior becomes critical. This is particularly important as we work to overcome the plague of misinformation. Not only do we need to provide the initial communication to shift the misinformation to positive stories, but we also need to support an ongoing dialog. This ongoing effort is also needed in the policy development process, where many are moving forward with policies they do not truly understand. This can result in policies that are impossible to implement, such as the recent Kentucky requirement for a once-yearly vet visit to maintain a VCPR. This feat is not possible for the current veterinary workforce in the state. Engaging in policy development needs to go beyond the local and federal government. As the United Nations brings forward antibiotic use reduction targets, we cannot just push back; we need to provide viable commitments to stewardship that can be proposed to counter the reduction targets. Animal agriculture must continue to show up when we talk about antibiotic stewardship because by showing up, we counter the perception that we have something to hide.

# One Health lessons on antibiotic stewardship and AMR to celebrate and build upon

One Health brings together people across multiple sectors who all share a common goal. Sharing lessons learned across these sectors can provide valuable insight to others. Leah Dorman, representing Health for Animals, shared four big lessons learned in the fight against antimicrobial resistance. The first lesson is that prevention is vital. Adopting prevention practices is always more effective than discouraging antibiotic use. This can be seen in global data documenting declining antibiotic sales for food animal use while vaccine sales for these animals have steadily risen. Though disease prevention can slow the development of resistance, a second lesson learned is that the transfer of resistance from animals to humans is a critical moment in the fight against resistant bacteria. Reports from the European Union demonstrate low levels of resistance to critical antibiotics among animals, indicating a low risk of resistance transfer between animals and humans for these antibiotics. In the U.S., the CDC antimicrobial resistance threats report includes only two diseases directly linked to livestock, representing well below 1% of antibiotic resistance deaths each year.

This evidence of a relatively low risk of antibiotic resistance transfer points out another lesson learned: Focusing on antibiotic use reductions in food animals alone will not solve the resistance problem. In fact, despite the importance of antimicrobial stewardship in animal agriculture, this alone does little to impact resistance in human pathogens. Even though all fluoroquinolone use in poultry was *National Institute for Animal Agriculture*  halted, National Antimicrobial Resistance Monitoring System (NARMS) data indicates that fluoroquinolone-resistant human infections continue to climb. These data suggest that a balanced focus on all aspects of One Health is vital to success. We still need to forge ahead with stewardship in animal agriculture to continue to improve animal health and assure food security across the globe.

Mirroring the lessons from Health for Animals, one of the primary goals of antimicrobial stewardship programs at the Centers for Disease Control and Prevention (CDC) is prioritizing prevention. Dr. Dawn Sievert of the CDC shared that these prevention practices go beyond infection control. Priorities in this area include reducing the unnecessary use of antibiotics while ensuring access to these medications when needed, tracking data on resistance, investing in developing better vaccines and diagnostics, and addressing sanitation and the environment. The CDC's investment in data and diagnostics is vast. The Antimicrobial Resistance (AR) Laboratory Network standardizes testing methodology for rapid detection and actionable data to affect a public health response. The global Antimicrobial Resistance Laboratory and Response Network provides similar benefits on a global scale.

Dr. Heather Fowler brought the conversation back to animal agriculture, sharing the importance of a One Health approach to antimicrobial stewardship. Just as the CDC invests in data, so does animal agriculture. Though many aspects of record-keeping in animal agriculture arise from residue avoidance practices, improving record-keeping methods could shift these practices already rooted in the industry into actionable data that can inform stewardship decisions. Whether for residue avoidance or antimicrobial stewardship, recordkeeping in the pork industry can be tied back to the "we care ethical principles" that drive the industry. These principles, which include food safety, animal wellbeing, the environment, public health, the people in the industry, and the communities the industry serves, clearly reflect One Health principles in action.

The first questions from the audience addressed AMR data management. Though there is a push to have data available quickly, there was concern that data without interpretation could be problematic. However, the CDC is working towards building platforms that provide data rapidly and with some level of interpretation so data is not misconstrued. The representativeness of these data was also clarified. Though the AR Lab Network is state lab-based and may not represent all resistant infections found in clinical laboratories, this is not the only data used to assess the prevalence and inform the Antibiotic Resistance Threats report. The AR Lab Network's strength is its ability to provide data in a manner that allows rapid response to public health threats.

Panel members shared stories of conferences and other large-scale events where animal agriculture was given all the blame for antibiotic resistance. The issue was quickly dealt with in one case because of the long-standing trust built between the animal and human health experts at the meeting. These relationships are critical, but we also have work to continue sharing the story of antibiotic stewardship in animal agriculture. These conversations can be built upon asking meaningful, open-ended questions and listening with an open mind. As we build trust and relationships across the One Health sector, we can speak with a single, stronger voice that can better combat misinformation.

