ANNUAL NRSP-7 SPRING MEETING 2009 MINUTES
January 26th and 27th, 2009

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MONDAY JANUARY 26TH, 2009
PLACE: Westin Meeting Room, Westin Washington, D.C. City Center, 1400 M Street NW Washington, DC 20005.
PARTICIPANTS: Babish, John - Cornell University (jgb7@cornell.edu); Tell, Lisa (latell@ucdavis.edu) - University of California, Davis; Webb, Alistair (Webb@ufl.edu) - University of Florida; Griffith, Ronald (rgriffit@iastate.edu) - Iowa State University; Bowser, Paul (prb4@cornell.edu) - Cornell University; Adams, Garry (gadams@cvm.tamu.edu) - Texas A&M; Baker, John (Baker@anr.msu.edu) - Michigan State University; and; Sherman, Gary (gsherman@CSREES.USDA.GOV) - USDA/CSREES; Oeller, Meg (moeller@cvm.fda.gov) - FDA/CVM; Lutschaunig, Mark (MLutschaunig@avma.org) - American Veterinary Medical Association; Luke, Gina - American Veterinary Medical Association; Smith, Brian (Bsmith@aavmc.org) - American Association of Veterinary Medical Colleges; Engelbach, Karl (kmengelbach@ucdavis.edu) - UC Davis; Miller, Diane (dlm72@cornell.edu) – Cornell University; Bryant. Dustin (dustinbryant@meyersandassociates.com) - Meyers and Associates for Texas A&M University; Schnick. Rosalie (RozSchnick@centurytel.net) - National Coordinator for Aquaculture New Animal Drug Applications; Rybolt, Michael – The National Turkey Federation.

8:30 – NOON NRSP-7 BUSINESS MEETING
PLACE: Westin Meeting Room, Westin Washington, D.C. City Center, 1400 M Street NW Washington, DC 20005.
PARTICIPANTS: The NRSP-7 National and Regional Coordinators: John Babish (Cornell University), Lisa Tell (University of California, Davis), Dr. Alistair Webb (University of Florida), Dr. Ronald Griffith (Iowa State University), and Dr. Paul Bowser (Cornell University). NRSP-7 Administrative Advisors Dr. Garry Adams, Chairman of Administrative Advisors (Texas A&M), Dr. David Thawley (University of Nevada), Dr. John Baker (Michigan State University) and (Cornell University). The USDA/CSREES liaison Dr. Gary Sherman (Washington, DC); and the FDA/CVM liaison Dr. Meg Oeller (Rockville, MD).

8:30 – 9:30 am
REPORT FROM USDA/CSREES

Dr. Gary B. Sherman, who reviewed the new appointments in USDA/CSREES as well as potential NRSP-7 funding in FY09 and FY10, gave the report from USDA-CSREES. As neither the FY09 nor the FY10 budgets had been released, Dr. Sherman's presentation focused on the speculative nature of their content.

REPORT FROM ADMINISTRATIVE ADVISORS

Dr. L. Garry Adams delivered the report from the Administrative Advisors. He began by praising the regional coordinators for their activities with university government relations personnel and the Stakeholders Advisory Committee. Also noted was the significant movement on project deliverables over the last six months. Dr. Adams gave special credit to the Regional Coordinators who have been managing limited funds extremely well and have enabled the Program to continue to move forward.

REPORT FROM FDA/CVM

Dr. Meg Oeller reviewed her stakeholder presentation for the group detailing the interactive role of NRSP-7 and the Center for Veterinary Medicine.

REPORT FROM THE NATIONAL COORDINATOR

Dr. John G. Babish presented an update on the Multi-Regional Funding request for FY10. The request was submitted January 23rd in the amount of $325,000 and would be reviewed by the SAAES Directors this upcoming spring.

Comments of the five-year review report were shared with the group. Overall, the Review Committee was impressed with the remarkably efficient productivity of the NRSP-7 program over its 24-year existence especially in the face of decreasing and uncertain funding. The Committee made several specific observations and recommendations for improvement in the programs effectiveness. A summary of some of those suggestions follows here:

- Funding levels are far below the level needed to adequately address the mission of this program. NRSP-7 should continue to work closely with university government relations personnel and stakeholders to address federal funding of the program and underscore the severe funding shortage.
- A greater emphasis should be placed pursuing all three aspects of the NRSP-7 Mission with equal vigor. That is the Technical Committee should consider (i) the identification of animal drug needs for minor species and minor uses, (ii) the generation and dissemination of data and (iii) the facilitation of FDA/CVM approvals with equal weight. All three activities are needed for a productive program.
- Thoughts should be given to form a central portal of PMF submissions through which all data would be passed before submission to FDA.
- Consideration of hiring a technical writer for a central protocol preparation and review, to put data packages in a FDA-friendly format and to insure a smoother flow of data. Quality assurance functions related to both GLP and GCP certifications could also be coordinated here, as could legislative activities that will be critical for continued funding.
- A re-evaluation of the managing off-site clinical trials to assure GCP criteria are met should be conducted.
- Under the current funding constraints, it is crucial that the four regions focus on a smaller number of drug approvals to achieve more successes in a timelier manner.
- Funding is orders of magnitude below what is minimally required to carry out the mission of the Program. The current landscape of drug regulation needs to be better defined as those areas addressed by major pharmaceutical manufacturers for "economically viable" options under MUMS, by PMFs to better defined the area under NRSP-7 and for other uses under AMDUCA, where NRSP-7 data are still required for proper use for dissemination through such programs as FARAD.

The Review Team concludes that NRSP-7 program provides an excellent example of how a relatively small investment of public funds can be leveraged to provide highly effective,

efficient outcomes that have significant economic impact and benefit to animal well being and public safety. However, without increased funding it is doubtful that the remarkable success of this program can continue.

