2022
IMPACT REPORT

International Consortium for Antimicrobial Stewardship in Agriculture

ICASA

A FFAR COLLABORATIVE

ICASA Vision Statement

The International Consortium for Antimicrobial Stewardship in Agriculture's (ICASA) investment in research creates practical solutions, such as new technologies and management practices that promote judicious use of antibiotics, produce healthier livestock and improve animal welfare.

Letter from Nikki Dutta, Interim Scientific Program Lead

Dear ICASA Participants,

Last year was a significant year for the International Consortium for Antimicrobial Stewardship in Agriculture (ICASA). We held an in-person convening, completed a joint competitive call for proposals for the Liver Abscess and Beef Stewardship Working Groups that produced four projects approved for funding and welcomed a new Associate Participant.

Located in Amarillo, Texas, the in-person convening brought Beef Stewardship and Liver Abscess Working Group Participants together to identify new opportunities for research. The convening kicked off with a feedlot tour at one of Cactus Feeders feedyards, followed by engaging discussions led by Cargill, Elanco, JBS USA and Tyson Foods representatives to better understanding of the growing challenges of liver abscesses. We also heard presentations from Dr. Paul Morley, professor and director of research at Texas A&M University's Veterinary, Education, Research & Outreach Center, and Dr. Dale Woerner, professor and Cargill Endowed Professor at Texas Tech University's Department of Animal and Food Sciences, to gain perspectives on microbiome, gut health and genetics. Facilitated by Kevin Ochsner, president at Agcellerate, the convening not only engaged stakeholders across the research and private industry sectors but also produced a strategy and list of recommendations for future scientific research.

The outcomes of the convening influenced the selection process for the four Liver Abscess and Beef Stewardship projects. With an aim to increase our understanding of basic liver abscess etiology, the 2022 awarded projects included research in the following key areas: (1) understanding pathogenesis and risk-factors of feedlot cattle reared in conventional beef versus dairy management systems, (2) modeling genomic, blood and microbiological markers for liver abscesses, (3) generating metabolomic analysis of blood plasma to identify unique abscess biomarkers, and (4) understanding associations between feeding and management practices of beef-on-dairy cattle with liver abscesses from birth to harvest.

Separately, ICASA supported a research project promoting antimicrobial stewardship through improved knowledge and data collection on metaphylaxis-use in feedlot cattle. Used as a mitigation strategy to combat diseases, metaphylaxis

administration and treatment decisions are often based on subjective assessments. To reduce subjectivity, there is an industry-wide need for a greater understanding of the perceptions, reasons, and/or information used to classify various cattle groupings based on disease risk-level to justify antimicrobial treatment decisions. The project's anticipated start date is Jan. 2023.

With the addition this year of Production Animal Consultation as an Associate Participant, ICASA continues to gain subject-matter expertise from across the livestock value chain. ICASA's Participants share knowledge and expertise to drive future investments in animal health research and encourage the judicious use of antibiotics.

In total, ICASA has now approved over 27 projects with a total value of over $12 million in research. Each project has contributions from at least ICASA Participant organizations, not including Foundation for Food & Agriculture Research (FFAR), enabling every Participant contribution to be leveraged across projects. ICASA exemplifies a collaborative framework that demonstrates impressive value.

I am extremely pleased with the momentum and successes of ICASA. Through collective engagement and collaboration, we continue to play an active role in the livestock welfare and production spaces. Lastly, after serving for six years as FFAR's scientific program director for the Advanced Animal Systems and as ICASA's consortium director, Dr. Tim Kurt left FFAR in September 2022 to tackle new animal health and welfare challenges in the dairy sector. I would like to recognize the leadership Dr. Kurt provided ICASA, and I am humbled to continue his legacy in managing this consortium, with your support. Together, through collective engagement and collaboration, we will continue to play an active role in the livestock welfare and production spaces.

Sincerely,

Nikki Dutta
Interim Scientific Program Lead, Advanced Animal Systems
Foundation for Food & Agriculture Research

CONTENTS

EXECUTIVE COMMITTEE REPRESENTATIVES

Hugh Aljoe
Noble Research Institute

Dr. Janet Helms
McDonalds Corporation

Dr. Kathy Simmons
National Cattlemen's Beef Association

Dr. Matthew Cleveland
Genus PLC

Dr. Ben Holland
Cactus Feeders

Dr. Miles Theurer
Veterinary Research and Consulting Services

Jessica Clowser Burkham
The Beef Alliance

Tom Jones
Hy-Plains Feedyard

Dr. Derek Vote
JBS USA

Samantha Conrad
Tyson Foods

Dr. Sarah Klopatek
JBS USA

Jennifer Williams
Tyson Foods

Joy Parr Drach
Advanced Animal Diagnostics

Dr. Joel Nerem
Pipestone Veterinary Services

Dr. Alyssa Word
Cactus Feeders

Dr. Heather Fowler
National Pork Board

Dr. Chelsey Shivley
USDA-APHIS

Nikki Dutta
Foundation for Food & Agriculture Research

Executive Summary

The International Consortium for Antimicrobial Stewardship in Agriculture (ICASA) funded a total of **$2,977,465.01 to six research projects** across four of the six Working Groups in 2022. In addition to the second-year renewal of the Swine Health Working Group proposal seeking to develop a surveillance protocol for antimicrobial resistance (AMR) in swine populations, the Metaphylaxis Working Group also funded a proposal aiming to promote antimicrobial stewardship in beef cattle through improved knowledge of metaphylaxis-use data.