Animal agriculture has forged many critical relationships with our human medical counterparts, but incorporating the environmental side of One Health is a newer endeavor for many. The National Pork Board Sustainability group, which oversees the We Care Ethical Principles, includes an environmental engineer with solid connections in the industry. With the diverse expertise within this group, even the questions asked among the group can drive development. We can also employ experts that can make the data more understandable. Through modeling, we can demonstrate stewardship practices' impact to understand better the return on investment (ROI) for these practices.

The focus on ROI is also crucial when we face hesitancy or resistance to participating in research or sharing data. Helping producers see the value of their contribution can help drive participation. This is particularly important when data collection work falls on the farm. Sharing data following the project can also help producers see the value of the research. In addition to ROI, data protection to assure confidentiality is critical to gaining participation. Having a team member who is invested in the industry and knows the producer's perspective can be invaluable. As opportunities to collect data grow, so will the need to communicate findings to policymakers in an understandable way. As we celebrate where the One Health approach has taken antibiotic stewardship, we learn many lessons that provide an opportunity to continue to improve stewardship practices.

## **Agency Partner Updates**

#### Food and Drug Administration Center for Veterinary Medicine (FDA-CVM)

FDA's Center for Veterinary Medicine regulates animal food, animal drugs, animal biotechnology, and animal cellular therapies. Their regulatory approach incorporates relationships across federal partners, state agencies, and industry stakeholders. FDA-CVM wants to continue risk-based regulations while keeping up with and supporting innovation in the animal health industry. This year marks the mid-point of CVM's 5-year antimicrobial stewardship plan. This plan evaluates the use conditions of already approved products, promotes stewardship among end users, and improves antimicrobial use and resistance data collection. Several guidance documents for the industry (GFI) have been updated or introduced recently. GFI #152 is in the process of being updated. This guidance maintains the purpose and scope of the original version. However, it updates the criteria for assessing the risk of food animal antimicrobial use on human health and ranking the importance of antimicrobials to human medicine. GFI #263, fully implemented in June 2023, brought all remaining over the counter, medically important antibiotics under veterinary supervision. Outreach efforts to small farms and small ruminant producers are ongoing, as these are expected to be the most affected areas of the industry. GFI #273 addresses approved products that do not have a defined duration of use. It aims to build defined duration ranges for in-feed products sold under veterinary supervision. The comment period for this guidance was ongoing at the time of the symposium.

Data collection activities, as addressed in the 5-year plan, are also progressing. The National Antimicrobial Resistance Monitoring System (NARMS) continues to provide data on resistance in foodborne pathogens. Antimicrobial Sales and Distribution data continue to be published yearly, with new biomassadjusted sales data introduced to improve data visualization. CVM continues to work towards a robust antimicrobial use data collection system. Despite compelling reasons to collect these data, many challenges remain. Though the diversity of production settings, data collection platforms, and metrics are challenging, confidentiality concerns are likely a more significant issue. CVM continues to work with the Regan Udall Foundation to build a public-private partnership to address these concerns.

#### **Centers for Disease Control & Prevention (CDC)**

The CDC keeps the pulse of antimicrobial resistance through domestic and global systems that gather both outbreak and surveillance data. NARMS is crucial in food safety monitoring, combining domestic surveillance with foodborne illness outbreak-associated data. These data feed into global surveillance systems for select pathogens. NARMS continues to use whole genome sequencing to capture emerging causes of resistance. These data and traditional susceptibility tests are available in real time to aid public health responses. To better facilitate data use, the CDC continues to improve the NARMS Now online dashboard with new visualizations and summaries ready for release. NARMS data is also presented through the Spectra of Activity Tool, a human health-oriented tool to improve clinician access to NARMS data.

Though it is relatively straightforward to track known resistance determinants, emerging antimicrobial resistance is more complicated. CDC has created an Emerging Antimicrobial Resistance Working Group that identifies genotypic and phenotypic resistance threats. NARMS also monitors what they consider "sporadic" resistant infections: those that reoccur, emerge, or persist (REP). Several of these REP infections are related to food safety and animal agriculture. Another new dashboard provides access to data beyond bacteria. The BEAM (Bacteria, Enterics, Amoeba, and Mycotics) Dashboard includes resistance data and outbreak information across a broader set of pathogens.

In addition to surveillance and data management, CDC is involved in collaborative investigations. This includes projects related to backyard chickens, as well as companion animals. Outbreak investigations have included human Campylobacter cases associated with companion animal contact and carbapenemresistant *Enterobacterales* (CRE) outbreaks among companion animals in veterinary settings. CDC is also working on many international projects, including a project on CRE and other resistant organisms in Guatemala and a collaborative *Salmonella* project in Spain. Domestically, CDC participates in several additional collaborations, including the Integrated Food Safety Centers of Excellence. As CDC's antibiotic resistance experts look to the future, the emergence of fungal antimicrobial resistance is a growing concern for the organization. CDC has leveraged and seeks to expand collaborations across human and animal health.

