

Antibiotic Stewardship: From Metrics to Management

An NIAA symposium held November 3rd to 5th, 2015, in Atlanta, Georgia

EXECUTIVE SUMMARY

Antimicrobial resistance (AMR) is an extraordinarily complex problem that is global and results from the actions of a broad and very diverse set of individuals and groups in the United States, including human and animal health professionals, hospitals and healthcare organizations, farmers and companies engaged in animal and field crop agriculture, Federal, state and local governments in the United States and especially consumers of healthcare and food products. Similar and comparable groups in other countries also can have a direct impact of the AMR problem in the United States. Through its series of annual antibiotic resistance symposia beginning in 2011, the National Institute of Animal Agriculture has sought to provide a platform where multiple stakeholders can come together and establish productive relationships and find common ground, with the goal of producing a consensus of opinion on how to move forward to address this problem of growing international concern. Each symposium has built upon the lessons and outputs of those that came before.

The theme of the 2015 symposium, *Antibiotic Stewardship: From Metrics to Management*, addressed the issue of how to determine whether the many efforts underway and planned to improve antibiotic use in animal and human health and in animal agriculture were succeeding. To this end, participants from previous symposia who had forged relationships across subject matter expertise and boundaries of professional discipline came together with an array of attendees attending NIAA antibiotic symposia for the first time. As at the preceding symposia, the 2015 conference combined information delivered during plenary sessions with facilitated discussions in breakout groups, each of which had defined tasks for developing output. The content and results of these efforts is summarized below.

Attendees heard presentations from scientists, animal and human health professionals, governmental public health officials, and representatives of companies involved in the animal protein supply chain. These presentations pointed out particularly the dramatic changes which have taken place since the first NIAA antibiotic symposium in 2011:

- Animal and human health professionals and medical practitioners are much more aware of the concept of antimicrobial stewardship
- Consumers have begun to drive change with their increasing interest in having “antibiotic-free” options at the retail groceries and restaurants
- Federal and state governments have instituted a variety of new guidelines and regulations covering both animal and human health pertaining to the labeling and use of antibiotics
- The Federal government has issued a new National Strategy and formed an independent advisory panel to address AMR and provide guidance to government agencies
- Virtually all stakeholders who use or prescribe antibiotics as well as consumers of healthcare and food products are changing their practices in an ongoing way and adopting new approaches that are highly variable as they seek to conform both to external expectations as well as their own evolving understanding of the AMR problem
- Despite the many reports, action plans, meeting and conferences which have taken place and the numerous initiatives announced by both public and private sectors organizations, there is a dearth of established, well-accepted metrics to assess the success of the efforts which are underway and planned.

The 2015 NIAA antibiotic symposium was designed to provide leadership by asking the diverse set of conference participants to take a first step in discussing, debating and creating quantifiable metrics for evaluating activities to improve antibiotic use and reduce the risk of resistant infections in people and animals were progressing optimally.

Tom Chapel, MA, MBA, who serves as the Chief Evaluation Officer at Centers for Disease Control and Prevention, in consultation with the 2015 NIAA Symposium program committee, developed a strawman roadmap and framework to guide the breakout groups in their discussions and creation of proposed metrics. A cadre of trained facilitators led the breakout groups which first revised the roadmap (**Figure**), and in subsequent sessions, developed four specific measures as a first step in leading the way to consensus metrics for progress in antimicrobial stewardship (**Table**). Symposium attendees were able to listen to plenary presentations on current stewardship efforts in animal and human health and drivers of change in antibiotic usage with an awareness of the revised roadmap and used the information presented in developing the measures.

These measures are:

1. The percentage of states with ongoing, working committees overseeing collection and dissemination of data on antimicrobial resistance from human, animal and environmental sources
2. The number of useful and practical new diagnostic tests for the rapid identification and characterization of infection and AR (developed within a specific time frame)
3. Proportion of production units that have a documented Veterinarian-Client-Patient Relationship (VCPR) with at least one veterinarian.
4. The degree to which new and alternative interventions are being used in practice by veterinarians

For each measure, the breakout groups identified potential obstacles to creating the metric, including possible barriers to obtaining needed data, as well as challenges in implementing the metric. In addition, these metrics were developed to incorporate both human and animal health concerns (numbers 1 and 2) or in parallel to metrics in development for human health (number 3, paralleling requirements for antimicrobial stewardship programs to be in place in all hospitals and nursing homes; number 4 assessing improvements in infections control among inpatients and reducing unnecessary antibiotic prescribing among outpatient physicians).