The Liver Abscess and Beef Stewardship Working Groups collaborated on a joint open call seeking novel research that improves our understanding of liver abscess pathobiology, epidemiology and metaphylactic treatment in beef cattle, resulting in four projects funded. A summary of the six Working Group projects funded is included in the table below.

WORKING GROUP	PROJECTS FUNDED	FFAR FUNDING	MATCHING CONTRIBUTIONS	TOTAL 2022 PROJECT VALUE
Liver Abscess / Beef Stewardship	4	$1,199,961.11	$1,122,482.78	$2,322,443.89
Metaphylaxis	1	$124,949.00	$124,961.00	$249,910.00
Swine Health	1	$202,555.56	$202,555.56	$405,111.12
Total	**6**	**$1,527,466.67**	**$1,449,999.34**	**$2,977,465.01**

In addition to funding research, the Foundation for Food & Agriculture Research (FFAR) hosted a group of ICASA Participants for an in-person convening to discuss recent research results and to identify future liver abscess research priorities — both for ICASA and the beef industry at-large. The convening featured presentations from private industry and academia, followed by small group breakouts to discuss key learnings, significance and causation in order to identify research priorities and opportunities. The 2022 ICASA Liver Abscess Convening Report provides more information.

To summarize, it has been another successful year for ICASA! We are excited by the fact that **Production Animal Consultation joined as an Associate Participant** to expand our impact across the U.S. livestock value chain. We look forward to continuing our efforts to support scientific research that promotes the judicious use of antimicrobials and advances animal and human health and wellness.

Research Grants Awarded in 2022

Project Title	Funding Mechanism	Institution	Principal Investigator	Project Length (Yrs)	Co-funders	FFAR Funding	Matching Contributions	Total Budget
Liver Abscess & Beef Stewardship Working Groups								
Modeling for genomic, blood, & microbiological markers for liver abscesses in fed beef cattle	Request for Applications	Texas Technical University	Dr. Dale Woerner	2	Texas Tech Univ.; Genus ABS; Hy-Plains Feedyard; VRCS	$300,000.00	$333,463.00	$633,462.78
Understanding liver abscess pathogenesis & risk-factors of feedlot cattle reared in conventional beef versus dairy management systems	Request for Applications	West Texas A&M University	Dr. Kendall Samuelson	2	West Texas A&M University	$299,957.78	$300,382.22	$600,340.00
Associations between feeding & management practices of beef-on-dairy cattle from birth to harvest with liver abscesses	Request for Applications	Kansas State University	Dr. Raghavendra Amachawadi	2	Animal Welfare Consulting; Syracuse Dairy, LLC; Cargill; Deer Creek Feeding, LLC; Hy-Plains Feedyard; Tyson Foods; VRCS	$300,000.00	$300,000.00	$600,000.00
Metabolomic analysis of blood plasma to identify unique biomarkers indicative of liver abscesses	Request for Applications	Kansas State University	Dr. T.G. Nagaraja	2	United Health Corp.; Kansas State Univ.	$300,003.00	$300,000.00*	$600,003.00
Metaphylaxis Working Group								
Promoting antimicrobial stewardship through improved knowledge on the subset of feeder cattle in which the value of metaphylaxis-use is most uncertain	Direct Solicitation	Kansas State University	Dr. Natalia Cernicchiaro	2	Innovative Livestock Services (Beef Alliance); Hy-Plains Feedyard; Veterinary Research and Consulting Services (VRCS); Five Rivers (Beef Alliance); Zoetis; Cactus Feeders	$124,948.89	$124,961.20	$249,910.00
Swine Health Working Group								
Developing a model protocol for tracking antibiotic use & AMR surveillance across a large-scale commercial swine production system: YEAR 3	Direct Solicitation	Pipestone Veterinary Services	Dr. Scott Dee	1	Pipestone Veterinary Services; National Pork Board; USDA-APHIS	$202,555.56	$202,555.56	$405,111.12

*Pending matching funds

Project Impacts & Key Findings

In pursuit of audacious science, we always have a wide range of projects in process. Given the nature of the scientific process, projects typically cover a period of a few years. This means that significant impacts or breakthroughs often emerge near the end of the project period or continue to emerge in the years after closure.

This report offers a snapshot of key research impacts that emerged in 2022 and 2023.

All "Key Project Findings" reported as follows are preliminary and subject to change.

Project Impact

2020 Metaphylaxis Working Group Open Call Key Project Findings

Development of a Science-Based Management Strategy to Reduce the Use of Antimicrobials in High-Risk Beef Cattle

Institution: Texas Tech University

PI: Dr. Kristen Hales

Funding Partners: Texas Tech University

PROJECT OBJECTIVES AND GOALS

During this reporting period the research team has submitted the manuscript titled "Infrared thermography or rectal temperature as qualification for targeted metaphylaxis in newly received beef steers and the effects on growth performance, complete blood count, and serum haptoglobin during a 42-day feedlot receiving period" to *Applied Animal Science*. The manuscript was accepted on May 10, 2023, and will be published in the June or July edition of *Applied Animal Science*. Likewise, we submitted the manuscript titled "An updated profile on the bovine acute phase response following an intravenous lipopolysaccharide challenge" to the *Journal of Animal Science*. The manuscript has been accepted and is listed online in the advanced articles section and should be in the June or July edition of the journal.

