Minutes
Minor Use Animal Drug Program/NRSP-7 Fall Meeting 2013
December 18th 2013 (Noon to 3:00 pm)

WEDNESDAY, DECEMBER 18TH 2013: **TELECONFERENCE**

TO VIEW THE MEETING REPORTS:

Connection Meeting Information
Meeting Name: MUADP Fal Meeting 2013
Summary:
Invited By: Amy Omer (Amy.Omer@fda.hhs.gov)
When: Wednesday, December 18th - 12:00 PM - 3:00 PM
Time Zone: Eastern Time (US and Canada)

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ATTENDEES

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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. John C. Baker (Michigan State University AES), Chairman of Administrative Advisors (AA), Margaret Smith (Cornell University, AES) and Phil Elzer (LSU, AES). The attending NIFA representative was Dr. Gary Sherman (Washington, DC) and the FDA liaisons were Drs. Meg Oeller and Amy Omer (Rockville, MD). Absent were administrative advisor Dr. Frances D. Galey (Western Region) and Regional Coordinator Thomas Vickroy (Southern Region).

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 NIFA/USDA, Administrative Advisors, the National Coordinator, FDA/CVM and the Regional Coordinators,

NIFA/USDA – DR. GARY SHERMAN
Funding for the FY 2013 NRSP-7 Hatch Multistate projects have all been awarded to CA, FL, IA and NY. 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.

Even if this were a good year, it is way too early in the FY-14 budget cycle to expect to

see distributions to states for the FY14. Because we are once again functioning on a CR, we are not permitted any prognostication about the timing of potential release of FY-14 distributions. Finally, what the Experiment Station System likely did was vote to fund at a projected level. Ultimately funding for any off the top subprogram in Hatch may be different if/when a budget is signed into law for FY-14.

Dr. Sherman, upon request, repeated his outline of the funding history of the MUADP delivered last spring.

1). Historically, MUADP/NRSP-7 enjoyed line item Special Grant funding from Congress (administered under NIFA's special grant authority) but this ended 3 years ago when 'earmarks' were greatly reduced.

2) MUADP/NRSP-7 is currently supported by Hatch funding. It was by virtue of the Program's legitimacy as an NRSP that, when special grant funding ended, there was a secondary (Hatch) Authority under which funding could be made available to the program, at the discretion of the directors of the system of US Agricultural Experiment Stations (AESs).

3) NIFA and Congress continue to support and fund the Hatch program. The Hatch Act authority provides funds to be distributed by NIFA on a formula basis to Ag Experiment Stations co-located at Land Grant colleges and universities. NRSPs and MultiState Committees, proposed and administered by AES Directors, are supported as a specified apportionment from Hatch funds. AES directors determine levels of funding for NRSPs and Multi-State Committees based on available funds.

4) NIFA Budget cuts for 2013 include loss of $180 M in mandatory funding that was not renewed, and the effects of Sequester. The ~18% overall cut to NIFA is expected to be applied roughly evenly across all NIFA programs. The Hatch program will likely experience this % decrease and this should be expected to impact Hatch sub-programming like NRSPs.

5) Efforts continue to search for a Western Region Administrative advisor for NRSP-7

6) NIFA is cognizant of the exploratory efforts underway related to a possible merger with IR-4. The Agency will consider consensus restructuring possibilities if and when the leaderships of both NRSP-7 and IR-4/NRSP-4 come to one or more mutually agreed upon potential merger strategy(ies).

7) Dr. Sherman, NIFA Liaison to NRSP-7, 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.

REPORT FROM THE ADMINISTRATIVE ADVISORS - DR. JOHN BAKER (CHAIR)

Dr. Baker reported that the Fall meeting of ESCOP on September 25, 2013, NRSP7 was approved for $325,000 for FY2014. Here are the official ESCOP NRSP actions taken during the fall ESCOP meeting, held on September 25, 2013 in Columbus, OH:

- NRSP_temp281 (now NRSP8) was approved for a new five-year term (10/2014 to 9/2019) with an annual OTT budget of $500,000.
- NRSP1 was approved for an increase from $50,000 to $75,000. New distributions: $53,410 should go to Colorado State for impact reporting and $21,590 goes to Rutgers to support the NIMSS system.
- All other NRSP OTT budgets will remain the same for FY2014 (assuming no cuts from sequestration):
    - NRSP3: $50,000
    - NRSP4: $481,182
    - NRSP6: $150,000
    - NRSP7: $325,000
    - NRSP9: $175,000

Dr. Baker reviewed the renewal process and outlined anticipated changes for this year. The NRSP-7 one-year proposal is due January 15th of 2014 and he and Dr. Babish have been working through the outline to complete the proposal on time.

