Minutes
Minor Use Animal Drug Program/NRSP-7 Spring Meeting 2014
June 19th 2014 (Noon to 3:00 pm)

TUESDAY, JUNE 19TH 2014: TELECONFERENCE

TO VIEW THE MEETING REPORTS:

Connection Meeting Information
Meeting Name: MUADP Spring Meeting 2014
Summary:
Invited By: Amy Omer (Amy.Omer@fda.hhs.gov)
When: Tuesday, June 19th - 12:00 PM - 3:00 PM
Time Zone: Eastern Time (US and Canada)

To join the meeting: **https://collaboration.fda.gov/r3reqnsmhtr/**

If you have never attended a Connect Pro meeting before:
Test your connection:
https://collaboration.fda.gov/common/help/en/support/meeting_test.htm

CALL IN NUMBER: **866-712-2714** PASSCODE: **2542087**

ATTENDEES

NAME	AFFILIATION	EMAIL ADDRESS
Amy Omer	FDA/CVM	Amy.Omer@fda.hhs.gov
Dorothy Bailey	FDA/CVM	dorothy.bailey@fda.hhs.gov
Francis Galey (AA)	AA/UWY/WAES	FGaley@uwy.edu
Gary Sherman	USDA/CSRESS	gsherman@nifa.usda.gov
John Babish (NC)	MUADP/NRSP-7	jgb7@cornell.edu
Lisa Tell (RC)	MUADP/NRSP-7/UC Davis	latell@ucdavis.edu
Margaret Smith (AA)	AA/NY AES	mes25@cornell.edu
Meg Oeller	FDA/CVM	margaret.oeller@ fda.hhs.gov
Paul R. Bowser (RC)	MUADP/NRSP-7/Cornell U	prb4@cornell.edu
Phil Elzer (AA)	AA/LSU/SAES	Pelzer@agcenter.lsu.edu
Rod Getchell	MUADP/NRSP-7/Cornell U	rgg4@cornell.edu
Ron Griffith (RC)	MUADP/NRSP-7/Iowa State	rgriffit@iastate.edu
Thomas Vickroy (RC)	MUADP/NRSP-7/U FL	vickroy@vetmed.ufl.edu

The MUADP/NRSP-7 technical committee is made up of a National Coordinator, four Regional Coordinators, four regional Administrative Advisors, and liaisons from USDA and FDA. The National Coordinator is Dr. John Babish (Cornell University). The Regional Coordinators are Dr. Lisa Tell (University of California, Davis), Dr. Ronald Griffith (Iowa State University), and Dr. Paul Bowser (Cornell University). The Administrative Advisors present were Drs. Margaret Smith (Cornell University, AES), Phil Elzer (LSU, AES) and Francis Galey (UWY, AES). The attending NIFA representative was Dr. Gary Sherman (Washington, DC) and the FDA liaisons were Drs. Meg Oeller, Dorothy Bailey, and Amy Omer (Rockville, MD). Absent was administrative advisor Dr. John Baker.

12:00 PM INTRODUCTIONS - *Introductions and meeting organization*

Dr. John G. Babish started the meeting, as custom, with a thank you to Drs. Omar and Bailey for their organizing efforts at FDA/CVM to have the teleconference conducted through the Adobe Connect facilities at Rockville, MD.

The National Coordinator then outlined the agenda of the meeting with reports from the Administrative Advisors, the National Coordinator, FDA/CVM, NIFA/USDA and accomplishments from the Regional Coordinators,

REPORT FROM THE ADMINISTRATIVE ADVISORS - DR. JOHN BAKER (CHAIR)
Dr. Baker was unable to attend the meeting, but had contacted Dr. Babish earlier in the day with the news that he had been selected as the new Dean of the College of Veterinary Medicine for Michigan State University. Both Drs. Baker and Babish recommended Dr. Margaret Smith as the new chair of the Administrative Advisors. Dr. Smith agreed and stated she was honored by the consideration. She also stated that she would work hard within the AES system to move NRSP-7 forward into a new era of funding.

REPORT FROM THE NATIONAL COORDINATOR - DR. JOHN G. BABISH

The central issue facing NRSP-7 is the loss of funding in the NIFA/USDA budget a number of years ago. The Hatch funds have been used to leverage support from stakeholders for the last several years, but these funds are at a reduced level from the previous NIFA/USDA funding. Our Hatch funding for 2014 has been approved. Due to a change in AES Guidelines on Hatch funds, however, this award is not continued for an additional year if our five-year proposal is not approved,.

