

Addressing Antibiotic Resistance

A REPORT FROM THE JOINT APLU | AAVMC TASK FORCE
ON ANTIBIOTIC RESISTANCE IN PRODUCTION AGRICULTURE



Association of Public and Land-grant Universities

The Association of Public and Land-grant Universities (APLU) is a research, policy, and advocacy organization representing 237 public research universities, land-grant institutions, state university systems, and affiliated organizations. Founded in 1887, APLU is North America's oldest higher education association with member institutions in all 50 U.S. states, the District of Columbia, four U.S. territories, Canada, and Mexico. Annually, member campuses enroll 4.7 million undergraduates and 1.3 million graduate students, award 1.1 million degrees, employ 1.3 million faculty and staff, and conduct \$41 billion in university-based research.

Association of American Veterinary Medical Colleges

The Association of American Veterinary Medical Colleges (AAVMC) is a nonprofit membership organization working to protect and improve the health and welfare of animals, people and the environment around the world by advancing academic veterinary medicine. Members include 49 accredited veterinary medical colleges in the United States, Canada, Europe and Australia, as well as 23 affiliate members.



Introduction

Since Fleming's discovery of penicillin in 1928, antibiotics have dramatically improved human, animal, and plant health. Antibiotics have enabled millions of people to live longer and more productive lives. They have dramatically lowered child and infant mortality rates and have helped to add significantly to our life expectancy. Antibiotics have significantly reduced morbidity and mortality in our animal populations and have improved gains in productivity. At the same time, there is a growing concern among scientists and healthcare workers that the effectiveness in treating infections with antibiotics is becoming compromised by increasing drug resistance.

In recent years, the pace at which we are discovering novel antibiotics has slowed drastically, while antibiotic use is rising significantly. Thus, the great strides forward made over the last few decades in controlling infectious diseases could be reversed with catastrophic consequences. In addition, as with all infectious diseases, the speed and volume of international travel is creating new opportunities for microbes to share genetic material and to spread globally. Antibiotic resistance is biologically complex

and poorly understood. The scope and scale of the problem threatens human, animal, and environmental health nationally and globally. There is a growing consensus that an integrated national plan is critical and that agriculture must be a full partner in both developing national strategies and taking action to address this growing and significant threat to health.

Background

In 2014, the President’s Council of Advisors on Science and Technology (PCAST) charged a group of experts to create a national strategy and recommendations to address antibiotic resistance. The report, ***Combating Antibiotic Resistance*** was issued in September 2014, and was quickly followed by a Presidential Executive Order that endorsed the report and the adoption of its recommendations. In addition, a high-level governmental task force co-chaired by the Secretaries of Health and Human Services, Agriculture, and Defense was formed. Using the information from the PCAST report and existing plans, the interagency Task Force for Combating Antibiotic-Resistant Bacteria was charged to create a National Action Plan. The critical features of the National Action Plan included: (1) slowing the spread of resistant infections; (2) strengthening national “One Health” surveillance efforts; (3) advancing the development of rapid and innovative diagnostic tests; (4) accelerating basic and applied research and development; and (5) improving international collaboration and capacities.

Prior to these activities, the FDA issued Guidances 209 and 213 which, in essence, called for the voluntary withdrawal of the use of medically-important antibiotics for growth promotion in livestock and poultry over the next three years. Almost all animal health pharmaceutical companies have already agreed to comply with these guidance documents. The FDA also added flexibility to the existing Veterinary Feed Directive (VFD) to enhance its use as a veterinary oversight tool for implementing Guidances 209 and 213. These actions by the FDA have changed the landscape for antibiotic use and accessibility in animal agriculture. Finally, the World Health Assembly of the WHO endorsed a global action plan for antimicrobial resistance in May 2015. Their recommendations were closely aligned to the National Action Plan of the United States.



A Call to Action

The new national and global plans to address antibiotic resistance have motivated a call to action. Many of the recommendations outlined in these plans fit especially well with the expertise, capacity, and missions of our colleges and universities.

Therefore, the Association of Public and Land-grant Universities (APLU) and the Association of American Veterinary Medical Colleges (AAVMC) created a Task Force on Antibiotic Resistance in Production Agriculture. The APLU|AAVMC Task Force brought together representatives from U.S. agriculture colleges/land-grant universities and veterinary colleges as well as key representatives from the production animal agriculture community and the pharmaceutical industry to leverage their respective strengths and expertise in education, outreach and research. Officials from key federal agencies also served as observers to the Task Force on Antibiotic Resistance in Production Agriculture, which was charged to make recommendations, advise and assist government agencies and the President's interagency Task Force for Combating Antibiotic-Resistant Bacteria. The APLU|AAVMC Task Force especially focused their

efforts on agriculture and animal health. Our recommendations emphasize where our assets can add value to implementing a national strategy; most importantly, we have adopted a “One Health” perspective in creating our strategies. The Task Force members believe that agriculture and animal health must be full partners with the human medical community in a truly or fully integrated national action plan. We accept the responsibility and challenge to be an integral partner in the future reduction and mitigation of antibiotic resistance.