Participants noted that these early efforts will require discussion and input from an even broader array of interested and concerned parties and that these four metrics can only be a start in identifying an agreed-upon set of process and outcome measures. However, as several plenary speakers had noted, and as the breakout group participants reiterated, difficulties in reaching consensus and implementing metrics must be overcome as ongoing evaluation and continuous improvement in antibiotic stewardship practices is an urgent imperative in which all stakeholders have a direct interest.

NEXT STEPS

Because antibiotic resistance is an extremely complex and multifaceted problem, no single solution is possible and no one scientific or professional discipline or sector of society can hope to address it alone. We will succeed in addressing this emerging crisis from a systems-based approach that strives to close gaps of misunderstanding and avoid implementing meaningful and effective interventions. While action

is urgently necessary, these actions must be based on a solid foundation of science, be economically and socially viable, grow out of transparent and open dialogue among all concerned parties and be evaluated carefully at each phase of implementation to ensure successful and sustainable outcomes.

The commitment to antibiotic stewardship from stakeholders throughout animal agriculture and the animal protein supply chain is clear and definitive, matching the seriousness and commitment we heard from representatives of human medicine and public health. High priority areas from the roadmap were chosen for metrics development because: 1) AMR and antibiotic use need to be carefully monitored and much better understood, 2) research on developing and implementing new, rapid and accurate diagnostic tests for antibiotic resistance that can be used in the field and at the bedside needs to be vigorously supported, 3) similarly, research to find alternatives to antibiotic use, including preventative treatments and improved production management practices requires both Federal and private sector support, and 4) the application of new regulations and guidelines will need to be thoughtfully and carefully assessed and assistance will need to be deployed to help practitioners and producers fully understand the changing requirements and put them into practice.

While the symposium succeeded in bringing together experts from diverse backgrounds to discuss the subject theme—*Antibiotics Stewardship: From Metrics to Management*—and resulted in the development of four potential metrics to monitor progress, participants and organizers understood that these efforts are a very early step forward and must lead to further dialogue and cooperative efforts to achieve the goals shared by the many stakeholders. NIAA will continue to provide leadership within animal agriculture and establish a platform to facilitate collaborations for identifying and helping to implement solutions to improve antibiotic use through stewardship and reduce the spread of antibiotic resistant bacteria. These collaborations will proceed from a One Health perspective, promoting a better understanding of the science and working to overcome political, social and cultural divides between the worlds of veterinary and human medicine, and between agriculture and food production industries and consumers.

FIGURE: Revised roadmap based on small group Tue discussion—**principal changes from initial roadmap in bold**

1 Activities	2 ST Outcomes	3 MT Outcomes	4 MT Outcomes	5 LT Outcomes
<p>[WHICH PLAYER(S)] ID and educates on best stewardship practices</p> <p>[WHICH PLAYER(S)] Monitors sales, use, and management practices</p> <p>[WHICH PLAYER(S)] Mobilizes, advocates, engages across sectors</p> <p>[WHICH PLAYER(S)] strengthens infrastructure for surveillance and reporting</p> <p>[WHICH PLAYER(S)] establishes regional PH lab network with standard platform for resistance testing</p> <p>[WHICH PLAYER(S)] provides R&D funding and support</p> <p>[WHICH PLAYER(S)] forms public-private research partnerships</p> <p>[WHICH PLAYER(S)] delivers education programs</p>	<p>Strong antibiotic stewardship in humans/healthcare</p> <p>(1) Strong antibiotic stewardship/vet oversight in food production and animal husbandry</p> <p>More regional cross-sectoral cooperation</p> <p>Consensus on strong and supportive policy</p> <p>Stronger lab capacity</p> <p>(2) One health surveillance; Integrated surveillance</p> <p>Development of new tests and technologies</p> <p>Development of mgmt. and production innovations</p> <p>Increased private sector interest and investment</p>	<p>Improved use of antibiotics in healthcare settings; Optimal treatment decisions</p> <p>Improved use of antibiotics in food production and animal husbandry</p> <p>Real-time info sharing on resistance and infections</p> <p>Increased trust and reduced blame</p> <p>Rapid recognition of resistance in humans, animals, and environment</p> <p>(3) Rapid ID and characterization of infection</p> <p>(3) New diagnostic tests</p> <p>(4) New antibiotic therapeutics; New non-antibiotic prevention methods and therapies</p> <p>(5) New and innovative animal management and food production innovations</p>	<p>Less drug resistance</p> <p>Preserve the usefulness of antibiotics and effective treatment of infection</p> <p>More effective prevention, control, and treatment of infection/disease in humans and animals</p> <p>Prevention of infection and disease</p>	<p>Reduced spread of antibiotic resistant pathogens</p> <p>Fewer resistant infections; Less disease in humans and animals</p>

