NIMBioS Working Group, Knoxville, TN, September 19-22, 2014

"Evaluating the Association between Shifts in Antimicrobial Use Practices and Antimicrobial Resistance Resulting from the FDA's Risk Mitigation Strategy"

The overall objective: To develop a systems approach to identify specific conceptual approaches, analytical methods, and quantitative data sources that are appropriate for **associating population-level changes in antimicrobial use in livestock with population-level changes in antimicrobial resistance**.

The specific aims:

1) Review the risk pathway(s) associated with **antimicrobial use in food-producing animals and antimicrobial resistance**.

2) Assess **current and possible future monitoring systems**.

3) Identify and develop a **proposed analytic methodology**.

4) Identify a prioritized list of **useful, quantitative variables to analyze the relationship between observed changes in antimicrobial use practices in food-producing animals and antimicrobial resistance patterns**

Day 1 (Friday, September 19, 2014): Data

8:00-8:40 Breakfast and Registration

8:40-9:00 Welcome: NiMBioS Directors

9:00-9:15 Introductory remarks: Organizers – Goals etc. CL & YTG
- Review Objectives:
"To develop methods to assess the impact of FDA Guidance 213 on population-level changes in antimicrobial use in livestock on population-level changes in antimicrobial resistance."
- Introduce Agenda
- Logistics

9:15-9:30 Participant introductions: Name, affiliation, expertise

9:30-9.45 Coffee Break

Session #1: **Antimicrobial Resistance (AMR) intro**

9:45-10:10 1.1. "**Public Health and Antimicrobial Resistance**" (Beth Karp, CDC)
10:15-10:40 1.2. "**Microbiology of Antimicrobial Resistance** (David White, FDA)
10:45-10:55 1.3. **"FDA's Current AMR Strategy"** (Craig Lewis, FDA)

Session #2: **AMR Risk Pathways**

11:00-11.25 2.1. "**Mapping Drivers of Antimicrobial Resistance**" (Carolee Carson, PHAC/CIPARS)
11:30-11:55 2.2. **"Primer on Animal Agriculture in the US"** (Kathe Bjork, USDA)

12:00-13:15 Lunch at NiMBioS

Session #3: Monitoring Systems

13:20-14:00 3.1. "**Monitoring Antimicrobial Resistance**" – (David White, FDA)
14:10-14:50 3.2. "**Monitoring Antimicrobial Use in Animal Agriculture**" (Craig Lewis, FDA)

15:00-15:40 **Discussion I: Focus Questions**
1. Which questions we want to tackle (i.e., how to divide the problem);
2. What we need to answer these questions; and
3. What we want to accomplish by the end of Day 4.

15:40-17:30 **Discussion II**: Clarify the available data and choose the exemplar biological system in which we expect to see a change following roll-over of the current strategy. Criteria to consider:

- which bacterial species are sampled and from which production systems/regions;
- which antimicrobials will be tested for resistance;
- expected change in usage of a given antimicrobial class or drug (frequency, intensity) in the production system/region;
- current prevalence of resistance to the antimicrobial(s) which usage is expected to change;
- confounding co-selectors of resistance: other antimicrobials used in the system/region and whether their increased usage is/is not expected, “natural” co-selectors common/not
- timeline of expected change in usage
- timeline of expected change in resistance given change in usage given the resistant biology

17:30-18:30 Reception at NIMBioS

Dinner on own

Day 2 (Saturday 20, 2014): Modeling and Statistics

8:00-8:30 Breakfast
8:30-8:45 Organizer remarks: Recap Day 1

Session #4: **Modeling approaches – statistical and mechanical models**

8:45-9:10 4.1. “**Reviewing statistical approaches used so far**” (Victoriya Volkova, KSU)

9:15-9:40 4.2. “**Geo-statistics approach to interpret the antimicrobial use and resistance patterns.**” (Thomas Van Becknel, Princeton)

9:45-10.15 Coffee Break

10:15-10:40 4.3. “**Reviewing available modeling approaches**” (Cristina Lanzas, UT, NiMBioS)

10:45-11:15 4.4 “**Lessons from the human antimicrobial resistance modeling literature**” (Ian Spicknall, CDC)

11.20- 11.45 4.5. “**Modeling AMR in health care settings**" (Shigui Ruan, Univ. of Miami)
11:45-11:55 Discussion

11:55-12:00 Workshop Picture

12:00-13:00 Lunch at NiMBioS

13:00-14:30 **Discussion III: Revisiting our Focus Questions**

1. Which questions we want to tackle (i.e., how to divide the problem);
2. What we need to answer these questions; and
3. What we want to accomplish by the end of Day 4.

Specifically: 1. Clarify the available approaches and choose which analytical approach(es) would allow us to reach the objectives, given the available data. 2. How are we going to proceed to further investigate the utility of each approach, and its implementation.