Beyond the research conducted at Texas Tech University (TTU), the team is planning to finish the proposal research by working work with Dr. Miles Theurer, Veterinary Research and Consulting Services (VRCS), and Tom Jones, Hy-Plains Feedyard, to plan the commercial feedyard experiment testing the infrared camera.

KEY PROJECT RESULTS

- During the lipopolysaccharide (LPS) challenge, a moderate correlation (correlation of 0.61) of body temperature measured via rectal probe or ocular infrared temperature was observed, but both methods had a similar temporal response and were sensitive to changes in body temperature. **Response of serum chemistry variables highlighted the links between metabolism and the inflammatory response.** The initial inflammatory response was initiated by cortisol and proinflammatory cytokines at hour 1 and tempered by anti-inflammatory cytokines at hours 3 and 4. **Beyond evaluating the relationship between methods to measure body temperature, these data offered an expanded view to our understanding of the bovine acute phase response.**

- In the study to evaluate rectal temperature and infrared thermography as qualification for targeted metaphylaxis, clinical health, growth performance, complete blood count and serum haptoglobin metaphylaxis was given to 48.9% of steers identified as febrile using a rectal thermometer and 48.6% of steers identified as febrile using an infrared camera. **Both methods of targeted metaphylaxis decreased the percentage of steers given antimicrobial therapy for bovine respiratory disease.** The total mg of active drug compound administered was not different between methods of body temperature measurement. Growth performance during the receiving period also did not differ between steers given metaphylaxis based on rectal or eye temperature using infrared thermography. **The use of targeted metaphylaxis with measures of body temperature decreased the proportion of cattle given metaphylaxis while maintaining optimal health and growth performance outcomes.**

- **The ICASA participants have been extremely helpful.** Dr. Miles Theurer visited TTU on the day we assigned metaphylaxis in our receiving study. It was great that he could visit and observe the experiment. Likewise, Dr. Hales consults with Dr. Ben Holland, Cactus Feeders, and Dr. Alyssa Word, Cactus Feeders, often on general research questions and questions about the project. They are helpful in ensuring our projects are relevant to the commercial feedlot industry.

Provided by Dr. Kristen Hales

Project Impact

2020 Metaphylaxis Working Group Open Call Key Project Findings

Predictive Model Development to Promote Science-Based, Strategic Metaphylaxis Administration in Beef Operations

Institution: Kansas State University

PI: Dr. Brad White

Funding Partners: Innovative Livestock Services (The Beef Alliance); Hy-Plains Feedyard; Veterinary Research and Consulting Services (VRCS); Five Rivers (The Beef Alliance)

PROJECT OBJECTIVES AND GOALS

- Work to procure and evaluate potential data for inclusion in predictive models.

- Create economic framework to evaluate total health impact to inform predictive models of decision to use metaphylaxis.

KEY PROJECT RESULTS

- Data were collected during the reporting period to populate predictive models. The data logistical infrastructure was modified to support a secured cloud system for efficient handling, processing and management of large data for subsequent evaluations.

- The economic framework was calculated through a project to generate a model to compare metaphylactic options. Cohorts (n=12,785) from 13 feed yards were given a standard entry date with pricing based on weight categories and each of three metaphylactic options: no metaphylaxis, a low cost/low efficacy metaphylaxis or a high cost/high efficacy metaphylaxis.

- **An economic model was developed that compared net returns of each cohort across the three metaphylactic options.** The economic model is currently static and deterministic, but once the formulas are verified it will be transformed into dynamic and stochastic.

Provided by Dr. Brad White

ICASA has been instrumental in developing public-private partnerships in the beef industry to improve antibiotic stewardship through research, outreach and implementation. The veterinarians at PAC provide beef cattle health services for ranchers and feeders tending to the care of over one million cow/calf pairs and three million head of cattle on feed in the United States. Along with veterinary services, PAC has active research, data system and education services to support beef industry clients. It is vital for us, and our clients, for PAC to be a member of ICASA to learn together with others in the beef industry and build on the public-private partnerships to leverage boots on the ground solutions for human, animal and ecosystem health while improving fiscal opportunities for all people in the beef industry.

Dr. Dan Thomson, DVM, Owner/Partner, Production Animal Consultation

Project Impact

2020 Late Morbidity in Beef Cattle Direct Fund Key Project Findings

Determining Risk Factors for Mid- & Late-Day Bovine Respiratory Disease Morbidity & Mortality

Institution: Kansas State University

PI: Dr. Brad White

Funding Partners: Veterinary Research and Consulting Services (VRCS); Five Rivers Feedyard (The Beef Alliance); Hy-Plains Feedyard

PROJECT OBJECTIVES AND GOALS

- Continued process on acquisition, cleaning and managing incoming operational feedyard health data.

- Complete descriptive analysis relative to health timing.

- Initiate project addendum for systematic field necropsies.