During our one-year renewal term the Program has outlined the following tasks:

1. Since the inclusion of the MUADP in the 2014 Farm Bill, the Program will work to identify Congressional support for stable and increased funding. Emphasize prudent use of antimicrobials in veterinary medicine necessitates the continuation of the MUADP.
2. Increase stakeholder base through inclusion of natural product manufacturers, pesticide manufacturers, etc.
3. Utilize CDC publications and news releases. The CDC has come down hard on antibiotic use in veterinary medicine. While strongly discouraging the use of antibiotics in veterinary medicine, they emphasize a more controlled use. This should be our position in describing the critical need for the program - more control over the use of antibiotics in minor species. Maybe this position by the CDC could serve NRSP7 in much the same way reregistration served the IR-4. Anyway, we have to come out ahead of this position and not be run over by it.
4. USDA and FDA need to realize that if the project closes there are ramifications. First off is the loss of faculty commitment, infrastructure and personnel that cannot easily be turned back on. Second, the loss of NRSP-7 is a serious food safety concern. This is (in my opinion) is the only viable option to get approval for pharmaceuticals used in minor species. Failure to do so leads to off label and sometimes illegal use of pharmaceuticals in minor species with subsequent risk to human health.

REPORT FROM FDA/CVM - DRS. MEG OELLER, AMY OMER AND DOROTHY BAILEY

1. Project Progress

- Erythromycin – Environmental Assessment (EA) pending with CVM due date of 7/13/2014. All other technical sections complete; Safety and effectiveness are for Chinook salmon only.
    - Next steps: Need to reach out to Chris Moffitt to see if data exists to expand this indication. Need to contact Bimeda to discuss their progress on the CMC technical section.
- CIDR-g – TAS, Human Food Safety (HFS) and Environmental technical sections are complete.Next steps: Effectiveness study report is nearing completion.
- Fenbendazole – HFS technical section complete. Target Animal Safety (TAS) technical section response submitted on 6/4/2014; CVM due date 12/2/2014.
    - Next steps: Request for Categorical exclusion denied; working on response. Need to request reaffirmation of Effectiveness technical section.
- Lasalocid – Effectiveness technical section complete.
    - Next steps: TAS response is closely related to fenbendazole TAS response; waiting for feedback on fenbendazole response. Categorical exclusion request is currently being prepared. HFS still pending.
- Ivermectin – Right of reference still pending; when it happens CVM will renegotiate requirements based on existing data.
    - Next steps: Working to get Merial and Postive Feeds to the table discuss path forward.

- SrCl – TAS protocol received concurrence from ONADE. Northeast region received OMUMS grant funding for TAS study.
    - Next steps: CVM to utilize existing data to support effectiveness technical section. CVM investigating how to prepare an environmental assessment as a white paper argument.
- Tulathromycin in Goats – TAS and Environmental technical sections complete.
    - Next steps: On hold.
- Tulathromycin in Sheep – Environmental technical section complete. Zoetis terminated designation.
    - Next steps: On hold.
- Nuflor Gold in Sheep – On hold.

2. Revisit prioritization of completion of these projects.

3. GLP Issues

What next steps are needed to move forward on the status of GLP concerns? Should we set up a meeting between University principals and Bernadette? Do the regional coordinators believe Meg's draft document is at least in part a feasible resolution to the issue? If the proposed budget allows for QA staffing, what affect will this have on the outlook of GLP studies at the universities?

NIFA/USDA – DR. GARY SHERMAN

Dr. Sherman noted that NIFA is cognizant of the exploratory efforts underway related to expanding the objectives of the program. Additionally, Dr. Sherman reminded the group that Secretary Vilsack and President Obama continue to strongly support revitalization of rural America. It is therefore appropriate to emphasize the roll of the MUADP in supporting a diversified, growing and vibrant rural economy.

Dr. Sherman then restated from the Fall meeting that funding for the FY 2014 NRSP-7 Hatch Multistate projects have all been awarded to CA, FL, IA and NY. He added that If grantees have not received the funds in their Treasury ASAP accounts, they should follow-up with NIFA's Financial Operations Division who has purview over fund certification. Emails should be sent to ASAPCustomerService@nifa.usda.gov. Grantees should provide the award number (per NIFA Award Face Sheet), and their ASAP account number when sending inquiries. We have not received any information regarding the FY 2014 Appropriation to date.