Once again, Dr. Baker stressed the need to develop a broader listing of stakeholder groups to align with additional NIFA priorities of sustainable agriculture and support of the rural, family farms.

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

One-Year Renewal

The NRSP-7 membership discussed at length either the 1-year renewal or 5-year renewal after the response from IR-4. The main issue facing NRSP-7 is the loss of funding in the USDA budget a number of years ago. The AES have been keeping the project alive for the last several years through "off the top" funds, which is at a reduced level than the previous USDA funding. There are serious concerns the project can remain viable if funding is reduce with the renewal (new guidelines, maintenance funding).

The application for renewal was submitted in Sept 2013 and the final application is due Jan 15th, 2014. The Sept application was sent around earlier this morning.

The decision to go with a I year renewal was based on the following:

1. Continue discussions with IR-4 in the area of collaboration. Even though they would remain separate projects there are opportunities for collaboration and cooperation between the two projects. A 1-year renewal would allow this process to move forward.
2. To provide time for one final appeal to Congress re Farm Bill, USDA and FDA for stable funding (and increased in funding). This would also allow more time for the engagement of stakeholders in this process. Emphasize prudent use of antimicrobials in veterinary medicine necessitates the continuation of the MUADP.
3. Increase stakeholder base through inclusion of natural product manufacturers, pesticide manufacturers, etc.
4. CDC publications and news releases. They have come down hard on antibiotic use in veterinary medicine. I'm attaching a copy of their publication. See especially pages 36-37. While coming down hard on 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.
5. 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.

Again, NRSP-7 is on life support right now. Reduction of funding from the AES by moving the project to maintenance support makes it difficult for the project to continue.

The application for renewal was submitted in Sept 2013 and the final application is due Jan 15th, 2014. The Sept application was sent around earlier this morning.

Schedule: Our funding for 2014 has been approved. The one-year renewal is for FY2015. If we are not approved for continued funding, we get one year (2016) to dismantle the program.

FDA Announced Minor Use/Minor Species (MUMS) Grant Program Request for Applications Open Period due January 3, 2014

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

Erythromycin Salmonids I-006013 – Environmental Assessment hopefully can be done by FDA/CVM; After that, NRSP7 will probably be done with this project

CIDR Goats I-011389 - Ron is working diligently with FDA/CVM to see what data for efficacy can be submitted. Conference call with CVM has occurred and Dr. Oeller is hopeful that the data that exists can be submitted and hopefully accepted.

Fenbendazole Pheasants I-010062 – Dr. Oeller says that she can address the efficacy portion and the Environmental. I believe Ron has sent the Response for Target Animal Safety to CVM.

Lasalocid Pheasants I-009096 - From what I understand, there are challenges with getting the old method bridged due to availability of materials. Dr. Vickroy had submitted a validation protocol. Not sure if there is a clear path to get this method validated.

Tulathromycin Goats I-011512 - If Human Food Safety is to be done, entire animal study needs to be repeated. Can't figure out a protocol for efficacy. This project needs to be put on low priority.

Tulathromycin Sheep I-011513 - Not planning to pursue this one.

Nuflor Gold Sheep I-011836 Drs. Oeller and Bailey are going to look into what can be combined with the old Nuflor and Nuflor Gold. Otherwise, this project would also be put on hold.

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 12/2013: No new progress on this project.

ADR#299 - Pirlimycin for Dairy Goats

Project on hold until funding is identified and CIDR goat studies are completed.

ADR#338 – Spectramast™ LC Sterile Suspension for Mastitis in Dairy Goats

Project on hold until funding is identified and CIDR goat studies are completed.

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 12/2013: 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). Update 12/2013: HFS report received concurrence from CVM, April 2014.

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 12/2013: 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.

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 accepted for pulication in AJVR.

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 is on line via early release.

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.

Laboratory Report:

Most of the activity continues as sample analysis in the laboratory. Results and plans 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:

Finish sample analysis for goat flunixin and tulathromycin studies. Publish data for all of these

NORTHEAST REGION: DR. PAUL BOWSER

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 are conducting a cooperative project with the USGS Tunison Laboratory of Aquatic Science in which we are evaluating the use of allicin as a nutritional supplement for the reduction of *Aeromonas salmonicida* in salmonids.

Usefulness of the findings:

In all cases, the findings to date over the course of these projects serve as the foundation for continued work on these compounds.

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 are in the early stages of developing 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 is under review by CVM FDA.