# U.S. Department of Agriculture – Animal and Plant Health Inspection Service (USDA-APHIS)

Though USDA-APHIS does not have regulatory capacity related to antibiotic use, it is still engaged in the antibiotic resistance conversation. The USDA has an Antimicrobial Resistance Action Plan that mirrors the National Action Plan but with a focus on animal health. Several areas of USDA-APHIS tie directly to antimicrobial resistance. Antimicrobial use, stewardship, and antimicrobial resistance on the farms are monitored as part of the National Animal Health Monitoring System (NAHMS) studies. Recent NAHMS studies include Bison 2022, which includes antibiotic use practices. A backyard animal study focusing on chickens, rabbits, pigs, and goats will also incorporate aspects of antibiotic use into the survey. In planning or progress are also sheep and equine studies. The National Animal Health Laboratory Network (NAHLN) monitors resistance from diagnostic specimens nationwide. Due to its success, the NAHLN project continues and has added new areas of data collection, including companion animals and horses. USDA also provides stewardship education through its accreditation programs and collaborates across the industry and academia to build relationships to address resistance.

As APHIS works towards a better understanding of antimicrobial use, they have found collaboration to be an effective avenue to acquire data. A recent collaboration with the swine industry has built upon industry-developed antibiotic use reporting systems to gather use data to understand the industry. Another collaboration within the dairy industry focuses on methods to improve the implementation of selective dry cow therapy, utilizing social science approaches. APHIS is also early in its efforts to build an AMR dashboard through public-private partnerships. Domestic collaboration is vital to reaching APHIS goals, but international engagement will be critical. The UN is considering an agreement to put arbitrary antimicrobial use reductions in place, a practice the U.S. does not support. Through a better understanding of current use and research to refine use, we can identify science-based alternatives to the proposed reductions. We must also remember that antimicrobial use is just one piece of the animal health puzzle. APHIS has also recognized that animals beyond food, such as wildlife and companion animals, must be included in the discussion of antibiotic use and stewardship.

#### U.S. Department of Agriculture – Food Safety Inspection Service (USDA-FSIS)

The mission of FSIS centers on food safety across meat, poultry, and egg products. They accomplish this through inspection activities, with over 85% of FSIS personnel working on the front lines of food safety inspection. FSIS is a critical participant in the NARMS program, providing sampling from the ceca of animals presented for slaughter and samples of food products collected through hazard analysis and critical control point (HACCP) programs. The cecal samples indicate potential pre-slaughter AMR threats without the impact of antimicrobial treatments that may be applied to the carcass through production.

Tracking *Salmonella* serotypes is important in providing early indicators for public health threats. They also provide opportunities to implement methods to reduce *Salmonella* presence in food. Though this has proven valuable, there are differences between cecal and product samples, highlighting that we still do not fully understand *Salmonella* from farm to slaughter. The data collected through FSIS sampling is presented through the NARMS Now dashboard. It is also presented in a report of FSIS NARMS data to provide better context to the data collected by FSIS. This reports some of the challenges in interpreting these data, particularly in the differences between cecal and product samples, which consistently demonstrate higher resistance levels in products than ceca.

Current work with FSIS NARMS includes a supplemental report analyzing the most recent data from NARMS. This report, though not yet published, demonstrates a decline in multi-drug resistance, but it will also report a rise in ciprofloxacin resistance, a critically important antimicrobial. It also shows a shift in the prevalence of *Salmonella* serotypes. FSIS continues to engage with stakeholders and federal partners to build our knowledge of antimicrobial resistance and use in

animal agriculture. They are reintroducing NARMS sampling in sheep and goats in conjunction with the upcoming NAHMS Sheep study and continue to build upon NARMS collaborations, research collaborations with USDA Agricultural Research Service (ARS), and other projects targeting the farm-to-fork continuum.

### **Environmental Protection Agency (EPA)**

The EPA categorizes antimicrobials as pesticides and uses the term antimicrobial to refer to surface-applied antimicrobial substances. The antimicrobial pesticides that the EPA regulates are used mainly on crops or as wood preservatives. Part of the regulatory requirement of the EPA is to determine that the product does not cause unreasonable adverse impacts on human health, which includes impact on resistance. Applying antimicrobials to plants is essential to growers, especially as climate change drives increased bacterial disease pressure. Antifungal use on crops is more common, but many of these products are related to human drugs.

The EPA is tasked with determining the balance of the costs and benefits of a product from economic, social, and environmental views. This results in a risk analysis and mitigation approach to regulating these products. The EPA utilizes an adapted format of the FDA's GFI #152 to assess the risk of release, exposure, and consequence to provide a qualitative risk assessment. This poses a challenge in an organization that largely relies on quantitative outcomes. The risk assessment of EPA-regulated antibiotic pesticides is a collaborative process involving CDC, FDA-CVM, and USDA, leveraging the knowledge of partners with daily experience with similar products.