REPORTS, DISCUSSIONS AND NEW PROJECT PROPOSALS FROM THE REGIONS

WESTERN REGION – DR. LISA TELL

Progress of Work and Principal Accomplishments:

Active Regional Projects:

ADR#325 – Florfenicol (Nuflor® Injectable Solution) for sheep for respiratory disease

The human food safety (HFS) and efficacy studies required by FDA/CVM for the old formulation of florfenicol (Nuflor Injectable Solution) have been completed. All of the data from this project have been published. The data from the HFS study has been organized and a technical report has been written. The final technical report for the human food safety study was reviewed for Quality Assurance in March, 2010. This report was submitted to FDA/CVM in July, 2010. On February 11, 2011, FDA/CVM concluded that the tissue residue depletion study was acceptable for supporting a withdrawal period determination, and assigned a 42-day withdrawal period. Other comments from FDA/CVM were that microbial food safety issues still need to be addressed which include the impact of florfenicol on antimicrobial resistance among bacteria of public health concern in or on treated sheep as well as human intestinal flora. Update 12/2013: No new progress on this project.

ADR#350 – Florfenicol (Nuflor Gold®) for sheep for respiratory disease

A pilot study evaluating administration route (IM vs. SC) and doses of 20 (IM) or 40 (SC) mg/kg was performed in September and October of 2009. All of the samples (n=672; 28 samples for 24 animals) have been analyzed. A product development meeting was held on November 18th, 2009 with CVM, the sponsor and the Minor Use Animal Drug Program. Another dose range finding study using the SC route of administration is to be performed. Once the proposed label dose is determined, the Target Animal Safety Study will be performed. This study is currently pending and will not progress until CVM provides further guidance. Update 06/2014: No new progress on this project.

ADR#299 - Pirlimycin for Dairy Goats
Project is not being pursued.

ADR#338 – Spectramast™ LC Sterile Suspension for Mastitis in Dairy Goats
Project is not being pursued.

ADR#135 – Erythromycin in Salmonids
The environmental assessment was sent to FDA/CVM for review and they requested a revision of certain sections and that a chronic toxicity study with *Daphnia magna* is performed. This chronic toxicity study has been performed and will address CVM concerns regarding chronic toxicity to aquatic insects. In addition, a study describing the physiochemical properties of erythromycin has been performed. Because of the physical characteristics of ERTT, an empirical pKa could not be established. The final environmental assessment report for erythromycin in salmonids was completed in May, 2010 and submitted to FDA/CVM for review. The results of this environmental assessment report supports the safe use of erythromycin thiocyanate in all freshwater-reared salmonids at a dose regimen of 100 mg/kg bodyweight/day for 21 to 20 days. Christine Moffitt (author) submitted the White Paper for erythromycin. This was revised and submitted to FDA/CVM in July, 2010. We received notification January 12, 2011 from FDA/CVM that the Final Study Report for the pivotal Daphnia magna chronic toxicity study entitled: "Chronic toxicity of erythromycin thiocyanate to Daphnia magna in a flow-through, continuous exposure test system" is considered complete. Dr. Oeller is working on the White Paper for this study. Update 06/2014: Awaiting final amendment of EA by CVM.

Collaborative Projects:

ADR#280 - Fenbendazole in Game Birds (Pheasants, bobwhite quail, partridge)
A conference call with Merck/Intervet/SP was held on February 25, 2010. A product development meeting was held with CVM on September, 9, 2010 to discuss the development plan for investigating the use of fenbendazole Type A medicated article for the treatment of nematode parasites in pheasants. The HFS protocol was submitted and received concurrence from CVM on 12/08/2010. The TAS study protocol was submitted to FDA/CVM for review in February 2011. Plans are in place to conduct the HFS and TAS studies in the summer of 2011. The Western region will perform the analytical testing of the samples. We have begun to re-establish the fenbendazole tissue method for pheasants by testing intra and inter-day precision and accuracy. We are testing liver, muscle (breast and thigh), and skin/fat. In addition to spiked samples we will assay incurred samples to verify the method. There were a total of 366 samples analyzed in our laboratory during the summer of 2011 (120 study; 138 stability; 108 validation). HFS report received concurrence from CVM, April 2014. Update 06/2014: No new progress on this project.