With the completion of the five-year business plan, the process of the 2004-2009 review, the Program review process is nearly finished. What remains is a written response to the review team report. All material will then be submitted to the National Information Management and Support System (NIMSS) database for review.

9:30 – 10:30

ACCOMPLISHMENTS FROM THE REGIONS AND NEW PROJECTS:

Northeastern – Dr. Paul R. Bowser

Progress of the work and principal accomplishments

Hydrogen Peroxide Project:

INAD 9493 Hydrogen Peroxide as a Therapeutic Compound for Bacterial Gill Disease in Fish. No additional work has been performed on this project during this study period.

Species Grouping Project:

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

A primary constraint in the availability of therapeutic compounds for the Aquaculture Community is the relatively large number of fish species that are currently cultured or that have significant potential as commercial species. Currently, research in support of a label for a therapeutic compound must be performed separately for each species for which the label is desired. We have undertaken a project designed to show the similarities in how drugs are handled by different fish species with the goal of supporting a species (crop) grouping concept for fish. We have conducted these studies in a collaborative effort with the Western Region NRSP7. Within this context, to date we have completed the following preliminary Human Food Safety/Tissue Depletion Studies using the following test articles as model compounds:

Oxytetracycline:

1. Walleyes, freshwater fish, 15C and 20C
2. Tilapia, freshwater fish, 25C and 30C
3. Hybrid Striped Bass, saltwater fish, 20C and 25C
4. Summer Flounder, saltwater fish, 17C and 20C
5. Rainbow Trout, cold water trial (8C)

Romet-30:

1. Walleyes, freshwater fish, 20C and 25C
2. Tilapia, freshwater fish, 25C and 30C
3. Hybrid Striped Bass (would not accept ration; Species removed from Romet trials)
4. Summer Flounder, saltwater fish, 17C and 20C

Florfenicol (10 mg/Kg/d, 10d):

1. Walleyes, freshwater fish, 20C and 25C
2. Tilapia, freshwater fish, 25C and 30C
3. Hybrid Striped Bass, saltwater, 20C, 25C

Florfenicol (Effect of fish size)

1. Tilapia – 100 gm, freshwater fish,
   25C, 15 mg/Kg, 10d
2. Tilapia – 250 gm, freshwater fish,

25C, 15 mg/Kg, 10d

3. Tilapia – 500 gm, freshwater fish,
   25C, 15 mg/Kg, 10d

Several attempts were made to conduct human food safety studies for Romet-30 in hybrid striped bass. Additional trials where the new Romet-TC was used were also met with a lack of palatability. Therefore, we will not include hybrid striped bass in our efforts with Romet.

Usefulness of the findings:

In all cases, the findings of these projects serve as the foundation for continued work on these compounds. The Human Food Safety Studies completed to date 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 (Florfenicol) in trout, salmon and catfish.

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

Future work is being hampered by a lack of funds in the Northeast Region. Should funding become available, we propose to conduct 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.

Other:

We are also considering the development of a project that centers on the question of disinfection of fish eggs to prevent the vertical transmission of Viral Hemorrhagic Septicemia Virus.

Publications issued or manuscripts approved during the year: (**see "Principal Publications" at end of report)**

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.

Target animal safety studies have been completed in both rainbow trout and walleye. Information collected during these studies constituted the subject of eight manuscripts in the peer-reviewed literature and several presentations at scientific meetings. Our raw data and a

peer reviewed publication (see Saez and Bowser 2000 below) describing discharge kinetics of hydrogen peroxide from a fish hatchery were provided to the U.S. Geological Survey Upper Midwest Environmental Sciences Center, La Crosse, Wisconsin, for their use in the recent submission that resulted in a label for hydrogen peroxide. We also provided reprints of our eight peer reviewed publications to the Sponsor in response to their request as they prepared their "all other relevant information" submission. The manuscripts provided were the following:

Tort, M.J., A.J. Kuhl, G.A. Wooster and P.R. Bowser. 1998. Modification of tolerance of walleye (*Stizostedion vitreum*) to bath treatment with hydrogen peroxide. Journal of the World Aquaculture Society 29:499-504.

Saez, J.A. and P.R. Bowser. 2000. Hydrogen peroxide concentrations in hatchery culture units and effluent during and after treatment. North American Journal of Aquaculture 63:74-78.

Tripi, C.M. and P.R. Bowser. 2001. Toxicity of hydrogen peroxide to pre-exposed young-of-the-year walleye (*Stizostedion vitreum*): effects of water quality and age of fish. Journal of the World Aquaculture Society 32:416-421.

Tort, M.J., C. Jennings-Bayshore, D. Wilson, G.A. Wooster and P.R. Bowser. 2002. Assessing the effects of increasing hydrogen peroxide dosage on rainbow trout(*Onchorhynchus mykiss*) gills utilizing a digitized scoring methodology. Journal of Aquatic Animal Health 14:95-103.

Tort, M.J., D. Pasnik, C. Fernandez-Cobas, G.A. Wooster and P.R. Bowser. 2002. Quantitative scoring of gill pathology of walleyes (*Stizostedion vitreum*) exposed to hydrogen peroxide. Journal of Aquatic Animal Health 14:154-159.

Tort, M.J., C. Fletcher, G.A. Wooster, and P.R. Bowser. 2003. Stability of hydrogen peroxide in aquaria as a fish disease treatment. Journal of Applied Aquaculture 14:(3/4) 37-45.

Tort, M.J., G.A. Wooster and P.R. Bowser. 2003. Effects of Hydrogen Peroxide on Hematology and Blood Chemistry Parameters of Walleye (*Stizostedion vitreum*). Journal of the World Aquaculture Society 34:236-242

Tort, M.J., D. Hurley, C. Fernanzez-Cobas, G.A. Wooster and P.R. Bowser. 2005. Effects of hydrogen peroxide treatment on catalase and glutathione activity in walleye (*Sander vitreus*). Journal of the World Aquaculture Society 36(4):576-585.