Fungicide risk assessment is a much more challenging task. However, with the rise of fungicide-resistant human pathogens, a collaborative effort between EPA, HHS, and USDA is underway to build a framework to assess the risk of these products. One of the most significant challenges in assessing the risk of fungicides is the ubiquitous nature of several fungi that are plant and human pathogens, such as *Aspergillus fumigatus*. As resistance to fungicides grows in human pathogens, using a science-based approach to assess product safety and determine future approvals will be critical.

## **Questions and Answers with Agency Partners**

With such a wide variety of dashboards sharing antimicrobial resistance data, the agency partners were asked how to help producers navigate these dashboards and whether there will be tools in the future to combine data across dashboards. Despite the wide range of seemingly disconnected dashboards, there has been an effort to target dashboards to specific audiences. Further, there is an effort to provide multiple formats; for example, the same data could be presented in a researcher-oriented dashboard and a producer-focused factsheet or infographic. Context becomes critical to proper data interpretation with so many audiences and data sources.

Even with stakeholder input, a broad, integrated One Health dashboard may not be feasible. Improving data security is one possible avenue to increase the likelihood of an integrated dashboard. However, it is unlikely that this will completely solve the problem due to the wide variety of data sources, each requiring different interpretations. Testing methods differ between human and animal health, complicating data presentation and interpretation if combined into a single dashboard.

The federal partners all described collaboration across agencies and with industry stakeholders. Agency partners were asked how they collaborate with state and local partners to distribute information. USDA-APHIS has been trying to find partnerships to provide better access to data and resources. For example, California state legislation required reporting of antimicrobial resistance data, prompting a collaboration between the California Department of Food and Agriculture and APHIS to acquire data beneficial to both organizations. CDC collaborates through the Food Safety Centers of Excellence, as well as through collaborations built during outbreaks.

#### **Breakout Sessions**

The breakout sessions allow the conversations of this meeting to continue in a more targeted manner. Certified Angus Beef led the communications breakout, which focused on how antibiotic stewardship messaging can be shared with the public. Though there has been a shift to a more balanced view of the role of animal agriculture in the development and spread of AMR, there is still a need for messaging to the general public. How to frame these messages is an essential topic of discussion. NIAMRRE led the research breakout, which focused on how the U.S. could respond to the Muscat Manifesto, which proposes a considerable percent reduction in antibiotic use in agriculture. Though many countries are expected to sign on to this document, it does not align with U.S. goals. The group brainstormed how the U.S. could respond to this proposal with constructive ideas to improve stewardship without relying on an arbitrary reduction in usage, which is complicated by difficulties in appropriately measuring antibiotic use. The Relevant Classroom, A Division of Vivayic, led the education breakout session. This breakout focused on bringing agriculture-oriented One Health lessons into the classroom. Building lesson plans to assist teachers in sharing these lessons with youth in the

classroom is an important step. These breakouts were an opportunity to continue the conversation and build ideas to keep moving AMR topics forward.

## Public Health's focus for antibiotic stewardship and AMR

Public Health experts are an essential partner to have at the table as we tackle antimicrobial resistance. Dr. Karen Smith shared how the field of public health arose, how it has changed over time, and how it will need to continue to evolve. The origins of public health are likely as simple as assuring the latrine was placed away from the water source. As towns and cities grew, separating drinking water and wastewater became more challenging. This led governments to build sewage infrastructure as a public service, employing the first public health workers. Early forays into disease control were related mainly to quarantine for easily identifiable diseases like leprosy, but this disease control mission continued to grow.

Public health grew to encompass a wide variety of issues, yet it still evolves in modern times. Up until around 30 years ago, a primary function of public health departments was to act as a safety net healthcare provider for those without access to traditional healthcare. Though this function has primarily transitioned to the public sector, public health departments maintain vaccination clinics to ensure sufficient surge capacity in an outbreak. The focus of modern public health has shifted to protecting the population through prevention practices and policy development. Many public health policies, like requiring car seatbelts, have had substantial positive impacts on human health, but building public health policies can be challenging. The best and most effective policies are built through collaboration with those who will be most affected by the policy. This ensures that the policy is implementable in the community where it is needed.

The public health approach to solving problems starts with surveillance, which is critical to understanding what the problem is and the scale of the problem. With a well-defined problem, identifying risk factors can point to the cause of the problem. Once the cause is understood, interventions can be evaluated, and implementation plans developed. However, the public health approach does not end with implementation. Unexpected issues can quickly derail a public health intervention. An evaluation plan is critical to the implementation process so issues can be identified and addressed early to keep the intervention on track.

