

REPORT OF THE USAHA/AAVLD COMMITTEE ON FOOD AND FEED SAFETY

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The Committee met on October 16, 2016 at the Sheraton Greensboro Hotel in Greensboro, North Carolina from 1:30 to 5:30 p.m. There were 12 members and 13 guests present. Basic housekeeping tasks were covered, sign in and voting protocols were discussed.

Presentations and Reports

Interstate Shipment of Raw Milk and Listeria Outbreaks

Megin Nichols, DHHS/CDC/OID/NCEZID/DFWED/ORPB

The Centers for Disease Control and Prevention (CDC), along with federal and state partners, investigated Listeriosis in two people residing in California and Florida, linking them to consuming raw dairy products from Dairy Farm A in Pennsylvania. Dairy Farm A is an unregulated venue that ships milk interstate. Both illnesses occurred in 2014 and both ill people in this outbreak were hospitalized; the ill person from Florida died and the other recovered. Public health investigators used the PulseNet system to identify these illnesses. PulseNet is the national subtyping network of public health and food regulatory agency laboratories coordinated by CDC. DNA "fingerprinting" is performed on Listeria bacteria isolated from ill people by using techniques called pulsed-field gel electrophoresis (PFGE) and whole genome sequencing (WGS). Although the two illnesses occurred in 2014, the source of these illnesses wasn't known until January 29, 2016, when the U.S. Food and Drug Administration informed CDC that whole genome sequencing of Listeria bacteria from raw chocolate milk produced by Farm A showed that it was closely related genetically to Listeria bacteria from the two ill people described above. The Listeria isolates from these two ill persons had indistinguishable PFGE patterns and were highly related by WGS analysis to isolates from a sample of raw chocolate milk produced by Dairy Farm A. Because Listeria was recently found in raw milk produced by Farm A, CDC is concerned that conditions may exist at the farm that may cause further contamination of raw milk and raw dairy products distributed by this company and make people sick. Raw milk is milk from cows or other animals that has not been pasteurized to kill harmful bacteria. This raw, unpasteurized milk can carry dangerous bacteria such as Listeria, Salmonella, E. coli, and Campylobacter, which are responsible for causing numerous foodborne illnesses and outbreaks. We recommend that people drink and eat only pasteurized dairy products (including soft cheese, ice cream, and yogurt). Pasteurization is the process of heating milk to a high enough temperature for a long enough time to kill dangerous bacteria. This is especially important for people at higher risk for foodborne illness: children younger than five, pregnant women, adults 65 and older, and people with weakened immune systems.

<http://www.cdc.gov/listeria/outbreaks/raw-milk-03-16/index.html>

Updates from the FDA Vet-LIRN

Renate Reimschuessel, Vet-LIRN, DHHS/FDA/CVM/OFVM/CVM/OR

During the past six years, the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) has grown from an idea in August 2010 to a functioning network comprising 38 laboratories. The activities initiated during this time are varied yet all focused on forwarding CVM's mission to promote human and animal health. Dr. Reimschuessel reported on a short list of the activities and accomplishments of the Vet-LIRN.

Vet-LIRN

1. In December 2010, the newly formed Vet-LIRN staff consisted of a Director, a support scientist, a liaison to Office of Surveillance and Compliance, and a contract Oak Ridge Institute for Science and Education (ORISE) chemist. The network now has another support scientist and two veterinarians working on investigation and response to consumer reports.
2. Vet-LIRN held its first stakeholder meeting in March 2011, and by August 2011 we had 16 Vet-LIRN laboratory partners. The network has grown to 38 laboratories.
3. Vet-LIRN awarded 11 cooperative agreements to conduct a study evaluating Salmonella presence in diarrheic and non-diarrheic dogs and cats. <http://grants.nih.gov/grants/guide/rfa-files/RFA-FD-11-010.html>. Data from this study is being prepared for publication.
4. Vet-LIRN collaborated with six Food Emergency Response Network (FERN) laboratories to test a number of animal feed products for various contaminants. This study's results were published in 2014.
5. Vet-LIRN collaborated with three FERN laboratories to optimize methods and test pig tissues for triazine contaminants. This study's results were published in 2015.