ADR#324 - Progesterone CIDRs for Goats (TAS, Milk Residue Study, and Efficacy)
The target animal safety study technical report has been accepted by FDA/CVM (February 2008). The milk residue study has been completed and the quality assurance inspection has been completed. The final technical report was sent to FDA/CVM in December 2008 and accepted October 2009. FDA/CVM has provided comments regarding the efficacy protocol. The protocol has been accepted for concurrence. The efficacy study was started at UC Davis and Iowa State University during the Fall of 2009. A quality assurance inspection was performed for the stability of progesterone in goat tissue during frozen storage in September 2009. A quality

assurance inspection was performed in October 2009 for CIDR-G Insertion and Removal. All of the raw data from the UC Davis portion of this project was submitted to the Study Sponsor, Dr. Ron Griffith in August, 2010. The CIDR Efficacy study was initiated in August, 2010. A letter dated August 12, 2011 from FDA/CVM stated that the human food safety requirements for the use of CIDR-G in goats have been satisfied for toxicology, residue chemistry, and microbial food safety. The Human Food Safety technical section is complete as of August 12, 2011. A withdrawal period was established as zero and a milk discard time of zero. Update 06/2014: Nothing new to report.

ADR#340 - Tulathromycin in Goats (Collaborative project with the North Central region) The quality assurance was performed for the target animal safety study in February and March 2008. A tissue liquid chromatography/mass spectrometry method for analysis of the samples has been validated using 664 spiked samples to validate 4 tissues. Validation of analytical methods for liver, muscle, kidney and fat samples is complete. Plasma (444) and tissue (180) samples from the target animal safety have been analyzed. The quality assurance for the target animal safety report was completed November 2009. Plasma samples from the HFS study have been analyzed and the PK data has been generated. Tissue samples from the HFS study (205) have been analyzed. The method validation report has been submitted to the Central Region for quality assurance review. See North Central region report for further information. Tissue samples to re-establish data for freezer stability have been run and the data submitted to Dr. Griffith of the North Central region. A total of 102 freezer stability samples from Iowa State University were analyzed. The analytical data for the Human Food Safety Report has been provided to Dr. Kris Clothier and Dr. Ronald Griffith at Iowa State University. Update 04/2013: In March, 2013 an ERA amendment was requested by CVM for the HFS technical report but this study will result in a technical section incomplete due to some analytical challenges and freezer stability requirements. Update 06/2014: Nothing new to report.

Other Projects/Activities:

Quality Assurance: Since the Fall of 2012 FDA Inspection, and our efforts have been focused on addressing SOP revisions and internal operations. At this time these efforts are on hold due to funding challenges.

Excede in Sheep*:* Study has been completed in domestic sheep. Manuscript has been published.

Flunixin in Goats: Two cross over studies have been completed in domestic goats evaluating IV vs. IM administration. In addition, a pilot study has been completed in lactating goats. Update 12/2013: Samples were reanalyzed and the data is currently being evaluated.

Multidose flunixin Administration in Goats: This study was initiated to evaluate multi dose flunixin use in goats and milk residues. The study has been completed and the data is being analyzed. Initial study results were presented at the 2013 STAR meeting.

Plasma samples from a goat study study lead by Jamie Boehmer at the Office of Research evaluating inflammatory markers and flunixin have been analyzed. Dr. Tell is in contact with Dr. Boehmer and the manuscript is currently being written.

Tulathromycin pharmacokinetics in dairy goats: A UC Davis summer student, Bernadette Grismer, performed this study. A total of 448 samples (328 milk; 120 plasma) have been analyzed. Update 12/2013: Manuscript accepted by JVPT and has been published.

A food animal medicine resident (Matt Cuneo) performed a research study looking at a two time dose administration of tulathromycin in dairy goats. The samples are currently being analyzed. Initial results will be presented at UC Davis Goat Day 2014. Update 06/20/2014: Analysis of all milk samples just completed. Analysis of serum samples in progress.

Laboratory Report:

Some of the activity for the region continues as sample analysis in the laboratory mostly for studies focusing on drug use in small ruminants. Statuses of projects are reported under separate projects above.

Usefulness of the Findings:
The findings from most of the current studies (non-GLP) will be utilized to fulfill the mission of generating data relative to drug use in minor food animal species.

Work Planned for Remainder of the Year:
Publish data for all of these

NORTHEAST REGION: DR. RODMAN G. GETCHELL
Progress of the work and principal accomplishments:

Species Grouping Project:

INAD 10-320 Oxytetracycline in Fish
INAD 10-823 Romet-30 in Fish
INAD 11-145 Florfenicol in Fish

Efforts on this project consisted of providing administrative support and oversight to the New York State Department of Environmental Conservation in their conduct of field trials under our INAD 10-320 for the use of Oxytetracycline in fish.