The fight against antimicrobial resistance primarily reflects a public health approach, but it is a challenging issue regardless of the approach. Antimicrobials are a critical tool to save lives, but their use also causes resistance. Even the first step of a public health approach, surveillance, is challenging in the AMR arena. Much of the surveillance data in human medicine comes from hospitals, yet most antibiotics are prescribed in outpatient settings. These types of challenges are not unique to human medicine. We see similar issues within animal agriculture, making a One Health approach to this issue even more critical.

One Health is an intentional collaboration across the silos that still divide human, animal, and environmental health. By building this collaboration, we get to know one another, and we get to know aspects of health we may have never considered before. This helps us see opportunities to improve that may have gone unnoticed otherwise. This intentional collaborative effort will become even more critical as climate change continues to impact our world. Even though we cannot fix the climate, we can work together to protect the health of people and animals.

### Why is it important for a One Health conversation to continue?

Dr. Heather Fowler served as moderator and opened this session with some One Health history. She shared several definitions of One Health, including the One Health High-Level Expert Panel (OHHLEP) definition, which incorporates multiple societal factors and the impact of climate change, both of which are critical aspects of the One Health conversation as it continues in the future. This session brought together some of the most diverse speakers from geographical and expertise standpoints to discuss why we must continue the One Health conversation.

Though the focus of this meeting is animal agriculture, the AMR conversation is incomplete without the perspective of veterinarians in companion animal medicine. Dr. Benjamin O'Kelley is an emergency and critical care specialist who leads the antimicrobial stewardship efforts at BluePearl Pet Hospitals, part of Mars Veterinary Health, comprising around 3,000 veterinary hospitals worldwide. Companion animal veterinarians are impacted regularly by AMR. They see patients with resistant and multi-drug resistant infections, many of which are zoonotic. When resistant infections arise, it can significantly increase the cost of care, an ever-escalating issue in companion animal medicine. Though some companion animal vets believe that animal agriculture is the cause of resistance, they must also look at their industry, where high-power antibiotics can be prescribed, often with little oversight.

These high-power drugs are frequently employed when illness becomes emotional. For many people, pets are family. This devotion to an animal can lead to medical decisions where antibiotic after antibiotic is employed to save a beloved family member. However, these emotional ties can be invaluable for pet owners and a reason why vets need access to antibiotics. Dr. O'Kelley shared a story of a pet that survived a house fire. His injuries put him at risk of bacterial infection, so antibiotics were a critical aspect of his treatment plan. These interventions did ultimately save the dog, which helped this family recover as they grieved the death of their daughter, who had lost her life in the same fire. Access to antibiotics in such situations can be a gift to patients and their owners. However, companion animal veterinarians must also respect these drugs because every decision regarding antibiotics has an impact. BluePearl Pet Hospitals have built a stewardship program that recognizes the challenges faced in companion animal medicine, builds knowledge across all skill levels in the clinic, and develops a culture of stewardship. Dr. O'Kelley urges animal agriculture to keep moving the conversation forward. A better understanding of our strides in food animal antibiotic use could help motivate change among companion animal veterinarians.

Shifting from a conversation just beginning, Jim Lanier of the HEB grocery chain shared the long-standing story of responsible antibiotic use at HEB. The chain is a grocery retailer across Texas and Mexico with a responsible antibiotic use policy that has been in place for over 20 years. They have a historic policy because they recognize the importance of knowledge and understanding across their chain. When headlines about food hit the press, people ask questions where they buy their food. However, when HEB asked store managers if they were comfortable answering these questions, particularly about antibiotics, most were not. Even more concerning, many provided incorrect answers when asked about antibiotic facts. HEB works to educate their managers and employees on the responsible use of antibiotics in food animals and build agricultural expertise within their management structure.

This knowledge can help shoppers make more informed decisions across the 16 lines of beef HEB carries. This array of beef options includes a "raised without antibiotics" line and premium products like Wagyu beef. However, in a state where a quarter of the population lives in poverty, HEB believes it is vital to hit all price points. Their value beef line provides high-quality, affordable protein from cattle that were just as well taken care of as those from their premium lines of beef. HEB continues to move the conversation around antibiotics forward, even as they respond to activists and advocacy groups that attack the company from outside the state of Texas. They also continue the One Health conversation beyond antibiotics, recognizing that customers will ask tough questions about tough topics; HEB focuses on educating their personnel so they can confidently join the conversation.

For a different perspective, Dr. Paul Morley of the Veterinary Education Research & Outreach Program shared why he feels the AMR conversation needs to shift away from animal agriculture. Though AMR is undeniably an important public health issue, Dr. Morely brought us back to when the dogma of AMR was that antibiotic use in animal agriculture was the main driver of resistance. Unfortunately, this notion has stuck in some circles, leading to pressure to reduce or even eliminate antibiotic use in animal agriculture. Dr. Morely suggests that even though it is again viewed as dogma by many, the notion that reducing antibiotic use will reduce resistance has yet to be proven. To prove a need for antibiotic use reductions in animal agriculture, he suggests we need better evidence along the entire chain from antibiotic use in food animals to resistance in animals to infection in humans and finally to illness in humans.