Education and Outreach Recommendations

An effective educational and outreach strategy will be key to the implementation of the National Action Plan. With the issuance of Guidances 209 and 213 by the FDA and changes in the Veterinary Feed Directive giving veterinarians increased oversight authority, there will need to be a greater emphasis on stewardship programs, education and training to ensure our efforts to address antibiotic resistance are successful.

A variety of educational and outreach programs – utilizing customized content to accommodate a wide variety learners – will be required to meet the needs of diverse audiences. Proposed initiatives include:

- **DESIGN AND IMPLEMENT A MODEL CURRICULUM TO IMPROVE AWARENESS, UNDERSTANDING AND HELP IN THE IMPLEMENTATION OF EFFECTIVE ACTIONS TO COMBAT ANTIBIOTIC RESISTANCE.** The contents of a model curriculum would include a common body of knowledge but would also have customized content based on targeted audiences that would include undergraduate, graduate, professional health sciences, agriculture, community colleges and veterinary technology students. Collecting and building an inventory of existing academic courses and curricula would be extremely useful. In addition, the model curriculum would be available on-line, widely distributed and constantly improved through an active learning network that would accommodate both national and global interests. This recommendation envisions both the development of case studies and inter-professional educational workshops and forums over time.

- **CREATE AND DELIVER COURSES AND PLANS ON ANTIBIOTIC STEWARDSHIP THROUGH A VARIETY OF EDUCATIONAL AND CONTINUING EDUCATION (CE) PROGRAMS.** These courses would specifically target human and animal health professionals who need CE credits to maintain their professional licenses. Veterinary antibiotic-focused programs are needed for both food and companion animal practices. Stewardship is a key element of the National Action Plan for Combating Antibiotic-Resistant Bacteria. While there is a sense of urgency to develop effective programs; as of yet, the stewardship concept is not standardized, well-defined, or consistently adapted and applied outside of in-patient human healthcare settings. Inherent with this recommendation is the need to define core principles and to partner with specific specialty groups and human health organizations such as the Infectious Diseases Society of America (IDSA) and Centers for Disease Control and Prevention (CDC).
- **IN COLLABORATION WITH U.S. DEPARTMENT OF AGRICULTURE (USDA) ANIMAL AND PLANT HEALTH INSPECTION SERVICE (APHIS) VETERINARY SERVICES (VS), ASSIST IN DEVELOPING AND INCORPORATING NEW TRAINING MODULES AND INITIATIVES ON COMBATING ANTIBIOTIC RESISTANCE AND IMPLEMENTING STEWARDSHIP PROGRAMS FOR VETERINARIANS AS PART OF USDA’S NATIONAL VETERINARY ACCREDITATION PROGRAM (NVAP).** Some modules would be used to both acquire accreditation for new graduates and to maintain accreditation status for practicing veterinarians. The U.S. Food and Drug Administration (FDA) would also be an essential partner in helping to develop these modules.
- **ALONG WITH OTHER EDUCATIONAL PROVIDERS AND ORGANIZATIONS, INCLUDING ANIMAL AGRICULTURE COMMODITY GROUPS AND THE AMERICAN VETERINARY MEDICAL ASSOCIATION (AVMA), DEVELOP KEY MESSAGES AND PERTINENT INFORMATION TO INFORM AND EDUCATE PRODUCERS AND FARMERS OF THE CHANGING LANDSCAPE FOR ANTIBIOTIC USE AND ACCESSIBILITY IN ANIMAL AGRICULTURE – INCLUDING RECENT FDA GUIDANCES, CHANGES TO THE VETERINARY FEED DIRECTIVE, ON-FARM DISEASE PREVENTION STRATEGIES AND EMERGING STEWARDSHIP PROGRAMS.** USDA’s Cooperative Extension Service should be considered in implementing this recommendation because of their existing infrastructure, experience, and significant reach across the agricultural communities. Consistent and simple messaging is a critical feature of this recommendation as is the need to accommodate the diversity of animal species,



production practices, and different geographic settings. The translation of messages and information into Spanish language versions would also be very useful.