Ovadine (Western Chemical) Disinfection of Fish Eggs:

We have been evaluating the efficacy of Ovadine (PVP-Iodine, Western Chemical) as an egg disinfection compound for fish eggs with a particular emphasis on the reduction of Viral Hemorrhagic Septicemia Genotype IVb from walleye eggs. Our trial will build on preliminary efforts, funded by New York Sea Grant Program, in which we found that the consensus treatment protocol of the Great Lakes Fishery Commission (50 mg/L iodine for 30 minutes) was not completely effective in the elimination of VHSV IVb. A disinfection trial was conducted during the 2010 walleye spawning season with the collaboration of the New York State Department of Environmental Conservation. Treatments included iodine doses of 0, 50 and 100 mg/L for 30 minutes. Two manuscripts on this work have been published in the peer-reviewed literature.

Allicin for the reduction of *Aeromonas salmonicida* infection in salmonids:

We conducted a cooperative project with Dr. H. George Ketola of the USGS Tunison Laboratory of Aquatic Science, Cortland, NY in which we evaluated the use of allicin as a component of the ration to increase production efficiency in salmonids. More specifically, we determined if allicin in the ration will result in a reduction in losses due to Aeromonas salmonicida in salmonids. We developed a challenge model with A. salmonicida in rainbow trout and conducted two preliminary trials in which allicin was added to the ration at three different concentrations (0.0%, 0.5%, 1.0% and 2.0%). The fish were then challenged with an intraperitoneal injection of Aeromonas salmonicida. Upon preliminary evaluation of the data, there appeared to be some benefit from the addition of allicin at 0.5% and 1.0% and an adverse effect at 2.0%. Future effectiveness trials will involve a challenge with the pathogen administered via the water. The standard target animal safety model (1X, 3X, 5X dose for 3X duration) was utilized to further evaluate the effect of supplementation of allicin to the diet. Fish were fed allicin supplemented rations (0.0%, 0.5%, 1.5% and 2.5%) for 30 days. At the end of the trial select serum chemistry, hematology and histopathology parameters were evaluated. A preliminary evaluation of the data indicated significant ($P<0.05$) differences between treatments for some of the parameters. Upon microscopic evaluation of select tissues from treated fish, an increase in pigment containing macrophage centers in the posterior region of the kidneys of the fish receiving the highest dose (2.5% for 30 days). This was interpreted to be a possible indication of tissue damage. The presence of a potential adverse effect at the highest dose was consistent with the potential adverse impact of the highest treatment concentration in the challenge studies.

The effort served as the basis for the Master of Science thesis research for Dr. Kate E. Breyer, a Resident in the Laboratory Animal Medicine Program at Cornell. She successfully defended her Thesis in June of 2013. A manuscript based on these studies has been submitted and is currently under review.

Usefulness of the findings:
In all cases, the findings to date over the course of the above described projects serve as the foundation for continued work on these compounds. The Human Food Safety Studies completed to date for oxytetracycline, Romet-30 and Florfenicol in fish are consistent with what was expected; namely that the elimination of therapeutic compounds from the edible portion of the fish tested are within the withdrawal times currently specified for labels, or available in the literature for oxytetracycline, Romet-30 and Aquaflor (Florfeniol).

Work planned for next year:
Species Grouping Project:

INAD 10-320 Oxytetracycline in Fish
INAD 10-823 Romet-30 in Fish
INAD 11-145 Aquaflor (Florfenicol) in Fish

We anticipate our efforts on this project to center around the continued provision of administrative support and oversight of Efficacy Studies of oxytetracycline in a collaborative effort with the New York State Department of Environmental Conservation. The particular focus of the efficacy trials will be for the treatment of bacterial diseases not currently on the label for treatment of bacterial diseases of cool water species such as walleyes, muskellunge and tiger muskellunge (hybrid muskellunge X northern pike). These studies will be initiated when diagnosed field cases can be identified that will lend themselves to the implementation of controlled field studies.

Ovadine (PVP-Iodine, Western Chemical) Disinfection of Fish Eggs

Data from the Ovadine work is being summarized with one publication and a second manuscript in press. We are investigating the potential of indexing Ovadine.

Strontium Marking of Fish Otoliths

We have developed a project to complete the data package needed to obtain a label or to index the use of Strontium Chloride for marking fish otoliths. Our protocol has been reviewed and accepted by CVM FDA. We submitted an application for funding from the MUMS Program to conduct this project. We were recently informed that our MUMS application was successful. We anticipate the commencement of the Strontium Chloride effort in the fall of 2014 when fish of appropriate size and age become available. This summer we will conduct an assay validation trial for strontium chloride measurements in water.

Allicin for the reduction of Aeromonas salmonicida infection in salmonids

We completed two efficacy trials and one target animal safety trial in which allicin was added to the ration of rainbow trout as a nutritional supplement to increase production efficiency of fish culture. We do not anticipate any future studies on allicin at this time.