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

Our efforts have focused on evaluation of a species grouping concept for finfish. Within this effort we have conducted Human Food Safety/Tissue Elimination Studies as follows:

Oxytetracycline

Tilapia (25C, 30C) - completed
Walleye (15C, 20C) - completed
Hybrid Striped Bass (20C, 25C) - completed
Summer Flounder (17C, 20C) – completed

Results of studies conducted in the above four fish species are summarized in the publication:

Chen, C.-Y., R.G.Getchell, G.A.Wooster, A.L. Craigmill and P.R. Bowser. 2004. Oxytetracycline residues in four species of fish after 10-day oral dosing in feed. Journal of Aquatic Animal Health 16:208-219.

Rainbow Trout, cold water trial (8C) - completed

Romet-30
Tilapia (25C, 30C) - completed
Walleye (20C, 25C) – completed
Summer Flounder (17C, 20C) – completed

Results of studies conducted in the above three fish species are summarized in the publication:

Kosoff, R.E., C.-Y. Chen, G.A. Wooster, R.G. Getchell, Clifford, A.L. Craigmill and P.R. Bowser. 2007. Sulfadimethoxine and Ormetoprim Residues in Three Species of Fish After 5-day Oral Dosing in Feed. Journal of Aquatic Animal Health 19:109-115

Hybrid Striped Bass (20C, 25C) - did not accept feed medicated with Romet-30; palatability problems; two additional trials were attempted with feed medicated with Romet-TC (a product developed to avoid palatability problems). These additional studies were also unsuccessful because of lack of feed acceptance due to apparent palatability problems by the hybrid striped bass. No further work with Romet-30 or Romet-TC is currently planned.

Aquaflor (10 mg/Kg/d X 10 days)
Tilapia (25C, 30C) - completed
Walleye (20C, 25C) - completed
Hybrid Striped Bass (20C, 25C) - completed

Aquaflor (15 mg/Kg/d X 10 days)
Tilapia
100 gm fish - completed
250 gm fish - completed
500 gm fish - completed

Results of studies conducted with Aquaflor are summarized in the following two publications that have been accepted for publication:

Kosoff, R.E., C.-Y. Chen, G.A. Wooster, R.G. Getchell, A. Clifford, J.L. Craig, P. Lim, S.E. Wetzlich, A.L. Craigmill, L.A. Tell and P.R. Bowser. 2009. Florfenicol Residues in Three Species of Fish After 10-day Oral Dosing in Feed. Journal of Aquatic Animal Health. In press

Bowser, P.R., R.E. Kosoff, C.-Y. Chen, G.A. Wooster, R.G. Getchell, J.L. Craig, P. Lim, S.E. Wetzlich, A.L. Craigmill, and L.A. Tell. 2009 Florfenicol Residues in Nile Tilapia After 10-day Oral Dosing in Feed: Effect of Fish Size. Journal of Aquatic Animal Health. In press

Our protocol employed the optimum culture temperature for each fish species, plus one additional lower temperature at which the species might be cultured in an economically viable manner. A preliminary evaluation of our data suggests that Oxytetracycline and Romet-30 were eliminated from the edible portion of the fish at rates that will very likely be within the current label for salmonids and channel catfish.

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. Additional work is currently being impacted by a lack of funds in the Northeast Region.

3) Incomplete work or areas needing further investigation:

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

Principal Publications (during the past year):

Kosoff, R.E., C.-Y. Chen, G.A. Wooster, R.G. Getchell, A. Clifford, J.L. Craig, P. Lim, S.E. Wetzlich, A.L. Craigmill, L.A. Tell and P.R. Bowser. 2008. Florfenicol Residues in Three Species of Fish After 10-day Oral Dosing in Feed. Journal of Aquatic Animal Health. In press

Bowser, P.R., R.E. Kosoff, C.-Y. Chen, G.A. Wooster, R.G. Getchell, J.L. Craig, P. Lim, S.E. Wetzlich, A.L.Craigmill, and L.A. Tell. 2008. Florfenicol Residues in Nile Tilapia After 10-day Oral Dosing in Feed:Effect of Fish Size. Journal of Aquatic Animal Health.In press

NORTH CENTRAL – DR. RONALD W. GRIFFITH

Sheep CIDR-G Tissue Residue Study

This study was performed by Dr. Dennis Hallford at New Mexico State University in cooperation with both the Western and North Central Regions. NRSP-7 was informed on January 5, 2009 that the Office of New Animal Drug Evaluation had accepted the study report. This completed the data package required of NRSP-7 for approval of CIDR-G's in sheep for a zero time withdrawal period.

Goat CIDR-G Milk Residue

Both the NC and Western Regions of NRSP-7 are supporting these studies. The in-life phase of milk residue study was performed at UC-Davis in fall 2007 and Dr. Hallford at New Mexico State University performed the analytical phase. The study report has been recently submitted to the FDA/CVM. The data indicate that progesterone levels in the milk of pregnant goats are greater than progesterone levels in the milk of CIDR-treated goats.

Goat CIDR-G Tissue Residue

Currently planned for Fall 2009. Dr. Dennis Hallford at New Mexico State University plans to perform both the in-life phase and residue analysis.

Goat CIDR-G Effectiveness

Re-revision of the protocol is underway. Hopefully study will begin in late summer/fall 2009.

Draxxin Target Animal Safety in Goats

The in-life phases of the study were completed on March 22, 2008. The tissues from the untreated control and high-dose-group goats were examined for histopathology. Some minor lesions were observed in both groups and it was decided to examine the tissues from the 1X and 3X groups just in case ONADE would want that data. All the goats remained in good health except for one untreated control goat that developed respiratory disease. A few of the goats had some scattered gross lesions that seemed to be related to infectious processes rather than any toxic effects of the drug. In addition to the TAS portion of the study, we collected tissues and plasma for tulathromycin analysis for publication purposes.