Vet-LIRN Laboratories

1. Vet-LIRN awarded a contract to document feed contamination events between 2006-2011 to help CVM prioritize efforts and resources.
2. In 2012, Vet-LIRN initiated a proficiency testing (PT) program in collaboration with the Moffett Center and Iowa State University. We conduct, on average, three proficiency tests per year. These can be chemical, microbiological or pathology. During 2015 the PT's were: 1) Listeria in pet food PT, 2) inter-laboratory comparison of Vitamin E in animal serum, 3) Vitamin E in animal serum PT. In collaboration with NVSL, Vet-LIRN laboratories also participated in a Salmonella Group D serology PT.
3. In 2012, Vet-LIRN initiated an infrastructure funding opportunity to provide infrastructure funding for Vet-LIRN laboratory activities including testing during investigations. <http://grants.nih.gov/grants/guide/pa-files/PA-12-194.html>. Currently 30 laboratories have received funding. In 2015 and 2016, supplemental funds were awarded to facilitate travel and training for our partner laboratories.
4. Vet-LIRN program office participated in multiple National Level Exercises (NLE) and Integrated Consortium of Laboratory Networks (ICLN) exercises. These activities contribute to overall preparedness of our network for emergency response.
5. Vet-LIRN conducts approximately 30-50 in depth case investigations per year. These cases evaluate consumer reports of potential problems with animal feed or animal drugs.
6. Vet-LIRN continues to lead the Center's testing program to investigate the root cause of pet jerky treat associated illness. We are focusing on Fanconi cases, but also developed a multifaceted product testing program.
7. In 2013, Vet-LIRN initiated a new Cooperative Agreement program to develop and validate methods in our network. <http://grants.nih.gov/grants/guide/pa-files/PA-13-244.html>. There are currently 11 funded projects. A new request for applications (RFA) to evaluate feed-irradiation markers was developed and funded in 2016 <https://grants.nih.gov/grants/guide/pa-files/PAR-16-132.html>.
8. Vet-LIRN sponsored a meeting in January 2016 for awardees of methods grants to present their progress reports to FDA and each other.
9. Vet-LIRN was named, along with NAHLN, as a partner in the president's "Combating Antibiotic Resistant Bacteria" initiative. Vet-LIRN is initiating a pilot study to test antibiotic susceptibility of selected veterinary pathogens and conduct whole genome sequencing on a subset of these isolates.

Vet-LIRN plans to approach any new tasks needed by CVM with the same energy and innovation that has brought the program to its present state.

<http://www.fda.gov/animalveterinary/scienceresearch/ucm247334.htm>

Review of Multistate Foodborne Outbreaks 2015-2016

Colin Basler, DHHS/CDC/OID/NCEZID/DFWED/ORPB

This presentation provided an overview of the methodology used for multi-state foodborne outbreak identification and investigation. In addition, recent multi-state foodborne outbreaks of *Salmonella* and *E. coli* including outbreaks linked to new food items, e.g., pork, shell eggs, frozen stuffed chicken entrees, sushi, organic nut butters, protein supplements, cucumbers, ground beef, and flour were reviewed.

Finally, emerging issues such as the rise of multi-drug resistant foodborne outbreaks and the implementation of whole genome sequencing in foodborne outbreak detection were discussed.

Here is a link to the details of the outbreaks that were discussed:

<http://www.cdc.gov/foodsafety/outbreaks/multistate-outbreaks/outbreaks-list.html>

- Pork- *Salmonella* enterica serotype I 4, [5],12:i:-
- Eggs- *Salmonella* Oranienburg
- Frozen Stuffed Chicken Entrees- *Salmonella* Enteritidis
- Frozen Yellowfin Tuna Sushi- *Salmonella* Paratyphi B variant L(+) tartrate(+) and *Salmonella* Weltevreden
- Sprouted Nut Butters (sprouted almonds, cashews, and hazelnuts)- *Salmonella* Paratyphi B variant L(+) tartrate(+)
- Raw Powder Supplements and Meal Replacements- *Salmonella* Virchow
- Cucumbers- *Salmonella* Poona
- Ground beef- STEC/E coli O157
- Flour- STEC/E coli O121 and O26