- **DEVELOP AND DELIVER A SERIES OF PUBLIC EDUCATION AND COMMUNICATION PLANS, STRATEGIES AND MESSAGES.** Currently, there is a lack of knowledge and appreciation for the role of agriculture and animal health in combating antibiotic resistance as well as the need for a strong human and animal health partnership. Our universities and colleges offer a credible, objective, and trusted voice – our institutions also have a wide array of experts with multiple perspectives and views. The “One Health” approach should provide a useful framework to help explain antibiotic resistance and critical interventions to combat the problem. Editorials, media communications and interviews, publications, webinars, and social media channels should be used to deliver educational messages and services. To help ensure the effectiveness of this recommendation, joint messages that involve both animal and public health – emphasizing collaboration and cooperative actions and views – will be especially helpful.
- **DEVELOP AND IMPLEMENT EDUCATIONAL AND INFORMATIONAL STRATEGIES, TOOLS AND PROGRAMS THAT FOCUS ON DIFFERENT GROUPS EXTENDING ACROSS OUR EDUCATION SPECTRUM.** Agricultural youth groups – including 4-H, FFA and

STEM educational groups – represent emerging leaders, decision-makers, and ideal populations upon which to build a culture of understanding and commitment to address antibiotic resistance. Education programs and messages should be tailored to youth groups by using YouTube and other social media channels that also include youth leaders themselves to help deliver key messages.

Research Recommendations

Our universities and colleges have enjoyed a productive and collegial relationship with government agencies and federal researchers for decades. Our recommendations are built upon this strong partnership and past success. At the same time, our research recommendations on antibiotic resistance emphasize some of the critical principles needed to successfully conduct future research on this topic. These principles include: the need for trans- and inter-disciplinary scientific teams; the use of social, behavioral and economic sciences; a special recognition for the necessity of incorporating the private sector as strategic collaborators; an emphasis on innovation and the use of exciting new scientific tools and methods; the need to design and develop on-farm studies to assess the success of proposed policies and guidances and other interventional strategies; and, the integration and organization of national teams and consortiums that connect government, private and university researchers and further connect agricultural and veterinary medical researchers with biomedical and human health researchers to avoid duplication of effort and optimize synergies.

Finally, researchers should embrace the holistic concept of “One Health” in designing and carrying out research in human, animal, and environmental health and antibiotic resistance. This important organizing principle will help ensure a more complete picture of the complexities of antibiotic resistance and will be helpful in improving both our understanding of the phenomenon and finding new interventions and strategies to prevent or reduce resistance to antibiotics.

Research on antibiotic resistance should reflect the interconnectivity of people and animals and, as such, the National Action Plan should recognize and endorse a common portfolio of research needs that incorporates both animal agriculture and biomedical research and studies, especially in terms of basic research.

Basic Research Needs

Sufficiently understanding antibiotic-resistant bacteria

- Improve our understanding of how resistance is transferred across species and the environment
- Characterize fully, all impacts of both antibiotic and non-antibiotic co-selective pressures on the emergence and dissemination of resistant organisms and genes
- Improve our understanding of the interaction between host immunocompetence and the emergence of resistance during bacterial infections
- Generate and analyze appropriate metagenomic data to provide population baseline values and variability estimates

Finding alternatives to current antibiotics

- Identify and evaluate new products to combat and/or prevent bacterial infections
- Identify and fully evaluate the efficiency and impact of potential alternatives to antibiotics used in agriculture
- Collaborate with human and animal health pharmaceutical corporations to help develop a more robust pipeline of new antibiotics and alternative products

Applied Research Needs

Developing essential methods and tools

- Develop new computational methods and tools to carry out metagenomic analyses of isolates and specimens
- Develop essential ecological and mathematical models for antibiotic use and resistance risk assessment
- Collaborate in the creation and development of state-of-the-art and point-of-care diagnostic tests—many of these diagnostic tools could have a dual use in both veterinary and human medicine



Assessing antibiotic resistance in production agriculture

- Characterize the incentives and motivations for antibiotic use across agricultural systems and sectors
- Compare, contrast and assess best practices to reduce both antibiotic usage and resistance through on-farm and production system interventions including: disease prevention, biosecurity, hygiene, management practices, effective vaccine use and housing and transportation changes
- Quantify and evaluate the success of stewardship programs for both farm and companion animal populations
- Evaluate changes in antibiotic use to accurately and fully assess the impact and effectiveness of FDA Guidances 209 and 213 in reducing antibiotic resistance
- Develop studies to estimate the economic impact of implementing FDA Guidances 209 and 213 as well as changes to the Veterinary Feed Directive for both producers and consumers

- Evaluate the impact of eliminating medically-important antibiotics for growth promotion and quantify the impact on animal welfare and health
- Develop essential ecological and mathematical models and conduct longitudinal studies for various species and production systems that can measure changes in antibiotic resistance patterns and accurately measure and predict the true attributable risk to human health