Draxxin Efficacy in Goats

The protocol for a natural exposure model has been accepted by CVM. However, the studies were predicted to take three to six years to complete and require a significant portion of the financial resources of the NC Region. An alternative protocol based upon determination of AUC/MIC was prepared and submitted. However, ONADE wanted us to base statistical significance by comparison to cattle AUC/MIC. We were asked to provide an alternative target for determining effectiveness. It was decided that we needed some preliminary analytical and MIC data in order to set a realistic target. We have procured and tested a small group of bacterial isolates for MIC's. The MIC's are very close to those described for cattle. Plasma samples were collected from 6 goats and these have been analyzed for tulathromycin levels.

Draxxin Tissue Residue

The protocol has been reviewed by ONADE and there were relatively few comments. The protocol was amended and sent to Scott Wetzlich (Western Region NRSP-7) who will be doing the analysis. The methods for tissue extraction and tulathromycin analysis are currently being developed and validated. This study can begin whenever assay validation is complete. We will have tissues from goats at 2-, 3-, 4- and 5-weeks post treatment for determination of a target end point for the tissue residue study.

Lasalocid Efficacy in Pheasants

Drs. Larry McDougald and Lorraine Fuller at the University of Georgia performed the study with the assistance of Dr. Thomas McQuistion from Milliken University. A draft of the final report and an associated paper for publication was received on April 16, 2008. The full study report has been received and forwarded to Sandy Ogletree at UC-Davis for QA.

Lasalocid TAS in Pheasants

The protocol for this study was submitted to ONADE for review and was returned in early July. Drs. McDougald and Fuller have agreed to perform this study as well.

Lasalocid Human Food Safety in Pheasants

The protocol for this project is being revised and the study may be conducted in 2009 if the assay is validated.

Regulin (melatonin) implants for sheep

No activity to report. There does not seem to be much interest in this product either from the manufacturer or the sheep and goat industry.

Bioclip for Sheep

No activity to report. Does not seem to be much interest.

Fasinex (Triclabendazole) for Deer and Elk

No Activity to report. A major obstacle is that the drug is not currently marketed for cattle in the U.S.

WESTERN – DRS. LISA TELL

PROGRESS OF WORK AND PRINCIPAL ACCOMPLISHMENTS:

ACTIVE Regional Projects:

ADR#325 - Florfenicol for sheep for respiratory disease

Schering-Plough has been contacted and is interested in pursuing a bioequivalence study for the sheep using the new formulation. We are preparing to re-initiate communication with FDA/CVM to find out what is needed and possibly repeat the studies.

ADR#324 - Progesterone CIDRs for Goats (TAS and Milk Residue Study)

Target Animal Safety report has been accepted by FDA/CVM (February 20, 2008). Milk residue study has been completed. The final technical report was sent to FDA/CVM in December 2008.

ADR#272 - **Romet for Game birds**

See species grouping report.

ADR#299 - Pirlimycin for Dairy Goats

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

ADR#295 - Strontium Chloride for Salmonids. Steve Schroeder

There is nothing to report. Status of the project needs to be changed.

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

Mark Gaikowski with the U.S. Geological Survey (Upper Midwest Environmental Sciences Center in La Crosse, Wisconsin) is working in conjunction with NRSP-7 to revise and review specific sections of the Environmental Assessment Report for resubmission to CVM.

Work continues to summarize the physical chemistry of erythromycin thiocyanate. All samples have been processed and analyzed. Because of the physical characteristics of ERTT, an empirical pKa could not be established. However, it is expected that a derived pKa will be calculated. A draft manuscript is presently in preparation.

The report for the range-finding chronic toxicity study for *Daphnia magna* is in USGS review and should be finalized in the first quarter of 2009. A regulated chronic toxicity study will be initiated the week of Jan 26, 2009. The chronic study will provide the pivotal toxicity endpoint for the EA. The resultant final study report will likely be completed in the second quarter of 2009.

ADR# 311 –Lincomycin soluble powder for foulbrood disease in Honeybees

Dr. Margaret Oeller is coordinating the data summary/report preparation for CVM submission.

Collaborative Projects:

ADR#280 - Fenbendazole in Game Birds (Pheasants, bobwhite quail, partridge)

See Southern Region Report.

Ms. Ogletree and Dr. Webb met in February 2008 and discussed concerns regarding the QA portion of this project. Dr. Webb will be submitting his final report to FDA/CVM in January 2009.

Species Grouping Fish:

See North Eastern Region Report.

Sample analysis for florfenicol is complete and the two manuscripts have been accepted for publication.

ADR# 235-Lasalocid in Ring-Necked Pheasants

See North Central Region Report. The study director for this study was reverted back to Dr. Ronald Griffith of the North Central Region and is currently under quality assurance review (by Ms. Sandy Ogletree) for the efficacy portion of the study.

ADR#324 – Progesterone CIDRs for Goats: Efficacy Study

See North Central Region Report.

Dr. Griffith submitted the study protocol to CVM. The UC Davis portion of the study is to be performed in fall of 2009. UC Davis Animal Care and Use protocol for this study has been approved.

ADR#340 - Tulathromycin in Goats

The plasma method was established and our laboratory analyzed 440 samples from the TAS and preliminary PK studies. Emphasis will now shift back to establishing and validating the tissue methods. At this time, the Western region is working on establishing the approved analytical method in our laboratory. Validations of liver and muscle are nearly complete. Validation of kidney is underway and fat will follow shortly.

Other Projects:

Avian Species Grouping

Kristy Cortright finished work on the *in vitro* and *in vivo* studies. She is completing her last manuscript resulting from her PhD thesis. The manuscript should be published this year.