CRITICAL REVIEW (Northeast Region)

1) Work accomplished under the original project:

The original objectives of the project were to conduct a national program to obtain minor and specialty animal-drug clearances (tolerances, exemptions and registrations) in cooperation with state, federal and industry personnel. The mission of NRSP-7 is:

- To identify animal drug needs for minor species and minor uses in major species.
- To generate and disseminate data for safe and effective therapeutic applications, and
- To facilitate FDA/CVM approvals for drugs identified as a priority for a minor species or minor use.

Under the framework of this mission, progress has been made in the following areas:

(A) Use of hydrogen peroxide for the control of bacterial gill disease in fish.
(B) Species Grouping in Fish, using the compounds Oxytetracycline, Romet-30/ Romet-TC and Aquaflor as test articles.
(C) Use of Ovadine for the reduction of Viral Hemorrhagic Septicemia Virus on fish eggs.

(D) Uses of allicin as a component of the ration to reduce th impact of Aeromonas salmonicida in salmonids.
(E) We have been successful in obtaining funding through the MUMS program that will augment the NRSP-7 funding and allow the program to undertake a project to evaluate the use of strontium chloride as an otholith marker.

2) The degree to which the objectives have been met:
Work has focused on a number of important therapeutic compounds in aquatic animals. The work is being conducted in a deliberate manner with the goal of developing appropriate data that will be submitted in support of a label for these compounds. An initial step in this process is the publication of the data in the peer reviewed scientific literature. While we consider it extremely important to have such peer-reviewed information available for the veterinary community, should they consider an extra-label use, the ultimate goal is to secure a label for the product. As an additional goal, the work is being done in a manner that could justify a species grouping concept for finfish cultured in the United States.

3) Incomplete work or areas needing further investigation:
(A) The development of a crop (species) grouping concept is seen as imperative for supporting efforts to gain labels for therapeutic compounds for fish. Our work on Oxytetracycline, Romet-30/Romet-TC and Aquaflor (Florfenicol) in fish is proposed to be part of an effort to utilize those compounds as models in this effort. Further work on species grouping will require securing additional funding.

(B) Discussions with a researcher from U.S. Dept. of Agriculture, Agricultural Research Service Harry K. Dupree - Stuttgart National Aquaculture Research Center (USDA ARS HKD SNARC) suggests there is an interest in investigating the anti-viral properties of copper sulfate for the treatment of baitfish eggs. We have the capability to conduct in vitro work with fish cell cultures and/or in vivo work with baitfish eggs similar to the Ovadine disinfection project. The baitfish industry has asked the HKD SNARC about disinfectants on eggs, so that they could inactivate any viruses on the outside of eggs during hatching (most are outside the egg).

In some testing this spring, the iodine product Ovadine, at the recommended rate for fish eggs (100 mg/L for 10 min), caused mortalities in golden shiner and fathead minnow eggs. The preliminary results also suggested that Ovadine was toxic to hybrid striped bass and largemouth bass eggs at the recommended dose. This researcher has conducted studies that demonstrate that copper sulfate works well for fungus on eggs and relatively high doses are safe. Their previous drug approval research showed that 10 mg/L copper sulfate is safe and effective for catfish eggs, but they also have used 100 mg/L with good results. Copper sulfate treatment of eggs has been used in the catfish industry as well as with hybrid striped bass and a largemouth bass hatchery. Since copper sulfate is being used for egg fungus, the baitfish industry brought up copper sulfate as a possible disinfectant for fish viruses. We will be proposing an effort to the NRSP7 that will investigate copper sulfate treatment of fish eggs for the control of external viral fish pathogens.

SOUTHERN – DR. THOMAS VICKROY

Progress of Work and Principal Accomplishments:

Active Regional Projects:
1. Ivermectin Medicated Feed Block for Control of Cattle Fever Tick in South Texas (ADR#352)

This project is a collaborative effort among the North-Central Region of MUADP (Iowa State University), the Southern Region of MUADP (University of Florida), USDA-ARS, USDA-APHIS, the Texas Animal Health Commission and the Cattle Fever Tick Eradication Program. The study represents a minor use in a major food animal species as determined by FDA-CVM. Work conducted thus far at UF has involved determination of ivermectin content in samples of medicated feed blocks. Analyses have been carried out using a modified version of the approved regulatory method for ivermectin determination in beef liver samples. The method has not yet undergone FDA review for concurrence. The medicated blocks contain a

proprietary undisclosed mixture of nutrients, minerals, other ingredients and molasses as a taste enhancer that is used for oral drug delivery to free-range cattle in pastures. Analysis of feed block samples for consistency and reproducibility of ivermectin content has continued during the report period. Unfortunately, the project faces several major hurdles before it can be considered for possible concurrence by the CVM. The most significant problem has been the continued impasse between Texas-based Postive Feeds and Merck-Merial to reach an agreement to support release of a Right of Reference letter. At present, the future direction of this project remains uncertain.