Allicin for the reduction of Aeromonas salmonicida infection in salmonids

We were approached by Dr. George Ketola of the USGS Tunison Laboratory of Aquatic Sciences, Cortland, NY about a potential project to evaluate the ability of allicin, a garlic extract, to reduce the severity of various pathogens of fish. We initiated a collaborative project in which we are evaluating the ability of the allicin to reduce the severity of Aeromonas salmonicida infection in rainbow trout. Dr. Ketola has had a long career of fish nutrition research (the former name of the Cortland facility was the USFWS Tunison Fish Nutrition Laboratory) that spans well over 30 years. In this collaboration, Dr. Ketola formulates the rations and we utilize our biosecure fish research laboratories for the conduct of the challenge trials. The effort will serve as the Master of Science thesis research for Dr. Kate E. Breyer, who is a Resident in the Laboratory Animal Medicine Program at Cornell. She is pursuing the MS degree through the Cornell University Employee Degree Program. Thus, her salary support is from sources other than NRSP7. Given the financial limitation we are facing in the NE Region NRSP7, this collaboration between the Tunison Laboratory of Aquatic Sciences and the Laboratory Animal Medicine Program at Cornell is seen as an extremely economic means to conduct this research.

To date we have developed a standard bacterial challenge model to achieve an appropriate level of *Aeromonas salmonicida* infection following an IP challenge. This was followed by the first trial. Prior to the trial, for 14 days the fish were fed a diet in which allicin was added at 0.0, 0.5, 1.0 or 2.0% of the diet by weight. Fish were fed at 2% body weight per day. In this trial we did not observe a benefit from the addition of allicin to the diet at 0.0, 0.5, 1.0 or 2.0% of the diet when fish were fed at 2% of body weight per day. This protocol was based on a protocol reported in the literature in which the challenge pathogen was *Aeromonas hyhdrophila*. We will be repeating this trial to confirm the results of the first trial. If we again observe a lack of effect, we may continue the effort, but with a challenge that involves a water borne challenge with the bacterium.

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.

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:

The development of a 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. We expect that our efforts in developing a species grouping concept for fish will be a major undertaking in the upcoming years.

SOUTHERN – DR. THOMAS VICKROY

Progress of Work and Principal Accomplishments:

Active Regional Projects:

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

This pending project is a collaborative effort between the North-Central Region (Iowa State University) and the Southern Region (University of Florida) of MUADP. The primary role of the Southern region is to carry out drug analyses of all tissue samples. Previously, attempts to bridge the approved regulatory method for lasalocid analysis in bovine liver were unsuccessful in liver or skin from pheasants, which led to the failure of a human food safety trial. However, we have now solved all of the analytical problems and have a robust and reliable working method. That method has undergone a partial validation in samples of liver and skin with adhering fat from pheasants. In view of the previous difficulties in mounting a working analytical method, the validated method was submitted to the CVM along with the protocol for the in-life phase of studies. Pending CVM review and concurrence with the study protocol and the analytical method, this project will be in position to move forward with the in-life phase studies in the North-Central Region. The anticipated time line for project start up is October of 2012.

2. Ivermectin Medicated Feed Block for Control of Cattle Fever Tick in South Texas (ADR#352)

Preliminary work has continued slowly on this project. The study represents a minor use in a major food animal species and is a collaborative effort among several agencies and institutions, including the North-Central Region (Iowa State University) and the Southern Region (University of Florida) of the MUADP as well as USDA-ARS and APHIS. The project has not yet received concurrence from the CVM and it is unclear whether it will proceed or be completed. The primary role of the Southern Region is to conduct analytical testing of ivermectin levels in medicated feed blocks that are formulated by Postive Feeds, Inc. These blocks, which will be used for drug delivery to cattle in pastures, contain a complex mixture of nutrients, minerals and numerous other ingredients, including molasses as a taste enhancer. We have been successful in adapting the approved regulatory method for ivermectin analysis in order to determine ivermectin levels in the feed blocks. At this time, we have completed analysis of three batches of medicated blocks, each containing 16 to 24 individual blocks. Work is currently in progress as we continue to analyze medicated blocks for consistency of drug levels.

3. Fenbendazole in Game Birds (ADR#280)

This is a collaborative project among the North-Central, Western and Southern regions. The Southern Region has no principal role related to in-life studies (North-Central Region) nor the analytical phase (Western Region), so any progress updates will be contained in those regional reports.

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 for tracking the status of regional projects. In addition, the Southern Region coordinator organizes and coordinates monthly teleconferences among the regional coordinators and administrators. The next teleconference is scheduled tentatively June 2012.

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

Goat CIDR-G Effectiveness

The study report is still in preparation.

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 Tissue Residue

ONADE asked for additional data and clarification for the study report. The Western Region is leading the response effort.

Draxxin Efficacy in Goats

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

Fenbendazole Human Food Safety in Pheasants

The Western and North Central Regions combined to do this study. The technical section is complete.