Excede in Goats:

In collaboration with Drs. Rowe and Angelos, Dr. Elizabeth Dore (UC Davis 3rd year Food Animal Resident) completed a study evaluating the use of Excede in lactating and non-lactating goats. The data from this study were compiled and presented at two scientific venues for which Dr. Dore received a resident award at one of the meetings. The serum and milk samples have been analyzed and the PK data modeled. Dr. Dore is currently working on the manuscript and the manuscript will be submitted to JVPT for publication.

New Projects:

Nothing to report at this time.

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 all of the studies above will be utilized to fulfill the data requirements for the FDA/CVM approval of these drugs for use in minor species.

Work Planned for Remainder of the Year:

This year our primary goals are to start the CIDR-G Efficacy study, continue the method validation and analyses for the goat tulathromycin project, and finish up the salmonid erythromycin environmental assessment. Obtaining CVM concurrence for a florfenicol bioequivalence study will also be a major focus.

Publications issued or manuscripts approved since the last meeting:

Rowe, J, Tell, L, and Wagner, D. Animal safety report on intravaginal progesterone controlled internal drug releasing devices (CIDRs) in sheep and goats. J Vet Pharmacol Therap, In Press.

CRITICAL REVIEW:

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 to include:

a. Determination and prioritization of minor-use needs and data requirements.
b. Review, analysis and evaluation of minor-use research proposals.
c. Development and assembly of data for minor-use registrations.
d. Preparation and submission of petitions for drug registrations.

Considering these objectives, considerable progress has been made towards achieving them for each of the active projects listed above, particularly in the development of the data (the actual research), its analysis, assembly and interpretation, and submission to the FDA/CVM for review.

2. *The degree to which objectives have been met*

The degree to which these objectives have been met varies from project to project, however, in most all cases there has been progress. Those projects on which there has been no movement are reevaluated during each meeting of the NRSP-7 Technical Committee and decisions made on whether to continue to pursue them or move them into the inactive project list.

3. *Incomplete work or areas needing further investigation*

All of the projects listed above have some work that needs to be completed before they are approved by the FDA/CVM. In some cases this is just the FDA/CVM review, while in others there is work needed by the NRSP-7 project. The NRSP-7 work, which is undertaken each year within the Western Region, is based on the availability of qualified and interested investigators, the capacity of the regional laboratory to validate methods and analyze samples, and cooperation of the pharmaceutical manufacturers whose products are investigated.

SOUTHERN – DR. ALISTAIR I. WEBB

Projects in Progress:

RABBITS

ADR – 0107 Ivermectin & Rabbits

The human safety and target animal safety reports are being prepared. This task is being treated as secondary to the fenbendazole in game birds.

FISH

ADR - 0271 Crude Carp Pituitary

The project is dead with no response to FDA/CVM's concerns from the investigator.

BIRDS

ADR - 0280 Fenbendazole & Game birds

The human safety report has been submitted to FDA-CVM. The concerns of UC-Davis QA resulted in (a) withdrawal of quail part of the report [QA problem with Webb's dual role as study director and QA inspector plus very problematic withdrawal conclusions; (b) letters from site personnel submitted to try and mitigate lack of in vivo QA inspection; (c) in vitro section QA was certified. The TAS report continues to be incomplete but lacks investigator's final input and QA we are planning a 60-day completion. This will be submitted to FDA within 30 days.

DEER

ADR – 0210 Fenbendazole & Red Deer & ADR – 0216 Fenbendazole & Fallow

Intervet / Schering Plough are still working on their combined project pipeline priorities so this project id on hold.

ADR - 0294 Lasalocid and Deer / ADR - 0298 Lasalocid and Goats

Problem is that Alpharma will only proceed if there is a zero withdrawal time. We are well into validating an assay and will carry out initial pilots on two deer and two goats to see if the lasalocid levels are below tolerance. See below for TAMU collaboration.

The assay method has been had problems with recovery and there is no internal standard available. Once this is solved formal validation for pheasants, goats and deer will be carried out.

Dr Fajt [TAMU] has sent a draft of the HFS protocol for lasalocid in goats. It is being reviewed and hopefully can soon be submitted to FDA. TAMU is developing a drug development program and will probably have it's own QA unit.

BEES

ADR – 0343 Remebee and Honey bees

The Remebee project is with Beeologics for an Israel Acute Paralysis Virus [IAPV] specific double strand RNA product for prevention of collapsing colony disorder. The company has obtained an INAD and following a teleconference with FDA/CVM last month has gained both EA exclusion and approval for consumption of honey from treated hives [treatment has to end before honey flow. NRSP-7's role is of a possible advisor until FDA considers all the data submitted to determine what gaps there are and how large.

Work Planned for the remainder of the Year:

- Maintain lab and staff at GLP level
- Submit by summer all the ivermectin for rabbit reports and the TAS in game birds fenbendazole reports.
- Organize collaborative studies for gaining approval of fenbendazole & lasalocid in deer, and lasalocid in goats.
- Prepare, in coordination with the National Coordinator, INAD submissions for studies conducted under the aegis of the Southern Region. Initial preparation of written responses to CVM review of all of the data submitted for each project. This is often a time consuming and unrecognized activity associated with the completion of each project and may require considerable correspondence and conversation.
- Continued collaborative work with the other regions is anticipated and may include unplanned studies to address critical needs and opportunities to collect data.
- Continue the development of the NRSP-7 web site with possible re-implementation of the RUSTi database.

New / Proposed Projects:

With no assured funding in sight, no new projects are under consideration with primary effort being made to complete existing studies and we are trying to collaborate with TAMU to start work on lasalocid deer & goat projects.

Web Site

The NRSP-7.org web has continued to function well but is need of some development such as PowerPoint Presentations. The University is cranking-up security and is centralizing control of IT. We are concerned but we have been model citizens plus we actually got our original permission to host the web site without obvious use of the ufl.edu domain from the current head of IT. The MUMSRx web database continues to be updated – it alone receives 1-2 hits each day. RUSTi is alive but with loss of biological scientist we have kept a low

profile. Further development will have to wait upon program's choice of a successor on the current coordinator's retirement in May 2010.