2. Lasalocid for Treatment of Coccidiosis in Pheasants (ADR#279)

This project is a collaborative effort between the North-Central Region (Iowa State University) and the Southern Region (University of Florida) of the MUADP. This study remains on hold with no activity during the past six months. At this time, both regions are awaiting guidance from the FDA regarding on-going GLP study requirements as well as future needs for quality assurance oversight of this and other projects. As background, a tissue residue depletion study protocol (number 2012-235-HFS) was submitted in September 2012 to the INAD exemption file for a project to investigate the use of lasalocid (Avatec®) Type A medicated article for the control of coccidiosis associated with infection by Eimeria colchici, E. duodenalis or E. phasiani in pheasants. If this project moves forward, the in-life phase of studies will be conducted at Iowa State under the supervision of Dr. Ron Griffith and the Southern Region will carry out marker (lasalocid) residue analyses of all tissue samples.

3. Fenbendazole in Game Birds (ADR#280)

This is a collaborative project among the North-Central, Western and Southern regions, although the Southern region has no direct role related to the in-life studies (North-Central Region) nor the analytical phase (Western Region). For details on the project history, please refer to those regional reports for progress updates.

Update on Other Programmatic Efforts and Changes

1. NRSP-7 Website: The Southern Region is responsible for maintaining and updating the NRSP-7 website, including MUMsRx and the RUSTi system that is used for tracking the status of regional projects. The information posted on the website has been updated with recent progress reports but remains in need of a major overhaul. Efforts on the website have been scaled back pending a decision on the future status of the program.

2. Anticipated Use of Project Outcomes: The findings from all of the studies above will be utilized to fulfill the data requirements for Public Master Files and, ultimately, for FDA/CVM approval of these drugs for use in minor species.

NORTH CENTRAL – DR. RONALD W. GRIFFITH

Progress of Work and Principal Accomplishments:

Goat CIDR-G Effectiveness

The study report is nearing completion.

Lasalocid in Pheasants Target Animal Safety

We have a technical section incomplete letter from ONADE. We are waiting on the outcome of the fenbendazole TAS technical report before re-submitting this one. The work has been published in the Avian Diseases journal.

Lasalocid in Pheasants Human Food Safety

The study protocol for the in-life phase at Iowa State was submitted from the Southern Region and we have received protocol concurrence. The FDA had questions on the analytical method and we had planned to complete method validation beginning in June, 2013. The method validation is on-hold pending guidance from the FDA primarily concerning requirements for GLP studies for the MUADP. The study itself has been given a lower priority due to lack of funding and uncertainty over GLP issues.

Draxxin Efficacy in Goats
This is now largely in the hands of the FDA/CVM. Zoetis may be working on this.

Fenbendazole Target Animal Safety in Pheasants
We received a technical section incomplete letter on the study report. Additional data, clarification revised statistical analysis and justification of study procedures have been submitted. The reproductive safety portion of the work was not acceptable but the label will just state that reproductive safety has not been demonstrated. A paper covering this work and the reproductive safety data has been published in Avian Diseases.

Ivermectin Cattle Fever Tick Efficacy
This project is being done in conjunction with Tom Vickroy in the Southern Region and a whole host of individuals with the Texas Animal Health Commission, the USDA-APHIS and the Cattle Fever Tick Eradication Program as well as with Postive Feeds, Ltd. A conference call was held in November to discuss how to proceed with this portion of the project. Two herds (pastures) have been totally cleared of cattle fever ticks and additional data is available on pastures with low tick burdens on which the cattle were fed the ivermectin tubs. It was concluded that a study report covering the data we have to date will be prepared and submitted to the FDA/CVM The right of reference from Merial is remains unresolved.

Pregnant Mare Serum Gonadotrophin-ADR 0353
A request was received to investigate the feasibility of performing studies to support FDA/CVM approval for Pregnant Mare Serum Gonadotropin to be used as a reproductive aid in small ruminants. A current review of the literature is being prepared with the goal of subsequently requesting a product development conference. No further action at this point.