STRAWMAN Roadmap – Antibiotic Resistance – Based on National Action Plan and 2014 White Paper

TABLE: PROPOSED MEASURES AND METRICS DEVELOPED BY BREAKOUT GROUPS

METRIC 1: Percentage of states with ongoing, working One Health committees overseeing collection and dissemination of data on antimicrobial resistance from human, animal and environmental sources

Outcome to which the measure/metric is applied:

- Need for integrated one health surveillance with accessible, useful data for decision-making and assessment

Supporting measures:

- Include but not limited to:
 - Resistance rates for targeted bugs from humans, animals, food sources, environment
 - Antimicrobial use in a variety of human (hospital, outpatient, etc.), animal (farm, companion animal practice, etc.), and environmental sources

Issues/concerns with the metric:

- Would need to create a functional, integrated repository for human, animal and environmental AMR data
- Would need to incorporate some existing data which is publicly available (but in different places and systems), some data which exists but is not easily accessible or available, and some data which would need to be generated
- Would need to include the “right” data in the “right” form—too much data (“data dumps”) is of limited value
- Criteria include:
 - Accessible data
 - Downloadable data
 - Real-time data
 - Consistent case definitions (we all need to agree on what we’re measuring)
- Each state would need to establish a governing body with necessary funding and knowledgeable and trained staff. Other criteria might include (but not be limited to):
 - A charter defining goals, explicitly establishing public sector/private sector cooperation, and purposes and intents of how the data will be used for policy decisions
 - Agreements for data-sharing (e.g., memoranda of understanding [MOUs])
 - Appropriate protections for individual privacy and confidential and proprietary business information
- How would data from other states/other countries be handled (travelers, visitors, imported food/products)?

Could such a measure/metric be developed?

- Yes, and recent improvements in NARMS are a good example of an appreciated effort in this direction. However, there is a great deal more data already available, and as described in the CARB National Action Plan, several Federal agencies have committed to developing additional data sources. However, these data are not well-integrated and optimally interpretable now; additional data may only compound that problem.
- Suggest we need a special meeting with broad public/private participation to talk about AMR data: needs, sources and gaps, availability, accessibility, privacy and confidentiality protections, and who

will be responsible for what. Participants would need to come prepared to work on developing solutions for integrating one-health data, not just presenting organization-specific plans.

Challenges in defining/creating the data source and implementing the metric:

- Ensuring that information of value regarding antimicrobial resistance and antimicrobial use is available to human and animal health practitioners, interested organizations and the public appropriately available in a timely manner.
- Really need to ensure greater participation from folks in environmental fields and science. This is often overlooked by the human and animal health people.
- There are very significant challenges to accomplishing this metric, but we cannot effectively address the AMR problem without really understanding all the complicated aspects of it and we need the data to do that. Among the barriers to overcome are:
 - Lack of funding; government will need to be the main supporter in terms of funds
 - Lack of coordination at Federal and state levels. The CARB Advisory Panel may be able to help but they would need to prioritize this issue. The CARB National Action Plan is encouraging but the coordination plans for how the agencies will work together are not clear.
 - Public and private sectors need to coordinate better as well. There is already a great deal of data out there that is not being used effectively.
 - Some states don't have a functioning One Health component within their health departments
 - The increasing use of culture independent diagnostic testing (CIDT) is a threat to collecting good AMR data. Lots of groups are discussing this but addressing it with a specific plan it needs to be priority for ensuring the availability of required AMR data.