Fenbendazole Target Animal Safety in Pheasants

We received a technical section incomplete letter on the study report. Additional data, clarification 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 conference call is scheduled for Dec. 23 with the stats reviewer to address one of their concerns. A paper covering this work and the reproductive safety data was submitted to Avian Diseases and is currently in press.

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

1. 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.

2. 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.

3. Spitsbergen, J. M., Frattini, S. A., Bowser, P. R., Getchell, R. G., Coffee, L. L., Wolfe, M. J., Fisher, J. P., Marinovic, S. J., and Harr, K. E. (2013) Epizootic neoplasia of the lateral line system of lake trout (Salvelinus namaycush) in New York's Finger Lakes, Vet Pathol 50, 418-433.

4. Snook, T. S., White, S. D., Hawkins, M. G., Tell, L. A., Wilson, L. S., Outerbridge, C. A., and Ihrke, P. J. (2013) Skin diseases in pet rabbits: a retrospective study of 334 cases seen at the University of California at Davis, USA (1984-2004), Veterinary dermatology.

5. Shelver, W. L., Tell, L. A., Wagner, S., Wetzlich, S. E., Baynes, R. E., Riviere, J. E., and Smith, D. J. (2013) Comparison of ELISA and LC-MS/MS for the Measurement of Flunixin Plasma Concentrations in Beef Cattle after Intravenous and Subcutaneous Administration, J Agric Food Chem 61, 2679-2686.

6. McDonnel, S. J., Tell, L. A., and Murphy, B. G. (2013) Pharmacokinetics and pharmacodynamics of suberoylanilide hydroxamic acid in cats, J Vet Pharmacol Ther.

7. Macpherson, M. L., Giguere, S., Hatzel, J. N., Pozor, M., Benson, S., Diaw, M., Sanchez, L. C., Vickroy, T. W., Tell, L., Wetzlich, S., and Sims, J. (2013) Disposition of desfuroylceftiofur acetamide in serum, placental tissue, fetal fluids, and fetal tissues after administration of ceftiofur crystalline free acid (CCFA) to pony mares with placentitis, J Vet Pharmacol Ther 36, 59-67.

8. Grismer, B., Rowe, J. D., Carlson, J., Wetzlich, S. E., and Tell, L. A. (2013) Pharmacokinetics of tulathromycin in plasma and milk samples after a single subcutaneous injection in lactating goats (Capra hircus), J Vet Pharmacol Ther.

9. Goetting, V., Lee, K. A., Woods, L., Clemons, K. V., Stevens, D. A., and Tell, L. A. (2013) Inflammatory marker profiles in an avian experimental model of aspergillosis, Medical mycology 51, 696-703.

10. DeDonder, K. D., Gehring, R., Baynes, R. E., Tell, L. A., Vickroy, T. W., Apley, M. D., and Riviere, J. E. (2013) Effects of new sampling protocols on procaine penicillin G withdrawal intervals for cattle, J Am Vet Med Assoc 243, 1408-1412.

11. Dechant, J. E., Rowe, J. D., Byrne, B. A., Wetzlich, S. E., Kieu, H. T., and Tell, L. A. (2013) Pharmacokinetics of ceftiofur crystalline free acid after single and multiple subcutaneous administrations in healthy alpacas (Vicugna pacos), J Vet Pharmacol Ther 36, 122-129.

12. Cornwell, E. R., Labuda, S. L., Groocock, G. H., Getchell, R. G., and Bowser, P. R. (2013) Experimental Infection of Koi Carp with viral hemorrhagic septicemia virus type IVb, J Aquat Anim Health 25, 36-41.

13. Cornwell, E. R., Bellmund, C. A., Groocock, G. H., Wong, P. T., Hambury, K. L., Getchell, R. G., and Bowser, P. R. (2013) Fin and gill biopsies are effective nonlethal samples for detection of viral hemorrhagic septicemia virus genotype IVb, J Vet Diagn Invest 25, 203-209.

14. Coffee, L. L., Casey, J. W., and Bowser, P. R. (2013) Pathology of tumors in fish associated with retroviruses: a review, Vet Pathol 50, 390-403.

15. Coffee, L. L., Bogdanovic, L. B., Cushing, T. L., and Bowser, P. R. (2013) Pharyngeal odontoma in an adult walleye (Sander vitreus), Vet Pathol 50, 483-487.

DEVELOPMENT OF NEW ACTION ITEMS

1. Going forward on funding, renewal discussions for monthly teleconferences

OTHER BUSINESS

None brought forward

SPRING 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 3:05 pm.

RESPECTFULLY SUBMITTED:
John G. Babish, Ph.D. Date: 3/12/14
Minor Use Animal Drug Program/NRSP-7 National Coordinator