KEY PROJECT RESULTS

- **Four peer-reviewed manuscripts have been published.**

    1. An Evaluation of Temporal Distributions of High, Low, and Zero Cohort Morbidity of Cumulative First Treatment Bovine Respiratory Disease and Their Associations with Demographic, Health, and Performance Outcomes in US Feedlot Cattle. Johnson et al. -*Veterinary Sciences*—2023 https://doi.org/10.3390/vetsci10020089

    2. Determining Frequency of Common Pulmonary Gross and Histopathological Findings in Feedyard Fatalities. Schmidt et al. -*Veterinary Sciences*—2023 https://doi.org/10.3390/vetsci10030228

    3. Evaluation of Frist Treatment Timing, Fatal Disease Onset, and Days from First Treatment to Death Associated with Bovine Respiratory Disease in Feedlot Cattle. Smith et al. – *Veterinary Sciences*—2023 https://doi.org/10.3390/vetsci10030204

    4. Determining relevant risk factors associated with mid- and late-feeding-stage bovine respiratory disease morbidity in cohorts of beef feedlot cattle. Smith et al. -*Applied Animal Sc.*—2022 https://doi.org/10.15232/aas.2022-02312

- The lead graduate student on the project, Kristen Smith, completed her masters degree in summer 2022 and additional graduate students were initiated. A student has started work on generating predictive models relative to late day disease.

- **The project addendum to investigate late day death loss was approved by project collaborators and ICASA Participants. It was initiated in summer 2022 resulting in systematic necropsies and data collection on over 300 feedlot mortalities.** Data are still being summarized and cataloged.

Provided by Dr. Brad White

The National Cattlemen's Beef Association values the public-private partnership model for research funding at FFAR that has facilitated user-driven and actionable research benefiting the U.S. beef cattle industry in the area of antimicrobial use/antimicrobial stewardship through our participation in ICASA.

Dr. Kathy Simmons, DVM, Chief Veterinarian, National Cattlemen's Beef Association

Project Impact

2020 Technologies Working Group Open Call Key Project Findings

A Rapid Chute-Side Antibiotic Resistance Detection Tool to Improve Antimicrobial Stewardship & Optimize Risk Management While Controlling Bovine Respiratory Disease

Institution: Texas A&M University

PI: Dr. H. Morgan Scott

Funding Partners: Five Rivers Feedyard (The Beef Alliance); Cactus Research; NG Biotech; Texas A&M University

PROJECT OBJECTIVES AND GOALS

The research goals were to have completed the first round of cattle trials at the two feedyards, focusing on evaluating the rapid chute-side assay targeting cephalosporinase resistance targets in bovine feces. Because of some development constraints involving both the plasticware (lateral flow assay [LFA] device including sample well was prototyped and 3-D printed, then commercially produced) as well as some fine tuning of the resistance targets. Instead of a single bla_{CTX-M} target, the team now has two protein (enzyme, not gene) fecal matrix targets and one enzyme activity assay: bla_{CTX-M}, bla_{CMY-2}, and cefotaximase activity (3rd generation cephalosporins), respectively. The two enzyme targets are on a single LFA while the enzyme activity assay is a single LFA. Both require a short period of incubation which may limit the use in the field to better-equipped facilities. The trials were delayed to fall 2022. Two hundred head of cattle were procured at each of two feedyards and sampled at Day 0 and Day 7. Different antibiotics were administered at Day 0 (negative control, cephalosporin, macrolide, phenicol and fluoroquinolone) in accordance with feedyard policies in place. Fecal samples were taken per rectum and a nasal swab was taken from every fifth animal to aid in development of the BRD targets and for beta testing. In the meanwhile, diagnostic device development has continued on schedule for the respiratory targets. Some sensitivity issues have arisen with the macrolide targets. Use of recombinant products show good sensitivity while pure isolates of E. coli harboring the macrolide resistance genes yield low sensitivity. Sample preparation options are currently being explored to overcome these issues which likely relate to the target protein availability *in situ*.

KEY PROJECT RESULTS

- **Two devices for assessing the presence of resistance to 3rd generation cephalosporins in cattle feces have been developed.** One is in production and has both: bla_{CTX-M} and bla_{CMY-2} targets. The other looks more broadly at enzymatic activity against a 3rd generation cephalosporin (3GC: cefotaxime); this, enabling capture of additional enzymes

beside the two in the first assay). The research team has fine-tuned the protocols and are getting much better sensitivity and fewer false negatives with additional liquid and switch to buffered peptone water from brain-heart infusion.

- The team is getting reliable positive results as low as at 10^3 with three hours incubation and as few as one hour at 10^6. Also have a separate cefotaximase enzymatic activity assay which will cover additional ESBL and carbapenemase targets that are less common but of greater concern.

- Both assays are currently under validation with the cattle feeding trial samples collected in fall 2022. **The results suggest that there are cattle at arrival harboring higher levels of 3GC beta-lactamase producing coliforms.**

- Antimicrobial stewardship practices might suggest avoiding antibiotics for metaphylaxis that over-select or co-select for such resistance. Results of our work thus far (2/3 completed) suggest that (as expected) ceftiofur directly selects for both 3GC enzymes and enzymatic activity. The former two targets have much better sensitivity than the latter.