Many factors support continued antibiotic use in animal agriculture, such as the ever-growing population, food insecurity abroad and at home, veterinary and producer concern about animal welfare in RWA systems, and the environmental impact of these less efficient RWA systems. Dr. Morley suggests that we have a moral obligation to use antimicrobials in food animals. Though some in attendance had differing opinions, most would agree with Dr. Morely's other suggestions: Animal agriculture has made great strides in antibiotic use reductions, which deserves applause. We need new technologies, not just better diagnostics but also antibiotic alternatives. Finally, a better understanding of the host through microbiome, resistome, and transcriptome analysis may open even more options to minimize animal disease.

The final speaker in this panel brought a unique perspective to the One Health and AMR discussion. Dr. Alex Tasker's career focuses on One Health issues in complex and challenging settings. As was shared in Dr. Karen Smith's talk, Dr. Tasker reiterated the importance of surveillance but reminded the audience that entire supply chains exist that cannot be surveilled. He shared a story of a mass reindeer die-off in far northern Russia. With climate change, this area has become vulnerable to permafrost melt, which has revealed wooly mammoth ivory, a valuable resource in this food-insecure population. Unfortunately, this ivory may have harbored 9,000-year-old anthrax that was still viable. Anthrax is what killed the reindeer. This ivory was sent into black market trading channels where human exposure to this pathogen was possible. Who provides surveillance to these illegal markets? These criminal networks are designed to avoid surveillance, so the criminals themselves are the only source of surveillance. Another criminal network with direct ties to the AMR discussion is the counterfeit drug trade. This global issue has impacted many popular drugs in the U.S., life-saving drugs like antimalarials in other areas of the world, as well as antibiotics.

Internationally, there have been great strides in reducing antibiotic use in animal agriculture. In the United Kingdom, the pig and meat poultry industries have reduced high-importance antibiotic use by 99% since 2014-2015. The AWaRe classification system, which stands for access, watch, and reserve, guides appropriate antibiotic use. Nowhere does this program prohibit antibiotic use; instead, it encourages antibiotic use that is employed with forethought, particularly for certain reserved drugs. The world faces many risks. AMR is one of them, yet it is interconnected with numerous other global risks. The One Health discussion needs to continue because each issue must be addressed with other connected risks. A One Health approach must move beyond siloed thinking, engage non-traditional disciplines to create new solutions, and reframe how we view complexity and uncertainty, as these can bring new opportunities.

As an animal agriculture-centric audience, we rarely get to discuss antibiotic stewardship in companion animal medicine. An audience member asked Dr. O'Kelley what he sees as opportunities to address AMR in companion animal medicine. As in animal agriculture, point-of-care testing is important, but often, clients cannot afford these tests. Even with better education for vets and clients alike, the cost of care can still derail stewardship. Veterinarians often do not respond well to mandated treatments or prohibited drugs. However, peer comparisons, when presented non-judgmentally, are another opportunity to help veterinarians choose to change prescribing practices.

The sentiment that all antibiotic use in animal agriculture is bad continues in many areas. A question arose about how to stop misinformation regarding animal agriculture from university professors. Speakers were quick to note that these statements are not only coming from universities and that we need to start educating kids much earlier on the truths of animal agriculture. We cannot have conversations without all parties having an open mind, and we need to avoid the use of "all." It is just as easy for those in our industry to say "all universities..." as for opponents to say "all farmers..."

## Antibiotic Stewardship, emerging fungal pathogens in livestock, and AMR on the Horizon ... what should we be watching/engaging in?

#### Dr. Paul Plummer – NIAMRRE

Dr. Patricia S. Gaunt - Mississippi State University CVM Fish Diagnostic Laboratory Dr. Tom Chiller - Centers for Disease Control & Prevention Dr. Alexandra Medley (moderator) - Centers for Disease Control & Prevention

To conclude this symposium that focused on "thriving in a changing landscape," we looked to the edge of that landscape to see what is emerging on the horizon and what the AMR community needs to be watchful for in the future. Dr. Paul Plummer of NIAMRRE started the discussion by bringing together four big themes across the symposium that point toward the future of antibiotic stewardship and its relationship to animal agriculture. As antibiotic stewardship in livestock continues to progress, the focus of stewardship beyond human health may shift away from livestock. Aquaculture, companion animals, and crop production are likely the future targets of a One Health approach to antibiotic stewardship. Though stewardship in livestock is challenging, the aquaculture industry brings even more significant challenges. The diversity of animals raised in *National Institute for Animal Agriculture*  the industry is vast, encompassing vertebrates like catfish to invertebrates like mollusks or clams. To further complicate things, there are few labeled antibiotic choices, limited diagnostics, and few breakpoints to evaluate resistance even when diagnostics are available.