Whole Genome Sequencing and Plasmid Genomics of Antimicrobial Resistance: *Salmonella*'s Mobile Genetic Elements and the Antimicrobial Resistance Genes They Carry

Jonathan Frye, USDA-ARS, U.S. National Poultry Research Center

This presentation highlighted ongoing research projects that are part of the work of the Bacterial Epidemiology and Antimicrobial Resistance Research Unit. With the emergence of antibiotic resistance (AR), multidrug resistance (MDR), and carbapenem resistant Enterobacteriaceae (CRE), the specter of widespread untreatable bacterial infections threatens human and animal health. The ability of these emerging resistances to transfer between bacteria on mobile genetic elements (MGEs) could cause the rapid establishment of MDR bacteria in animals leading to a foodborne risk to humans. To sample the diversity of AR genes and MGEs in *Salmonella*, we selected animal isolates collected from 1997-2011 by the National Antimicrobial Resistance Monitoring System (NARMS). The ~70,000 *Salmonella* in the collection were isolated from beef and dairy cattle, chicken, swine, turkey, their meat products, the processing environment, and from farms. To obtain the greatest variety of AR genes and MGEs, 193 isolates were chosen based on their resistance phenotypes, serovars, and PFGE patterns, resulting in 75 serovars with diverse PFGE patterns. Whole genome sequencing (WGS) and bioinformatics analysis were used to identify AR genes and MGEs. Most isolates had AR genes detected as well as MGEs such as plasmids, integrons, or both. The AR genes were often located on the MGEs and many were arranged into MDR cassettes of several contiguous AR genes. Some of the MGEs and AR genes have been previously found in *Salmonella*; however, they are arranged differently and have not previously been found in animal isolates, in the serovars analyzed, or in isolates from human infections. Together this demonstrates that different factors may be affecting the development and spread of MGEs encoding AR in *Salmonella* found in animals as compared to humans. The next step will be to identify the animal environments that lead to the development and spread of AR so that these can be targeted with interventions to reduce this risk to human and animal health.

Food Safety Modernization Act/FSMA - Update

Michael J. Murphy, HHS/FDA/CVM/OFVM/CVM/OCD

As the implementation of the FDA Food Safety Modernization Act (FSMA) continues, the agency today issued two draft guidances to assist industry with the implementation of the Preventive Controls for Animal Food rule and another draft guidance to assist businesses in determining whether the activities they perform are within the “farm” definition. Two of the draft guidances are meant to assist domestic and foreign companies in complying with Current Good Manufacturing Practice (CGMP) requirements and with human food by-product requirements under the FSMA Preventive Controls for Animal Food Rule. <http://www.fda.gov/animalveterinary/products/animalfoodfeeds/ucm347941.htm>
<http://www.fda.gov/Food/GuidanceRegulation/FSMA/>

Veterinary Feed Directive/VFD – Update

Michael J. Murphy, HHS/FDA/CVM/OFVM/CVM/OC

In December 2013, the FDA took a significant step forward in addressing antimicrobial resistance by publishing Guidance #213, which calls on animal drug sponsors of medically important antimicrobials used in food-producing animals to withdraw production indications (e.g., “growth promotion” or “feed efficiency”) as approved uses from their labels, and to bring the remaining therapeutic uses of these products under the oversight of a veterinarian by the end of December 2016. The Veterinary Feed Directive (VFD) final rule, is an important piece of the agency’s overall strategy to promote the judicious use of antimicrobials in food-producing animals. This strategy will bring the use of these drugs under veterinary supervision so that they are used only when necessary for assuring animal health. The VFD final rule outlines the process for authorizing use of VFD drugs (animal drugs intended for use in or on animal feed that require the supervision of a licensed veterinarian) and provides veterinarians in all states with a framework for authorizing the use of medically important antimicrobials in feed when needed for specific animal health purposes.