- Phenicols also appear to disproportionately co-select for beta-lactamases, likely due to longstanding presence of *flo*R genes co-located with *bla* genes on plasmids. This would relate to the use and availability of chloramphenicol going back decades (up until 1984 in food animals). Florfenicol is the newer phenicol.

- Fluoroquinolones also appear to have some potential to co-select for 3GC resistance. This likely relates to the rapid spread of plasmid-mediated reduced susceptibility via *qnr* genes (*qnrA*, *qnrB*, *qnrS*), especially when co-located with bla_{CTX-M}.

- **Macrolides do not appear to co-select for beta-lactamases**; in terms of stewardship, this suggests that **at this point in time they may be the better choice for metaphylaxis where there is evidence of 3GC resistance among cattle on arrival.**

Provided by Dr. H. Morgan Scott

On the Horizon

Late Morbidity Working Group

The Working Group has been discussing Acute Interstitial Pneumonia (AIP) with a small external group of researchers including Dr. Matthew Scott, Dr. Amelia Woolums and Dr. Brad White. The group is aiming to improve case definitions and will likely suggest a project in 2023.

The National Pork Board and the producers we serve are committed to doing what is right for people, pigs and the planet. We also recognize the importance of research and surveillance in identifying and addressing knowledge gaps and identify trends. Thus, we are excited to support Dr. Scott Dee's AMR surveillance project for the third year. This work not only positions the swine industry as leaders in this space, but highlights the benefits of public-private collaboration in scientific research.

**Dr. Heather Fowler, VMD PhD MPH DACVPM PMP,
Director, Producer and Public Health, National Pork Board**

FINANCIALS

YEAR	PRINCIPAL INVESTIGATOR	FFAR FUNDING	CO-FUNDING	TOTAL PROJECT FUNDING
Technologies Working Group				
2020	Dr. H. Morgan Scott	$250,000.00	$272,833.33	$522,833.33
2020	Dr. Tim Robertson	$247,470.00	$247,470.00	$626,745.00
2020	Dr. Mohit Verma	$321,027.78	$178,970.43	$321,027.78
2020	Dr. Adam Rivers	$123,810.44	$102,740.00	$226,550.44
2021	Dr. Mike Apley	$200,000.00	$200,022.22	$400,022.22
Total		**$1,142,308.22**	**$823,065.55**	**$1,965,373.77**
Liver Abscess Working Group				
2020	Dr. Todd Milton	$342,000.00	$342,000.00	$684,000.00
2021	Dr. Kristen Hales	$125,000.00	$125,000.00	$250,000.00
2021	Dr. Rand Broadway	$86,000.00	$85,700.00	$171,700.00
2021	Dr. Vinicius Machado	$98,000.00	$97,739.00	$195,739.00
2021	Dr. Kendall Samuelson	$390,000.00	$401,771.68	$797,771.68
2021	Dr. Raghavendra Amachawadi	$125,000.00	$125,463.33	$250,463.33
2022	Dr. Dale Woerner	$300,000.00	$333,462.78	$633,462.78
2022	Dr. Raghavendra Amachawadi	$300,000.00	$300,000.00	$600,000.00
2022	Dr. T.G. Nagaraja	$300,003.00	$300,003.33	$600,003.33
Total		**$2,365,961.11**	**$2,411,522.34**	**$4,777,483.45**
Swine Health Working Group				
2020	Dr. Scott Dee	$313,839.00	$313,839.00	$627,678.00
2021	Dr. Scott Dee	$179,330.00	$329,330.00	$508,330.00
2021	Dr. Maria Pieters	$149,747.00	$209,870.00	$359,617.00
2021	Dr. Tim Johnson	$140,001.00	$171,353.00	$311,354.00
2021	Dr. Meghan Pierdon	$127,702.84	$140,789.00	$268,491.84
2022	Dr. Scott Dee	$202,555.56	$202,555.56	$405,111.12
Total		**$1,112,845.40**	**$1,367,736.56**	**$2,480,581.96**
Metaphylaxis Working Group				
2020	Dr. Brad White	$209,575.44	$217,693.33	$427,268.77
2020	Dr. Kristen Hales	$200,000.00	$200,000.00	$400,000.00
2021	Dr. Tom Darbonne	$63,000.00	$41,127.67	$104,127.67
2022	Dr. Natalia Cerrnichiaro	$124,949.00	$124,961.00	$249,910.00
Total		**$597,524.44**	**$583,782,00**	**$1,181,306.44**
Late Morbidity Working Group				
2019	Dr. Mariah Johnson	$186,644.00	$186,644.00	$373,287.83
2020	Dr. Brad White	$171,662.51	$176,444.44	$348,106.95
2021	Dr. Scott Speidel	$400,000.00	$664,000.00	$1,064,000.00
Total		**$758,306.51**	**$1,027,088.44**	**$1,785,394.95**
WORKING GROUP TOTAL		**$5,976,945.68**	**$6,213,194.89**	**$12,190,140.57**

Appendix A
Funding Eligibility
& Mechanism

The International Consortium for Antimicrobial Stewardship in Agriculture (ICASA) enables participants to drive significant advances that benefit both the public and private sectors, with $7.5 million funding and administrative support from the Foundation for Food & Agriculture Research (FFAR). For a Project to be eligible for funding, at least two ICASA Participants must contribute cash or in-kind contributions. The Participant-driven structure enables a wide-variety of Projects that may be broad in scope, or specific to particular species or environments. ICASA supports critical research across the following topic areas:

1. Cross-cutting Technologies *(on pause)*
2. Metaphylaxis
3. Liver Abscesses in Beef Cattle
4. Late Morbidity in Beef Cattle
5. Swine Health
6. Beef Stewardship.