PUBLICATIONS AND PRESENTATIONS

1) Rivera-Garcia, S., Angelos, J. A., Rowe, J. D., Byrne, B. A., Wetzlich, S. E., Van Liew, D. B., and Tell, L. A. (2014) Pharmacokinetics of ceftiofur crystalline-free acid following subcutaneous administration of a single dose to sheep, Am J Vet Res 75, 290-295.

2) McDonnel, S. J., Tell, L. A., and Murphy, B. G. (2014) Pharmacokinetics and pharmacodynamics of suberoylanilide hydroxamic acid in cats, J Vet Pharmacol Ther 37, 196-200.

3) Kinney, M. E., Lamberski, N., Wack, R., Foster, R., Neely, M., Tell, L., and Gehring, R. (2014) Population pharmacokinetics of a single intramuscular administration of tulathromycin in adult desert tortoises (Gopherus agassizii), J Vet Pharmacol Ther 37, 500-507.

4) Grismer, B., Rowe, J. D., Carlson, J., Wetzlich, S. E., and Tell, L. A. (2014) Pharmacokinetics of tulathromycin in plasma and milk samples after a single subcutaneous injection in lactating goats (Capra hircus), J Vet Pharmacol Ther 37, 205-208.

5) Griffith, R., Yaeger, M., Hostetter, S., Tell, L. A., Wetzlich, S., Vickroy, T., Lillie, B., MacFarlane, W., Laudenslager, T., Whitley, E., Dzikamunhenga, R., and Larson, W. (2014) Safety of fenbendazole in Chinese ring-necked pheasants (Phasianus colchicus), Avian Dis 58, 8-15.

6) Groocock, G.H., Getchell, R.G., Cornwell, E.R. Frattini, S.A. Wooster, G.A. and Bowser, P.R. (2013) Iodophor disinfection of walleye eggs exposed to viral hemorrhagic septicemia virus type iVB. North American Journal of Aquaculture. 75:25-33.

7) Wu, H., Baynes, R. E., Leavens, T., Tell, L. A., and Riviere, J. E. (2013) Use of population pharmacokinetic modeling and Monte Carlo simulation to capture individual animal

variability in the prediction of flunixin withdrawal times in cattle, J Vet Pharmacol Ther 36, 248-257.

8) Washburn, K. E., Fajt, V. R., Lawhon, S. D., Adams, L. G., Tell, L. A., and Bissett, W. T. (2013) Caprine abscess model of tulathromycin concentrations in interstitial fluid from tissue chambers inoculated with Corynebacterium pseudotuberculosis following subcutaneous or intrachamber administration, Antimicrobial Agents and Chemotherapy 57, 6295-6304.

ABSTRACTS

1. Smith J, Angelos J, Rowe J, Carlson J, Lee, L, Tell LA. Pharmacokinetics of flunixin meglumine in plasma and milk of domestic goats (*Capra aegagrus hircus*) following single subcutaneous dosing. UC Davis Goat Day, Davis, CA, February 1, 2014, UC Davis 36th Annual House Officer Seminar Day, Davis, CA, March 21st, 2014 and ACVIM Annual Meeting, Nashville, TN, June 4-7, 2014.

2. Breyer, K.E. 2013. Evaluating the efficacy of a low-dose Garlic Compound (Allicin) Against Infection With Aeromonas salmonicida In Rainbow Trout. Master Of Science Thesis, Cornell University. 45 Pp.

3. Breyer, K.E. , Getchell, R., Wooster, G., Ketola, G., and Bowser, P. (2013) Evaluating the efficacy of a low-dose garlic compound against Aeromonas salmonicida in Rainbow trout. 2013 Clinical Investigator's Day, Cornell University, Ithaca, New York. 18 March 2013. (Keb: Honorable Mention Award).

4. Breyer, K.E. , Getchell, R., Wooster, G., Ketola, G., and Bowser, P. (2013) Update! Garlic (Allicin): More than just flavor for your fish. 38th Eastern Fish Health Workshop, Gettysburg, PA. 29 April – 3 May 2013.

DEVELOPMENT OF ACTION ITEMS

- Going forward on funding, renewal discussions for monthly teleconferences

OTHER BUSINESS - None brought forward

FALL Meeting 2014 - The final decision on the timing of the meeting will be made during discussions at monthly teleconferences.

As there was no further business, the meeting was adjourned at 2:15 pm.

RESPECTFULLY SUBMITTED:
John G. Babish, Ph.D. Date: 8/1/14
Minor Use Animal Drug Program/NRSP-7 National Coordinator