ACTION ITEMS FOR ORGANIZING AND UTILIZING THE SAC

The group conducted a review of the action items to be discussed for organizing the roles of the government relations personnel and stakeholders with respect to contacting congressional members involved in agricultural appropriations. Talking points and a leave-behind one-page listing of bullet issues.

FALL MEETING

It was decided to hold the fall annual meeting on October 5th and 6th in a region to be decided depending upon travel costs and budgets.

IMPACT STATEMENTS FOR SPRING 2009

PEER-REVIEWED PUBLICATIONS

(1) Spitsbergen, J. M., Blazer, V. S., Bowser, P. R., et al. Finfish and aquatic invertebrate pathology resources for now and the future. *Comp Biochem Physiol C Toxicol Pharmacol* **2009**, *149*, 249-57.

(2) Wesley, I. V., Larsen, S., Hurd, H. S., McKean, J. D., Griffith, R., Rivera, F., Nannapaneni, R., Cox, M., Johnson, M., Wagner, D., and de Martino, M. Low prevalence of Listeria monocytogenes in cull sows and pork. *J Food Prot* **2008**, *71*, 545-9.

(3) Smith, G. W., Davis, J. L., Tell, L. A., Webb, A. I., and Riviere, J. E. Extralabel use of nonsteroidal anti-inflammatory drugs in cattle. *J Am Vet Med Assoc* **2008**, *232*, 697-701.

(4) Hurd, H. S., Brudvig, J., Dickson, J., Mirceta, J., Polovinski, M., Matthews, N., and Griffith, R. Swine health impact on carcass contamination and human foodborne risk. *Public Health Rep* **2008**, *123*, 343-51.

(5) Hawkins, M. G., Taylor, I. T., Craigmill, A. L., and Tell, L. A. Enantioselective pharmacokinetics of racemic carprofen in New Zealand white rabbits. *J Vet Pharmacol Ther* **2008**, *31*, 423-30.

(6) Groocock, G. H., Grimmett, S. G., Getchell, R. G., Wooster, G. A., and Bowser, P. R. A survey to determine the presence and distribution of largemouth bass virus in wild freshwater bass in New York State. *J Aquat Anim Health* **2008**, *20*, 158-64.

(7) Bartlett, S. L., Wooster, G. A., Sokolowski, M. S., Dove, A. D., and Bowser, P. R. Naturally occurring bacteraemia in American lobsters, Homarus americanus Milne-Edwards, in Long Island Sound. *J Fish Dis* **2008**, *31*, 19-25.

(8) Needham, M. L., Webb, A. I., Baynes, R. E., Riviere, J. E., Craigmill, A. L., and Tell, L. A. Current update on drugs for game bird species. *J Am Vet Med Assoc* **2007**, *231*, 1506-8.

IMPACT#1: Since the first drug approval in 1984 under the former IR-4 program, NRSP-7 has been responsible for generating 33 Public Master File (PMF) publications in the *Federal Register*, an average of 1.4 per year during its 24 years of funding.

IMPACT#2: In 2008, data from NRSP-7 was used in support of the FDA approval of Chloramine-T safety studies for control of bacterial gill disease in freshwater-reared salmonids. This formulation is used by immersion for control of mortality in freshwater-reared salmonids due to bacterial gill disease.

IMPACT#3: To date 342 drug requests have been submitted to the Minor Use Animal Drug Program for the development of data in support of the submission of a New Animal

Drug Approval. Currently there are 18 active research projects involving nine animal species and 12 different drugs.

Impact#4: During 2008 the regional coordinators published eight articles in peer-reviewed journals containing data developed in the Program.

AFTERNOON MEETING OF STAKEHOLDERS, GOVERNMENT RELATIONS REPRESENTATIVES AND NRSP-7 PERSONNEL

1:30 – 5:00

LOCATION: WESTIN MEETING ROOM

PARTICIPANTS: The NRSP-7 National and Regional Coordinators: John Babish (Cornell University), Lisa Tell (University of California, Davis), Dr. Alistair Webb (University of Florida), Dr. Ronald Griffith (Iowa State University), and Dr. Paul Bowser (Cornell University). NRSP-7 Administrative Advisors Dr. Garry Adams, Chairman of Administrative Advisors (Texas A&M), Dr. David Thawley (University of Nevada), Dr. John Baker (Michigan State University) and (Cornell University). The USDA/CSREES liaison Dr. Gary Sherman (Washington, DC). The FDA liaison Dr. Meg Oeller (Rockville, MD). Mark Lutschaunig,& Gina Luke representing American Veterinary Medical Association. Brian Smith or the American Association of Veterinary Medical Colleges. University Government Relations representatives Mr. Karl Engelbach of UC Davis, Dianne Miller, Director of Federal Government Relations for Cornell University, and Dustin Bryant of Meyers and Associates for Texas A&M University. National Coordinator for Aquaculture New Animal Drug Applications, Rosalie (Roz) Schnick. North American Deer Farmers Association was represented by Capital Consulting Group, and the National Turkey Federation by Michael Ribole.

PRESENTATIONS BY REGIONAL COORDINATORS

NORTHEAST REGIONAL COORDINATOR – DR. PAUL BOWSER

An outline of the species grouping research conducted in the Northeastern Region was given by **Dr. Bowser**.

Focus has been on Human Food Safety (tissue elimination studies)

- Model Species (Species Matrix)
- Tilapia
- Walleye
- Hybrid Striped Bass
    - Summer Flounder

Initial effort on:

- Extension of existing labeled drugs
- Terramycin for fish
- Romet-30
- Aquaflor (florfenicol)

Results to date indicate species grouping is a viable method for the reduction of animals used in research.