While deliverables will vary by Project, it is anticipated that all Projects will have practical outcomes that inform and help optimize the use of antimicrobials. With recent advances in precision agriculture, genomic sequencing, metagenomics and other fields, the consortium has been formed at a time when the combined efforts of multiple Participants can accelerate discoveries in ways not possible in the past.

For information on ICASA please contact Nikki Dutta at ndutta@foundationfar.org.

Appendix B Working Group & Objectives

ICASA & WORKING GROUP OBJECTIVES

Cross-cutting Technologies (on pause)

1. Identify and support technologies that improve animal health and the antimicrobial stewardship of animals.

Late-day Morbidity in Beef Cattle

1. Qualify and quantify the mid-day morbidity and late-day mortality, characterize the topic and define it so there is common understanding of the terms.
2. Identify possible explanations or causes of mid-day morbidity and late-day mortality as well as possible associated factors.

Metaphylaxis

1. Soliciting and supporting research focused on the use of metaphylaxis treatment practices in cattle and swine in order to enhance antimicrobial stewardship in food producing animals.

Liver Abscesses in Beef Cattle

1. Identifying a method or methods that allow for the management of liver abscesses in finishing cattle reducing or omitting the use of shared-class antibiotics while resulting in no detrimental effects to live animal performance, animal welfare or carcass quality.

Swine Health

1. Surveying and characterizing antimicrobial resistance at the farm level.
2. Investigating epidemiology and control of bacterial pathogens of swine. Specifically:
   - *Streptococcus suis;*
   - *Haemophilus parasuis; and*
   - *Actinobacillus suis.*
3. Improving swine gut health, specifically focusing on the following:
   - Neonatal diarrhea; and
   - Post-weaning diarrhea.
4. Generating a better understanding of the swine microbiome for improved pig health and performance.

Beef Stewardship

1. Supporting background research on antimicrobial use, rational and opportunities for improvement.
2. Supporting the development of peer-reviewed publications that can be used by diverse stakeholders to identify research needs and opportunities for improvement and/or policies.

Appendix C
Working Group Members

*Names in **bold** indicate the Working Group Chair*

BEEF STEWARDSHIP WORKING GROUP

Nikki Dutta, FFAR
Ben Holland, Cactus Feeders
Kathy Simmons, National Cattlemen's Beef Association
Josh Szasz, The Beef Alliance

Scott Eilert, Cargill
Glen Dolezal, Cargill
Tom Jones, Hy-Plains Feedyard
Miles Theurer, Veterinary Research Consulting Services

Ken Opengart, Tyson Foods
Christi Calhoun, Zoetis
Shawn Blood, Zoetis
Jon Hixson, Yum! Brands

LATE DAY MORBIDITY IN BEEF CATTLE WORKING GROUP

Miles Theurer, Veterinary Research Consulting Services
Hugh Aljoe, Nobel Research Institute
Ben Holland, Cactus Feeders

Kathy Simmons, National Cattlemen's Beef Association
Matthew Cleveland, Genus PLC
Josh Szasz, The Beef Alliance

Dan Scruggs, Zoetis
Vickie Cooper, Zoetis
Dan Thomson, Production Animal Consultation
Nikki Dutta, FFAR

METAPHYLAXIS WORKING GROUP

Alyssa Word, Cactus Feeders
Brandon Depenbusch, The Beef Alliance
Josh Szasz, The Beef Alliance
Jessica Clowser Burkham, The Beef Alliance
Travis McCarty, Veterinary Research Consulting Services

Miles Theurer, Veterinary Research Consulting Services
Tom Jones, Hy-Plains Feedyard
Alyssa Word, Cactus Feeders
Joy Parr Drach, Advanced Animal Diagnostics
Paula Alexander, Tyson Foods
Scott Gustin, Tyson Foods

Shawn Blood, Zoetis
JP Pollreisz, Zoetis
Dan Thomson, Production Animal Consultation
Shane Terrell, Production Animal Consultation
Nikki Dutta, FFAR

LIVER ABSCESS IN BEEF CATTLE WORKING GROUP

Ben Holland, Cactus Research
Tony Bryant, JBS USA
Darby Allen, JBS USA
Madhi Elangovan, JBS USA
Miles Theurer, Veterinary Research Consulting Services
Todd Milton, The Beef Alliance

Paula Alexander, Tyson Foods
Scott Gustin, Tyson Foods
Robert Scherer, Tyson Foods
Grant Sardella, Genus PLC
Lee Bob Harper, Zoetis
Bryan Bernhard, Zoetis
Gerald Poppy, Cargill

Dan Thomson, Production Animal Consultation
Shane Terrell, Production Animal Consultation
Nikki Dutta, FFAR

SWINE HEALTH WORKING GROUP

Joel Nerem, Pipestone Veterinary Services
Heather Fowler, National Pork Board
Darin Madson, JBS USA