METRIC 2: The number of useful and practical new diagnostic tests for the rapid identification and characterization of infection and AMR (developed within a specific time frame)

Outcomes to which the measure/metric is applied:

- Need for rapid identification and characterization of infection and new diagnostic tests. (More rapid identification and testing for antimicrobial resistance will allow animal [and human] health practitioners to provide the best care and also be good stewards of antibiotics.)

Supporting measures:

- Number of new tests becoming available at the farm level, for field use, that enable veterinarians to make diagnostic decisions more quickly and more accurately
- Number of new tests becoming available for ensuring food safety at production and processing level (before going to market)
- Improvement in how rapidly diagnostic information is available (current three to five days wait for results is too long)

Issues/concerns with the metric:

- Tests need to be accurate, rapid, affordable, cost-effective, and specific
- Tests need to be targeted first at the most common problems that veterinarians face

Could such a measure/metric be developed?

- Yes, both FDA and USDA would have role in approving and assessing implementation and effectiveness of such tests, but would need to fully engage state health and agriculture departments, producers and veterinarians, especially to ensure that helpful tests are utilized as widely as necessary and appropriate

Challenges in defining/creating the data source and implementing the metric:

- Someone has to produce the test. Manufacturers may need help in furthering the basic science required (can NIH help?)
 - Would need to establish training and perhaps accreditation standards for dissemination and use of tests once they are developed; perhaps this could be part of continuing education
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METRIC 3: Proportion of production units that have a documented Veterinarian-Client-Patient Relationship (VCPR) with at least one veterinarian.

Outcome to which the measure/metric is applied:

- Need for strong antibiotic stewardship/veterinary oversight in food production and animal husbandry.

Supporting measure:

- Does a specific production unit have a VCPR with a veterinarian in place (yes/no)?

Issues/concerns with the metric:

- Can we be certain that all veterinarians with VCPRs have the appropriate training/accreditation to write FDA compliant veterinary feed directives?

Does an existing data source exist for this metric?

- No.

Could such a measure/metric be developed?

- Possibly, but it would require a great deal of cooperation from USDA, FDA, producers and the veterinary profession (e.g., AVMA)

Challenges in defining/creating the data source and implementing the metric:

- Definitions and criteria would need to be established, e.g., what constitutes proper documentation of VCPRs
 - Producers would need a guarantee of anonymity to cooperate, especially if data were shared with a regulatory agency, and would need support to correct identified gaps and meet requirements
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METRIC 4: The degree to which new and alternative interventions are being used in practice by veterinarians

Outcome to which the measure/metric is applied: Need for new antibiotic therapeutics, new non-antibiotic prevention methods and therapies, and new innovations in animal management and husbandry to reduce infection risk

Supporting measure(s):

- The number of new therapies approved by FDA/USDA/EPA
- The number of non-antibiotic alternatives for prevention and treatment tested and proven effective
- The number of applications for patents for new technology likely to reduce antimicrobial use on the farm
- The number of applications for small business innovation research (SBIR)¹ funding for new technology and products likely to reduce antimicrobial use on the farm
- The number of grants from relevant Federal agencies (e.g., NIH, CDC) for new technology and products likely to reduce antimicrobial use on the farm

Issues/concerns with the metric:

- We need to establish definitions:
 - what is an intervention likely to reduce antibiotic use;
 - what classifies as a new therapy—does it need to be a new class of antibiotic; does it need to be a non-antibiotic treatment
- Even if new interventions are developed, would they be cost-effective. People won't use new techniques just because they spare antibiotics; they need to be economically beneficial

Could such a measure/metric be developed?

- Although this is hard to measure, it is very important.
- Need further discussion to figure out how to measure progress in this area

Challenges in defining/creating the data source and implementing the metric:

- Definitions
- Who will do the measurement and what will they count
- How to measure what is actually useful in practice and then, if useful, whether it's being used

¹ Each year, Federal agencies with extramural research and development (R&D) budgets that exceed \$100 million are required to allocate 2.8 percent of their R&D budget to these programs. Currently, eleven Federal agencies participate in the SBIR program, including USDA and DHHS

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