15:00-15:30 Coffee Break

15:30-17:30 Additional working group planning, further discussion

Day 3 (Sunday 21, 2014): Modeling and Statistics continue and …

8:00-8:30 Breakfast

8:30-8:50 Organizer remarks: Recap Day 2, Summarize reports from groups from Days 1 and 2, Review "group charge"

Session #5: Are we still missing something?

9:30- 10:00 5.1. "**Parameter fitting for stochastic models.**" (José Miguel Ponciano, Univ. of Florida)

10:00-10:20 Discussion

10:20-10:30 Coffee Break

10:30-12:00 Group work

12:00-13:00 Lunch at NiMBioS

13:00-14:30 Group reports and then larger body discussion/feedback

14:30-15:00 Working group planning, further discussion

15:00-15:30 Coffee Break

15:30-17:30 Additional working group planning, further discussion

Day 4 (Monday 22, 2014): Next Steps

8:00-8:30 Breakfast

8:30-9:00 Organizer remarks: Recap Day 3, Summarize report from groups from Days 1-3, Review "group charge"

Session #6: Where do we go from here?

9:00-9:35 **6.1 "Progression to multi-scale models and the application to food system intervention strategies." (Yrjo Grohn, Cornell)**

9:35-10:00 **6.2 "How good are models – model validation." (Laura Pullum, Oak Ridge)**

10:00-10:20 Discussion: Systems approach to antimicrobial use and resistance

10:20-10:30 Coffee Break

10:30-12:00 Working group planning, further discussion, concluding remarks

(Early departure)

12:00-13:00 Lunch at NiMBioS

Participants (1-1.5 pages)

a. Table

Name	Affiliation (including departments)	Areas of PhD; Areas of expertise most relevant for the Working Group
Craig Lewis	DHHS/FDA/CVM	DVM/MPH; food-animal production medicine, veterinary preventive medicine, public health, public policy
Yrjo T. Grohn	Cornell University (College of Veterinary Medicine, Department of Population Medicine and Diagnostic Sciences)	DVM, MPVM, MS, PhD (Veterinary Medicine, Epidemiology, Genetics, respectively); food supply veterinary medicine, analytical epidemiology and modeling
David White	DHHS/FDA/CVM	PhD (microbiology); microbiology, antimicrobial resistance research and surveillance, public policy
Laura Hungerford	DHHS/FDA/CVM	DVM/MPH/PhD (Veterinary Epidemiology); veterinary epidemiology, public health
Beth Karp	DHHS/CDC/OID	DVM, MPH; public health, veterinary preventive medicine
David Andow	University of Minnesota (College of Food, Agriculture, and Natural Resources Sciences)	PhD (Ecology); genetic ecology
Carole Carson	Laboratory for Foodborne Zoonoses, Public Health Agency of Canada	DVM/PhD (Veterinary Epidemiology; antimicrobial use and resistance modelling); quantitative risk assessment, antimicrobial use and resistance surveillance
José Miguel Ponciano	University of Florida, Department of Biology	PhD (Bioinformatics and Computational Biology); stochastic models, parameter fitting for stochastic models
Cristina Lanzas	University of Tennessee in Knoxville (College of Veterinary Medicine, Department of Comparative Medicine)	DVM/PhD (Animal Sciences); Mathematical modeling, infectious disease epidemiology, food safety, quantifying the effect of control strategies
Shigui Ruan	University of Miami Florida (Department of Mathematics)	PhD (Applied Mathematics); differential equations, dynamical systems, and mathematical biology; nonlinear dynamics in

		structured biological and epidemiological models; mathematical modeling of the superspreaders of antibiotic-resistant bacteria
Laura Pullum	Oak Ridge National Laboratory (Computational Data Analytics Group)	DSc (Systems Engineering and Operations Research); software-intensive system dependability and intelligent systems
Ian Spicknall	DHHS/CDC/OID - ORISE fellow	PhD (Mathematical Modeling) Environmental determinants of infectious disease
Victoriya Volkova	ICCM, Department of Diagnostic Medicine/Pathobiology, College of Veterinary Medicine, Kansas State University	DVM, PhD (Veterinary Medical Sciences); pharmacokinetic modeling, modeling dynamics of infection and genetic transfer
Kathe Bjork	USDA/APHIS/VS/CEAH	DVM/PhD (biostatistics); public health and analysis of antimicrobial resistance data
Thomas Van Boeckel	Princeton University (Department of Ecology and Evolutionary Biology)	PhD; statistical and epidemiological models to characterize spatio-temporal distribution of the disease, calculate risk maps, and evaluate potential intervention scenarios
Min Li	Cornell University College of Veterinary Medicine (Department of Population Medicine and Diagnostic Sciences)	PhD (Food Science); Risk assessment and predictive models for foodborne pathogens in various food supply chains; Bayesian Belief Network as a monitoring tool.