Samantha Conrad, Tyson Foods
Steven Clifton, Tyson Foods
Daniel Boykin, Cactus Feeders
William Herring, Genus PLC

Maria Clavijo, Genus PLC
Brianna Fredrich, Zoetis
Jim Lowe, Production Animal Consultation
Nikki Dutta, FFAR

CROSS-CUTTING TECHNOLOGIES WORKING GROUP *(ON PAUSE)*

Alyssa Word, Cactus Feeders
Andrea Chu, Cargill
Andy Brudkuhl, National Pork Board
Joel Nerem, Pipestone Veterinary Services
Joy Parr Drach, Advanced Animal Diagnostics

Jessica Clowser Burkham, The Beef Alliance
Samantha Conrad, Tyson Foods
Jarrod Bumsted, Tyson Foods
Bill Hewat, Tyson Foods
Derek Vote, JBS USA
Kendra Waldbusser, JBS/Pilgrim's

Miles Theurer, Veterinary Research Consulting Services
Fabiana Mokry, Genus
Marilyn Corbin, Zoetis
Justin Sexten, Zoetis
Nikki Dutta, FFAR

Appendix D
Proposal Abstract
Summaries

(PLEASE CONTACT FFAR TO REQUEST ANY FULL PROPOSALS)

Liver Abscess/Beef Stewardship Working Groups

Dr. Dale Woerner, Modeling for genomic, blood & microbiological markers for liver abscesses in fed beef cattle

Multiple published research studies have evaluated thousands of animals to provide reference for the prevalence of liver abscesses in fed beef cattle, and it has been established and widely accepted that liver abscesses in cattle result from *Fusobacterium necrophorum* infections (Nagaraja *et al*., 2005). Development of these infections has been mostly attributed to some component of nutritional management. Subtherapeutic use of some antimicrobials has demonstrated efficacious results but not without concern of antimicrobial resistance. Yet, more than 40 years of research on the matter has not provided a conclusive solution and suggests that the problem is multifactorial. These existing studies on the subject lack individual animal data to model multiple factors with their relationship to liver abscesses, including genetic correlations, associations with blood chemistry and prevalence of pathogenic microorganisms. A large sample study is needed to effectively model these factors. In response to this RFA, the team of researchers will study >2,000 fed cattle with existing individual genomic data (n = 1,000) and a historical liver abscess rate of 50 to 60%, providing for nearly equal distribution of liver abscess presence/absence. This rare opportunity will be the first to allow for a true investigation for genetic markers and biomarkers, including blood chemistry and individual microbial pathogen prevalence, contributing to the causation of liver abscesses. Identifying genetic markers in cattle predisposed to developing liver abscesses would allow for breeding decisions to reduce susceptibility in the fed cattle population and reduce the reliance on antimicrobial usage.

Dr. T.G. Nagaraja, Metabolomic analysis of blood plasma to identify unique biomarkers indicative of liver abscesses

Liver abscesses in cattle fed high grain diets occur because pyogenic bacteria gain entry, via portal vein, into the liver. Origin of the pathogens is believed to be the rumen, and their entry into the portal circulation is facilitated by ruminal wall compromised by chronic acidity. Liver abscesses are a polymicrobial infection and *Fusobacterium necrophorum* is the primary etiologic agent. Cattle with abscessed livers seldom show any clinical signs and are detected only at the time of slaughter. Liver function tests and serological targeting *F. necrophorum*- specific antibodies are of limited diagnostic value. Changes in blood cell counts and liver function variables in cattle with liver abscesses are consistent with chronic active inflammation, therefore, are non-specific to aid in the diagnosis. Our objectives are to utilize metabolomics to determine and describe a comprehensive 'biochemical fingerprinting' in the plasma of blood collected at the time of slaughter from cattle with and without abscesses (control) in the liver. Liver abscesses will also be scored to categorize them as mild (A- or A) or severe (A+) to relate plasma metabolome to severity of abscesses. In addition to gaining insight into the pyogenic process, unique biomolecules in the blood of cattle with liver abscesses will be of diagnostic value. The biomarker will be a major fill in the knowledge gap to detect the onset and progression of liver abscesses in cattle before slaughter and will aid in finding an alternative to use of in-feed tylosin for feedlot cattle. Antemortem diagnosis of liver abscess is not likely to have major application although early diagnosis could aid in management decisions to decrease the impact of liver abscesses on animal health and animal performance. As an example, diagnosis will aid in determining the timing of liver abscess occurrence during the finishing phase. A major application of an antemortem diagnosis will be to monitor liver abscesses in studies designed to evaluate efficacy of interventions, such as vaccine, antimicrobial alternatives, etc.