NORTH CENTRAL REGIONAL COORDINATOR – DR. RONALD GRIFFITH

Dr. Griffith described the North Central Region's efforts on several of the active projects in his area relating to the present stakeholders.

CIDRg

- CIDR is a progesterone implant used to synchronize estrus cycles in sheep & goats
- Uses a steroid hormone, Progesterone

- Targets the hypothalamus in a negative feedback
- Targets mammary glands & uterus in a positive feedback

Success

- A study at North Dakota State using CIDR's resulted in 100% synchronization, the highest in comparison to any other technique
- Success can be determined by
- Ultrasound
- Watching for signs of estrus
    - Pregnancy

CIDRg in Sheep

- Progesterone-containing intravaginal sponge.
- Human Food Safety has not been completed in the U.S. thus it is not approved for use.
- Nearing Approval….
- Need to verify stability of progesterone in muscle and liver.

CIDRg in Goats

- Milk Residue Study close to submission.
- Effectiveness

Tulathromycin (Draxxin®)

- Macrolide antibiotic (like erythromycin, tylosin, tilmicosin).
- Single Injection.
- Long-acting (effective lung levels for a week)… long withdrawal time.
    - Currently approved for use in Cattle and Swine.

Current Status of Draxxin in Goats

- Target Animal Safety Study is nearing completion.
- Protocols for Efficacy have been submitted. AUC/MIC vs. Field Trials
- Protocol for Tissue Residues has been approved. Western Region is working on analytical phase.

Lasalocid in Ring-necked Pheasants

- Effectiveness Study was completed at the University of Georgia last fall.
- First draft of the study report was submitted on 4-16-08.
- TAS protocol has been submitted and study is planned for this summer at UGA.
- HFS protocol is nearing completion.

Bioclip (Epidermal growth factor)

- Merck-Merial has the rights to this drug
- Currently evaluating whether to market in the U.S.
- Seems to be very little interest from Merck-Merial

Regulin

- Melatonin implant
- Sheep are seasonally polyestrus
- Regulin implanted in May and June would allow early July breeding/late Nov. & early Dec. lambing.
- Approved for use in Europe and Australia

Fasinex® (Triclabendazole)

- Treatment of liver flukes in deer and elk.
- Not approved for any species in the US.
- Approved in Europe for cattle.

Other Drugs

Fecundin (Androstenedione-7HSA in DEAE dextran adjuvant)

- Increases rate of multiple births in sheep.
- Approved for use in Europe and Australia

SOUTHERN REGIONAL COORDINATOR – DR. ALISTAIR I. WEBB

Dr. Webb presented an overview of research in the Southern Region, focusing on project tracking, game bird projects and the NRSP-7 website.

WESTERN REGIONAL COORDINATOR – DR. LISA TELL

Dr Tell began her presentation by reviewing the historical NRSP-7 accomplishments of the Western Region as summarized in the following Table.

Table 1. Western Region Historical Projects

DRUG	FORMULATION	SPECIES	STATUS
Ivermectin	Injectable	Reindeer	Approved
Fenbendazole	Premix	Big Horn Sheep	Approved
Ceftifur	Injectable	Sheep	Approved
Formalin	Powder	Sheep	Approved
Tylosin	Powder	Honey Bees	Approved
Formalin	Powder	Finfish and Eggs	Approved
Ceftifur	Injectable	Goats	Approved
Albendazole	Oral suspension	Goats	Approved
Amoxicillin trihydrate	Injectable	Sheep	Public Master File

Table 2. Western Region Current Projects

DRUG	FORMULATION	SPECIES
Erythromycin	Premix	Salmonids
Lincomycin	Powder	Honey Bees
Progesterone	CIDRg	Goats
Tulathromycin	Injectable	Goats

Goat specific studies included:

1. Ceftiofur sodium (Bacterial pneumonia)
2. Decoquinate (Coccidiosis)
3. Monensin (Coccidiosis)
4. Fenbendazole (GI parasites)
5. Morantel tartrate (GI parasites)
6. Albendazole (Liver flukes)
7. Clorsulon (Liver flukes) 5440 PMF
8. Levamisole (GI parasites) 5117 PMF
9. Ivermectin (GI parasites) 3883 PMF

Finally, a detailed description was presented of the pharmacokinetics of ceftiofur crystalline free acid (CCFA) in non-lactating domestic goats (*Capra aegagrus hircus*) following a single subcutaneous (SC) injection.

Conclusions :

- A single subcutaneous injection of CCFA did not result in any adverse effects.
- Serum concentration of CCFA remained above therapeutic concentrations for at least 4 days.

ROLE OF FDA/CVM LIAISON IN NRSP-7

Dr. Meg Oeller, FDA liaison to NRSP-7 reviewed the mission and organization of NRSP-7 and the relationship between NRSP-7 and CVM.

NRSP-7 Process in a Nutshell

- Animal Drug Request (ADR) to Regional Coordinator (4 Regions)
- Accepted projects funded
- Data generated as by any sponsor
- Data availability published in Federal Register (Public Master File)
- Pharmaceutical company files NADA using NRSP-7 Public Master File by reference

NRSP-7 Liaison is like a Regulatory Affairs Person

- Logs in ADR officially
- Requests INAD, environmental categorical exclusion, & slaughter authorization
- Sets up pre-submission conferences and other meetings
- Submits protocols and studies for CVM review
- Writes FOI Summary sections
- Compiles 'technical section complete' letters, protocols, final study reports, and FOI Summary into a Public Master File
- Requests publication of a Federal Register Notice announcing availability of the data to support a New Animal Drug Application
- Celebrates when a pharmaceutical company files an NADA using these data!
- Communicates *a lot* with National and Regional coordinators, academic researchers, producers, consumers, regulated industry, other government agencies…
- Gives presentations to industry, veterinary groups, producers, and government in and outside of FDA

USDA AND THE BUDGET PROCESS

In brief overviews, **Dr. Sherman** described the activities of USDA/CSREES. CSREES' mission is to advance knowledge for agriculture, the environment, human health and well-being, and communities. CSREES-funded research spans problems and issues encompassed within 13 national emphasis areas.