Operationalizing Task Force Recommendations

The APLU|AAVMC Task Force was acutely aware that their recommendations would most probably not be executed without a thoughtful and realistic implementation plan. Thus, the group understood that implementation is fundamental to strategy and needs to shape it. The recommendations on education, outreach, and research outlined in this report will be incomplete and ineffective without establishing and acting on goals for implementation. Thus, the Task Force concurred and supported the following implementation strategies:

- **ESTABLISH A PROGRAM MANAGER POSITION AND HIRE A MANAGER FOR THE NEXT YEAR** to ensure that Task Force recommendations and strategies are implemented
- **WORK WITH APLU AND AAVMC MEMBER INSTITUTIONS TO FORM A NATIONAL CONSORTIUM OF EXPERTS AND RESEARCHERS** to execute critical studies and research recommendations and to work with federal agencies to focus and integrate a national research portfolio to help combat antibiotic resistance
- **ESTABLISH AND HOLD A SERIES OF ONGOING EDUCATIONAL WORKSHOPS AND LEADERSHIP FORUMS** to advocate for, explain, and discuss the Task Force recommendations. These forums can be jointly held and sponsored by agencies, industry, non-governmental organizations and academic institutions and colleges
- **MEET WITH FEDERAL AGENCIES (USDA, FDA, CDC), VETERINARY, ANIMAL HEALTH, AGRICULTURAL ORGANIZATIONS, PCAST REPRESENTATIVES, FEDERAL TASK FORCE MEMBERS, ADVISORY COUNCIL MEMBERS, CONGRESSIONAL OFFICES** and other interest groups to detail and discuss the APLU|AAVMC Task Force recommendations and establish collaborative initiatives
- **SCHEDULE AND HOLD HILL BRIEFINGS WITH INTERESTED LEGISLATORS AND STAFFERS** to gain support and advocacy for Task Force recommendations



- **SHARE THE TASK FORCE REPORT WITH INTERESTED INTERNATIONAL ORGANIZATIONS** including the World Organisation for Animal Health (OIE), Food and Agriculture Organization of the United Nations (FAO), World Health Organization (WHO), Inter-American Institute for Cooperation on Agriculture (IICA) and Pan American Health Organization (PAHO); in addition share the Task Force Report with APLU and AAVMC global members. The objective of this recommendation is to expand implementation and create opportunities for continuous learning and improvement and to share best practices for combating antibiotic resistance
- **WORK WITH AAVMC MEMBERS, CONGRESS AND THE USDA TO HELP RESOLVE THE IMPORTANT ISSUE OF THE LACK OF ACCESS TO VETERINARIANS IN MANY RURAL COMMUNITIES ACROSS THE U.S.** Key Task Force recommendations involving education, stewardship, surveillance, and established producer-veterinary relationships and on-farm disease prevention and judicious antibiotic use plans are all based on access to veterinarians. The initial step in this recommendation would be a survey to determine accessibility needs especially with regard to smaller livestock holders and farmers

- **CREATE SEVERAL UNIVERSITY-BASED PILOT PROJECTS FOCUSING ON COMBATING ANTIBIOTIC RESISTANCE.** Such pilots would be designed and executed at large universities that have substantial human medical centers and hospitals, veterinary medical centers and hospitals, colleges of agriculture and other health science, business, and education colleges. Collaborative efforts in research, education, and stewardship would become the focus from which to build larger state-level initiatives to combat antibiotic resistance
- **CREATE, AND STAND UP, A UNIVERSITY RESEARCH ORGANIZATION (URO)** to help coordinate and implement recommendations and facilitate collaborative research and educational initiatives
- The APLU|AAVMC Task Force will be sunset upon publication of this report; however, a small Executive Team including the APLU, AAVMC, the program manager and a few other strategic partners will continue to function to help ensure that implementation is achieved

Conclusion

Finding solutions to attain optimal health for people, animals, and our environment has never been more important. Inherent with this goal and embedded in this challenge must be a national effort to combat the vexing and disturbing trend of accelerating antibiotic resistance. Not only has antibiotic resistance become a critical challenge to the future of human health, it is now also considered to be a national security issue. The APLU and AAVMC strongly believe that the agriculture, animal health, and veterinary medical communities have a unique opportunity to assist federal agencies and other organizations in designing and implementing effective strategies and interventions to significantly reduce the speed and impact of antibiotic resistance across society. The recommendations outlined in this report represent how our universities and colleges can add value to the National Action Plan and how our organizations can become strategic partners to ensure that our collective health is improved by addressing the problem of antibiotic resistance.

TASK FORCE MEMBERS

THE TASK FORCE'S MEMBERS INCLUDE:

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