Another area of veterinary medicine that is coming into focus in stewardship efforts, both domestically and globally, is companion animal medicine. Though there are many opportunities for people and animals to interact and potentially spread resistant infections, perhaps the most intimate interface is that of the household pet. These pets are frequently treated with antibiotics, particularly for severe diseases that may necessitate high-power antibiotics not used in livestock production. The future will bring more focus and more regulation for this aspect of antibiotic use. There are also likely to be future changes in stewardship beyond the veterinary use of antibiotics. The publication of the CDC 2019 Antibiotic Resistance Threats Report brought the emerging concern of fungal resistance to light. With few antifungal classes and broad overlap with crop production, there are potential changes in crop management on the horizon that could result in downstream consequences on feed access and affordability for livestock producers.

Beyond impacts on antibiotic users, the future will also change how we view antibiotic stewardship. Historically, antibiotic stewardship has been measured by reductions in antibiotic use, but the true story of stewardship is far more complex. How to assess and appropriately measure stewardship will continue to change as the differences across industries and even operations are recognized. To elicit changes in antibiotic stewardship, the physical science side of AMR research must form a partnership with social science. The industry must view social science as an integral part of stewardship to leverage the knowledge of human behavior to enable change. The challenges faced in measuring and improving antibiotic stewardship go beyond domestic policy. For the animal agriculture industry, there is growing concern about the impact of one country's antibiotic regulations being "exported" to other countries, effectively imposing a barrier to trade unless the exporting country adopts the antibiotic use standards of the importing country. Further, these standards are often based on the flawed measure of reduced use. The U.S. and animal agriculture must engage globally to build antibiotic use policies that ensure a strong future. Absence from the conversation does not stop decisions from being made. It only ensures decisions are made without our input.

Aquaculture is one of the areas of antibiotic stewardship where there is likely to be more focus in the future. Dr. Patricia Gaunt shared some background on aquaculture, focusing on catfish production and the challenges of antibiotic stewardship in aquaculture. Disease treatment in commercial fish production can be challenging. Only three antibiotics are labeled for use in aquaculture, all of which are in-feed antimicrobials. As fish get ill, their feed intake decreases, complicating the ability to treat these fish. This makes disease prevention a critical aspect of antibiotic stewardship in aquaculture.

The key to disease prevention in aquaculture is water quality, so much so that water samples can be essential to disease diagnosis. Maintaining optimal water quality is a delicate balance. With a limited growing season, farmers want faster growth, meaning they need to feed more to the fish, but if there is excess feed, this results in ammonia buildup. Ammonia degrades into nitrites, which, just as in cattle, cause methemoglobinemia, impairing the blood's ability to carry oxygen. A warm growing season also increases the risk of issues with dissolved oxygen because warm water carries less dissolved oxygen than cool water. All these water quality issues can directly impair fish health, cause stress and increased risk of disease, and, in severe cases, even death. Beyond water quality, biosecurity is another key to disease prevention in aquaculture.

Open ponds face wildlife-related biosecurity issues, but even closed indoor facilities have biosecurity challenges. Due to water recirculation within an indoor fish facility, a pathogen can rapidly spread from tank to tank once it enters the facility. In many ways, biosecurity in fish facilities is much like that in other areas of animal agriculture, with practices like procuring eggs from pathogen-free hatcheries, using separate equipment at each facility, and maintaining appropriate stocking density. Though there are few labeled vaccines in aquaculture, autogenous vaccines are a growing method of disease prevention in the industry. When disease does arise, an evidence-based approach to treatment will include diagnostics, water quality, and environmental conditions that can impact disease. Interpretation of diagnostics can be challenging due to insufficient breakpoints to assess antimicrobial resistance.

Antibiotic stewardship in U.S. aquaculture could be improved with better diagnostics, better data on sales and use, and more veterinarians. Unfortunately, the aquaculture industry in the U.S. is shrinking as farmers find it increasingly more challenging to compete with imported products. In the U.S., 85 percent of seafood consumed is imported, with antibiotic use practices often varying widely from U.S. standards. Despite this, only a tiny fraction of imported seafood is tested. As the focus of stewardship shifts towards aquaculture, efforts to improve stewardship must address both domestic and international production.