- Agricultural & Food Biosecurity
- Agricultural Systems
- Animals & Animal Products
- Biotechnology & Genomics
- Economics & Commerce
- Education
- Families, Youth & Communities
- Food, Nutrition & Health
- International
- Natural Res. & Environ.
- Pest Management
- Plants & Plant Products
- Technology & Engineering

Dr. Sherman went on to compare the Mission and funding of the NRSP-4 (IR-4) program to the NRSP-7 program. IR-4 Project Mission Statement: Provide safe and effective pest management solutions for growers of specialty crops.

IR-4 Project Funding

Principal sources:

- USDA CSREES
- USDA ARS

- USDA Multi-State Hatch funds, through SAES]
- Agrichemical industry
- Specialty crop commodity group stakeholders.

Funding for the IR-4 program from USDA/CSREES is $10.4 million/year in comparison to the $0.58 M for NRSP-7, or 18 times the amount. This discrepancy is further emphasized when the effect of minor crops and minor species on the US economy is considered. While the impact of minor species on the US economy is approximately $33 billion, the IR-4 estimate of the effect of minor crops on the US economy is $7.

TABLE 3. NRSP-7 APPROVALS

DRUG	CLAIM	SPECIES
Monesin	Coccidiosis	Goats
Amprolium	Coccidiosis	Pheasants
Thiabendazole	Gapeworm	Pheasants
Ivermectin	Warbles	Reindeer
Decoquinate	Coccidiosis	Sheep
Oxytetracycline	Gaffkemia	Lobsters
Bacitracin	Ulcerative enteritis	Quail
Monensin	Coccidiosis	Quail
Sulfa/ormetoprim	Bacterial infection	Catfish
Ivermectin	Ear mites	Foxes
Decoquinate	Coccidiosis	Goats
Salinomycin	Coccidiosis	Quail
Lasalocid	Coccidiosis	Rabbits
Fenbendazole	GI parasites	Goats
Ivermectin	Hypodermosis	Bison
Fenbendazole	Lungworms	Bighorn Sheep
Sulfa/ormetoprim	Coccidiosis	Partridges
Morantel tartrate	GI parasites	Goats
Ceftiofur	Bacterial pneumonia	Sheep
Formalin	External protozoans	Shrimp
Ceftiofur	Bacterial pneumonia	Goats
Lasalocid	Coccidiosis	Partridges
Formalin	Fungus/protozoans	Finfish/eggs
Tilmicosin	Respiratory infection	Sheep
Oxytetracycline	Otolith marking	Finfish fry
Tylosin	American foulbrood	Honey bees
Albendazole	Liver flukes	Goats

INTERACTION WITH NRSP-7 GOVERNMENT RELATIONS REPRESENTATIVES

Mr. Karl Engelback lead the discussions concerning the organization of groups for visits to Capital Hill to provide information to legislators responsible for reviewing the President's budget and recommending the final, compromise budget of USDA. The following groups were created to meet with the legislators on Tuesday January 27th.

GROUP ONE: NORTHEAST REGION
Cornell University -- Dianne Miller, Paul Bowser and John Babish

GROUP TWO: SOUTHERN REGION
University of Florida/Texas A and M -- Dustin Bryant, Garry Adams & Alistair Webb

GROUP THREE: NORTH CENTRAL/MID-WEST REGION

Iowa State University/AAVMC/Michigan State –Ronald Griffith, Brian Smith and John Baker, American Veterinary Medical Association -- Mark Lutschaunig and North American Deer Farmers Association lobbyist.

GROUP FOUR: WESTERN REGION
University of California, Davis -- Karl Engelbach and Lisa Tell

SUBCOMMITTEE MEMBERS LISTED FOR VISITS AND ASSSIGNED GROUPS
SENATE APPROPRIATION SUBCOMMITTEE ON AGRICULTURE, RURAL DEVELOPMENT, FOOD AND DRUG ADMINISTRATION, AND RELATED AGENCIES

Democratic Subcommittee Members:
Senator Tom Harkin (IA) – Group Three
Senator Byron Dorgan (ND) – Group Four
Senator Dianne Feinstein (CA) – Group Four
Senator Richard Durbin (IL) – Group Three
Senator Tim Johnson (SD) – Group Four

Republican Subcommittee Members:
Senator Robert Bennett (Ranking Member) (UT) – Group Four
Senator Thad Cochran (MS) – Group Two
Senator Mitch McConnell (KY) – Group Two
Senator Sam Brownback (KS) – Group Three

DRUG ADMINISTRATION, AND RELATED AGENCIES
Democratic Subcommittee Members:
Representative Maurice D. Hinchey (NY) – Group One
Representative Sanford Bishop (GA) –Group Three
Representative Marcy Kaptur (OH) – Group One

Republican Subcommittee Members:
Representative Jack Kingston (Ranking Member) (GA) – Group Two
Representative Tom Latham (IA) – Group Three
Representative Jo Ann Emerson (MO)—Group Three

Mr. Engelbach reviewed the purpose of the visits to be (1) to educate members on the program and (2) raise the issue of increasing support for the Program to $1 MM in FY10.

TUESDAY, JANUARY 27, 2009
NRSP-7 ADVOCACY VISITS ON CAPITAL HILL

At the conclusion of the day, a short meeting was held to review the accomplishments of the day. All agreed that members were receptive and the time was well spent. Consideration was also given to moving the Minor Species Drug funding to a non-earmark line item in the USDA budget.

Respectfully Submitted:

John G. Babish, Ph.D.
National Coordinator
Chairman, Technical Committee

2/25/2009
Date