Dr. Raghavendra Amachawadi, Associations between feeding & management practices of beef-on-dairy cattle from birth to harvest with liver abscesses

The use of beef cattle semen to breed dairy cows to produce calves, called, beef-on-dairy crosses, for beef production has greatly increased in the past five years. The practice increases the value of calves produced from dairies as beef-on-dairy calves have better feedlot performance, carcass quality and meat attributes compared to male dairy calves (calf-fed Holsteins). Beef from beef-on-dairy cattle has similar meat quality attributes (tenderness, juiciness and flavor) as beef from conventional cattle. After evaluating both positives and negatives of the contributions of beef-on-dairy crosses to the beef supply chain, packers exercise a universal discount on crossbred, principally because of liver abscesses and associated economic losses. Although no published data on the incidence of liver abscesses in beef-on-dairy cross cattle, there is consensus the incidence in beef-on-dairy cattle is two to

three times greater than crossbred beef cattle. The economic losses are above and beyond those of abscessed livers because of higher occurrence of severely abscessed livers (A+) with extensive adhesion to diaphragm and abdominal viscera. The reason for the higher incidence is not known although likely explanations include management prior to the feeding phase, days on feed at the feedyard, roughage level and even weather fluctuations. Our principal objective is to conduct a comprehensive analysis of feeding and management practices, including data on morbidity and mortality, from birth to harvest to determine their associations with liver abscesses. Our secondary objective is to determine timing of liver abscess development through lifetime periodic survey assessments. An improved understanding of the epidemiology of liver abscesses in beef-on-dairy cattle will likely lead to identification of novel targets and provide opportunities to develop interventions to replace in-feed use of tylosin.

Dr. Kendall Samuelson, Understanding liver abscess pathogenesis & risk-factors of feedlot cattle reared in conventional beef versus dairy management systems

While the liver abscess complex has been thoroughly described, pathogenesis is not fully understood. Because little is known about the timing, stage of production and causality of liver abscesses development, use of antibiotics to control liver abscesses is common during the finishing phase of cattle production. Liver abscesses present a significant challenge to the fed beef industry, and incidence is increasing. Research also suggests that the rate of liver abscessation in dairy and crossbred dairy cattle is two to three times greater than beef breeds. This is increasingly concerning as the geographic location of dairies shifts to areas with high liver abscess rates, and the number of beef-on-dairy crossbreds entering the supply chain grows. Our hypothesis is that the calf management practices used by commercial dairies and calf ranches increase the potential for ruminal acidosis, negatively affect animal health/performance and contribute to increased liver abscesses compared to conventionally raised beef calves. The objective of this study is to delineate the impacts of the calf management system and pre-arrival management on liver abscess development. Additionally, investigating relationships between calf management, liver abscess prevalence and cellular and molecular mechanisms within the blood transcriptome, rumen and liver microbiome may provide insight into liver abscess pathogenesis and identify biomarkers to assess the risk of liver abscessation and targets for intervention. Therefore, this research intuitively addresses the following areas identified by ICASA: 1) "Development of basic knowledge in the etiology and pathogenesis of liver abscesses" and 2) "Improved understanding of liver abscess development and/or regression."

Metaphylaxis Working Group

Dr. Natalia Cernicchiaro, Promoting antimicrobial stewardship through improved knowledge on the subset of feeder cattle in which the value of metaphylaxis-use is most uncertain

Antimicrobials are one of the most significant interventions for reducing the deleterious health and economic effects of bovine respiratory disease complex (BRDC), the most important disease in the U.S. feedlot industry. The success of mitigation strategies, such as metaphylaxis administration, is often tied to expected BRDC incidence within the population, but without reliable data for accurately classifying BRDC risk, the decision to use metaphylaxis is often based on subjective assessments. An improved understanding of the perceptions, reasons, and/or information used to classify lots based on BRDC risk and make subsequent antimicrobial use decisions is warranted. The objectives of the study include: 1) to assimilate knowledge from industry stakeholders on the current practices, information gaps and development of subsequent metaphylaxis research that is relevant to, and could be implemented by, commercial cattle feeders; and 2) gather and interpret data and information from cattle feeders, through the implementation of a survey of feedlot managers, veterinarians and other decision-makers to establish what type of qualitative and quantitative information is used (or not used) in classifying BRDC risk, with a particular focus on medium or moderate risk groups in which the metaphylaxis decision is most uncertain. Obtaining data on perceptions and behaviors through direct industry partnerships, can be used to comprehensively assess health risks and interventions, and in turn, optimize health management strategies for specific cohorts within heterogeneous cattle populations. Our research outcomes will have direct impact on cattle producers who strive to improve animal management, promote health and well-being, price-differentiate cattle based on health risks, efficiently utilize sparse labor resources, and importantly prudently use antimicrobials.

Swine Health Working Group

Dr. Scott Dee, Developing a model protocol for tracking antibiotic use & AMR surveillance for the swine industry [Renewal Y3]

The threat of Antimicrobial Resistance (AMR) is a major concern to human medicine, veterinary medicine, public health and livestock agriculture and global society. Even though agriculture is often considered the source of AMR in humans, no data support this hypothesis. To complicate the matter, while AMR data are being tracked by the National Antimicrobial Resistance Monitoring System (NARMS) at the level of the meat case (FDA), the harvest facility (USDA) and across cases of human foodborne illness (CDC), no such effort exists at the level of the swine farm. Therefore, the U.S. swine industry must be proactive and begin to collect these data across pathogens of food safety significance and veterinary significance from swine farms using standardized approaches based on NARMS standards and correlate this information with antibiotic usage data for participants. This project will be the first attempt to accomplish this goal at the level of a large-scale commercial swine production system. It provides a platform for on-farm analysis, as well as lays the foundation for similar analyses to be applied at the processing plant.