<http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm448620.htm>

<http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm071807.htm>

Modeling the Transboundary Survival of Foreign Animal Disease Pathogens in Contaminated Feed Ingredients

Scott Dee, Pipestone Veterinary Services

Project Objectives were two-fold - to model if foreign animal diseases could survive in feed ingredients shipped from Asia to the USA, and to evaluate whether two chemical mitigants could reduce risk. The hypothesis was that pathogen survival will be influenced by ingredient and treatment. Based on the Swine Health Information Center pathogen matrix, ten Foreign Animal Disease (FAD) viral pathogens were identified as significant risks to the U.S. swine industry. Due to the inability to work with these actual agents, we used “surrogate viruses”, which allowed us to study closely related and structurally similar viruses, but not the actual FAD pathogens. The designated FAD and the selected surrogate were as follows: foot and mouth disease virus (FMDV), (Seneca Virus A), Campylobacter fetus subsp. venerealis (CFV), (Bovine Virus Diarrhea Virus), pseudorabies virus (PRV), (Bovine HerpesVirus-1), African swine fever virus (ASFV), (Vaccinia virus), Nipah virus (Canine Distemper Virus), Swine Vesicular Disease Virus (Porcine Enterovirus) and Vesicular Exanthema Virus (Feline Calici Virus). Other selected pathogens (PRRSV 174, PCV2 and Vesicular Stomatitis Virus) did not require surrogates. Using a model previously validated to study the risk of contaminated feed ingredients for the transboundary spread of PEDV (Dee et al 2016), we selected feed ingredients known to be imported from China to the USA based on the U.S. Government Harmonized Tariff Schedule (hs.usitc.gov). These included organic and conventional soybean meal, soy oil cake, dried distiller's grain with solubles (DDGS), lysine, choline, vitamin D, pork sausage casings, and several pet foods (dry and moist). Ingredients were inoculated with representative surrogates (5g ingredient and 100 uL virus). Controls consisted of complete feed inoculated with surrogate or saline (negative control) as well as stock virus alone (positive control) in the absence of feed matrix. The design involved non-treated control ingredients, along with 2 mitigants: SalCURB-treated ingredients and MCFA-treated ingredients. These samples were then incubated in an environmental chamber for 37 days programmed using actual T and % RH data recorded during a journey from China to the U.S. (Beijing to Shanghai to San Francisco to Des Moines) in December 2012 through January 2013 (SeaRates.com). Samples were tested by polymerase chain reaction (PCR), VI and bioassay for porcine surrogates or on primary cells for surrogates of non-porcine origin at two day postinoculation (DPI) (Beijing), eight DPI (Shanghai), 25 DPI (San Francisco) and 37 DPI (Des Moines) to represent specific points in the model.

Results: As of this writing, testing of the FMDV, CSFV and PRV surrogates has been completed. Preliminary data indicate the survival of the FMDV surrogate (SVA) and the PRV surrogate (BHV-1) at all points during the 37-day shipping period from China and into the U.S. Both surrogates survived in conventional soybean meal and soy oil cake, while SVA also survived in lysine, pet food, Vitamin D, complete feed and casings. Both positive controls (SVA and BHV-1 stock virus) did not survive. In contrast, the CSFV surrogate (BVDV) appeared to be less stable and did not survive the 37-day journey, independent of ingredient. It did, however, survive until the samples theoretically entered the port of San Francisco (25 DPI) in conventional soybean meal and moist dog food.

Discussion: Under the conditions of this study, these preliminary results suggest that contaminated feed could serve as vehicles for FAD introduction to the U.S., supporting our previous results which focused on PEDV. Phase 2 has begun, consisting of surrogates for ASFV, Vesicular Exanthema Virus and Nipah Virus along with PRRSV.

Reference

Dee S, et al. Modeling the transboundary risk of feed ingredients contaminated with porcine epidemic diarrhea virus BMC Vet Res, 2016, 12:51

Committee Business:

Dr. McDonough began with a review of the committee's past year discussion topics, the mission statement of the committees and that we need to be thinking of how our committee meets the strategic plans of both the USAHA and the AAVLD. He also explained that this joint committee functions within the concept of One Health that includes the complex interconnectedness of human and animal and ecosystem health. Finally, he announced that the USAHA seeks to evaluate its entire Committee structure, and we will be requesting input and comment in the near future from committee members as this process develops. We also discussed the need to continue the committee's business throughout the year in between annual meetings, perhaps via the mechanism of teleconferences or webinar links.

The meeting was adjourned at 5:30 p.m.