Fungal pathogens present unique challenges in disease management. They are the closest to mammals of any pathogen, making fungal disease difficult to diagnose and even more challenging to treat without significant side effects. Because of this, even human medicine has only three classes of drugs to treat invasive fungal infections. A public health mycologist, Dr. Tom Chiller of the CDC, shared three concerning fungal pathogens on the horizon. Though *Aspergillus* fungi are ubiquitous in the environment, they can cause disease in immunocompromised people. Typically, aspergillosis can be treated with antifungals, but mortality from this infection has grown as a new strain resistant to azole-class antifungal drugs has emerged. Unlike many drug-resistant pathogens, this strain does not appear to have arisen from human antifungal use but rather from the environment. The azole class of antifungals is commonly used in crop production, a likely contributor to the development of this resistant pathogen. Though eliminating crop use of azole antifungals may seem reasonable, effective fungicides are essential for crop health, so this is not a viable solution. More research will be needed to better understand this infection, its origins, and solutions to stop the development of fungicide resistance.

Though resistance in *Aspergillus* has ties to the environment, human antifungal use is likely a driver of another emerging resistant fungal infection. Dermatophytosis is the most common fungal disease in the world. It includes common conditions like ringworm and athlete's foot that can be easily treated. Worryingly, a new species is emerging with high levels of resistance to terbinafine, the first-line treatment, and growing resistance to azole drugs, the second choice for treating dermatophytosis. The result is a highly contagious infection often seen all over the body. Though there are no documented cases in other species, many dermatophytes are zoonotic, so spread to animals is likely. This pathogen is thought to have emerged from Southeast Asia, where multi-drug preparations for dermatophytosis are common.

Though they ultimately went with a less scary title, the conference planning committee originally titled this panel discussion "What Keeps You Up at Night." The last topic surely fits the bill for the original title. A new fungal disease is emerging in Brazil. This is a dimorphic fungus with the ability to cause infections in both of its forms. These fungi can infect many species, but cats have been central to its spread in Brazil. In cats, the disease causes severe, disfiguring facial and ocular lesions. Contact with the fungi, even on intact skin, can result in infections, so infections among veterinarians and dogs with vet clinic exposure have been seen. Though this disease is treatable with long-term administration of antifungal drugs, if it were to acquire resistance, the results could be devastating.

The discussion following these speakers revolved around benchmarking and defining antibiotic and antifungal stewardship and how the two are linked. The challenges with use-based benchmarks were discussed in depth earlier, but viable benchmarks are still elusive. Easily acquired data should be the first target, but even this can be problematic. One suggestion is to evaluate treatments per diagnosis to mimic the prescription rate in human medicine. However, this requires consistent recordkeeping from farm to farm. Virtually every possible measure has its challenges. Finding a thorough definition of stewardship and developing effective benchmarks will require all stakeholders to come to the table. It is imperative to have people who understand the context of antibiotic use to help guide these decisions.

More data is always helpful in building stewardship practices, but data privacy and protection are ongoing issues. The upcoming farm bill will hopefully include language that provides statutory data privacy coverage, much like HIPAA does in human medicine, to increase participation in animal agriculture. The world of antibiotic stewardship will continue to evolve and be shaped by those who participate. It is critical for voices from across the One Health spectrum, including animal agriculture, to be at the table as the landscape of stewardship changes and new issues emerge on the horizon.

## References

Dupré J, Baines R, Cripps E, Ferrier H, Fraser R, Frewer L, Greenfield A, Kaler J, Murcott A, Stevenson P, Whitelaw B. Genome editing and farmed animal breeding: social and ethical issues. Nuffield Council on Bioethics. 2021 Jan 12.

Mettenleiter, T.C., Markotter, W., Charron, D.F. et al. The One Health High-Level Expert Panel (OHHLEP). One Health Outlook 5, 18 (2023). https://doi.org/10.1186/s42522-023-00085-2

Shanthalingam S, Tibary A, Beever JE, Kasinathan P, Brown WC, Srikumaran S. Precise gene editing paves the way for derivation of Mannheimia haemolytica leukotoxin-resistant cattle. Proc Natl Acad Sci U S A. 2016 Nov 15;113(46):13186-13190. doi: 10.1073/pnas.1613428113. Epub 2016 Oct 31. PMID: 27799556; PMCID: PMC5135351.

Singer RS, Porter LJ, Thomson DU, Gage M, Beaudoin A, Wishnie JK. Raising Animals Without Antibiotics: U.S. Producer and Veterinarian Experiences and Opinions. Front Vet Sci. 2019 Dec 6;6:452. doi: 10.3389/fvets.2019.00452. PMID: 31867349; PMCID: PMC6910073.

Wall RJ, Powell AM, Paape MJ, Kerr DE, Bannerman DD, Pursel VG, Wells KD, Talbot N, Hawk HW. Genetically enhanced cows resist intramammary Staphylococcus aureus infection. Nat Biotechnol. 2005 Apr;23(4):445-51. doi: 10.1038/nbt1078. Epub 2005 Apr 3. Erratum in: Nat Biotechnol. 2005 Jul;23(7):897. PMID: 15806099.