National Research Support Project Summary

Project Number: NRSP_TEMP301 (renewal for NRSP-7)

Title: A National Agricultural Program for Minor Use Animal Drugs

Duration: October 2014 to September 30, 2015

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NIFA Reps:

Statement of Issues and Justification

Prerequisite Criteria

How is the NRSP consistent with the mission?
Broadly stated, National Research Support Projects (NRSPs) are created to conduct activities that enable other important research efforts. Examples of NRSP activities might include collection of data that are widely used by other research groups and efforts, development of databases, or development of critical technologies. In accordance with the focus of NRSPs, the missions of the NRSP-7 Minor Use Animal Drug Program are: 1. To identify animal drug needs for minor species and minor uses in major species, 2. To generate and disseminate data for safe and effective therapeutic applications, and 3. To facilitate FDA/CVM approvals for drugs identified as a priority for a minor species or minor use.

Minor uses include minor species (all species except dogs, cats, horses, cattle, swine, chickens, and turkeys), while minor uses in major species are those that occur infrequently or in limited geographical locations. The primary emphasis of the Program is on food-and/or fiber- (hair, wool, fur, feathers or hide) producing minor species with a secondary interest in non-food animals such as bees and tropical fish.

To accomplish these goals, NRSP-7 functions through the coordination of efforts among animal producers, pharmaceutical manufacturers, Food and Drug Administration/Center for Veterinary Medicine, United States Department of Agriculture/Cooperative State Research, Education, and Extension Service, universities, State Agricultural Experiment Stations and veterinary medical colleges throughout the country.

Globalization of food markets has allowed countries with less stringent animal drug approval requirements to dominate U.S. sheep, goat, farmed shrimp and fish, venison, honey and game bird production industries. At the same time, the growing concern in the U.S. over antibiotic resistance in human health and the use of antibiotics in food producing animals threatens to eliminate or severely curtail antimicrobial use in veterinary medicine. In April of 2013, the Center for Disease Control and Prevention (CDC) released their report entitled, Antibiotic

Resistance Threats in the United States 2013 . With respect to the issue of antibiotic use in food animals, the CDC report concluded Because of the link between antibiotic use in food-producing animals and the occurrence of antibiotic-resistant infections in humans, antibiotics should be used in food-producing animals only under veterinary oversight and only to manage and treat infectious diseases, not to promote growth. Since the release of this report, efforts have grown to sharply eliminate any use of antibiotics in animals without veterinary oversight. There appears little doubt that the next several years will introduce a new era of antimicrobial use in veterinary medicine. This movement may, in the end, assist NRSP-7 by curtailing unsupervised use of antibiotics in minor species production. Thus, our stakeholders will not have the unrestricted availability of antibiotics and become even more dependent on the Program.

The Minor Use Animal Drug Program is the only national program designed and organized to address the issues of the prudent use of antibiotics, anthelmintics and production drugs in minor species of food- and fiber-producing animals. Until 2006 NRSP-7 was consistently funded through as a line item in the Federal Budget at $588,000 per year. Due to the elimination of earmarks by Congress, the Program lost direct Congressional funding in 2007 and 2008. Federal support resumed in 2009 and 2010, but has been provided through Hatch funding by the SAES at a 70% level over the last four years. Overall, Hatch funding has supplied less than 40% of the operating budget of the Program, with all of these funds directly supporting research. While appreciated, the current level of support, with additional cuts through sequestration and increasing costs of research, is insufficient to maintain the NRSP-7 as a viable, robust national program.

Over the next year, the Program will pursue additional funding support from the Minor Use Minor Species Program of the FDA/Center for Veterinary Medicine and developers of organic or natural alternatives to antimicrobial and pesticide use in food animals. Additionally, USDA/NIFA has been exploring ways to consolidate related programs. This has been successfully implemented for a subset of programs related to plant protection, and task forces are currently working toward consolidation of selected water programs. Early-phase discussions concerning possible consolidation of animal protection and production programs, including NRSP-7, are now underway. Stakeholders will also be engaged to further Congressional interest in tighter control of antimicrobial use in food animals through NRSP-7 research. Additionally, the Program will continue communications with the IR-4 Pesticide program liaison Dr. Malamud-Roam to further assess critical pesticide approvals for animals. These efforts, we believe, will assist the Program to be federally funded once again. If sustainable funding cannot be obtained, however, consideration will be given to termination of the Program.

How does this NRSP pertain as a national issue?
Globalization of food markets has allowed countries with less stringent animal drug approval requirements to dominate our sheep, goat, rabbits, farmed shrimp and fish, venison, honey and game bird production industries. One-third of the lamb and 82% of venison consumed in the US comes from Australia and New Zealand. Nearly 90% of the commercially farmed shrimp are imported. Additionally, two-thirds of the honey consumed in the US is imported and half of that honey comes from China. In order to complete with these countries, American producers are forced to use therapeutics not approved in minor species.

The economic impact of minor animal species agriculture in the United States is great, but at risk. THE United States gross annual farm gate income from production of specialty animal species has been estimated by producer groups at over $4.8 billion. Further, these farm gate revenues produce an economic stimulus to the US Gross Domestic Product estimated at another $37 billion. Table 1 provides a breakdown of theses national figures by state. Lack of approved drugs for these producers is seriously threatening the growth and long-term viability of these collective industries and the security of our food supply. While the cumulative contribution of minor species to agricultural income is great, the return to pharmaceutical companies for research on therapeutics for this category, by species is small and generally unprofitable.

See attached Table 1 ECONOMIC IMPACT OF MINOR ANIMAL SPECIES BY STATE IN THE UNITED STATES AS OF 2013

Because of this substantial investment in time and resources, pharmaceutical companies must be assured that the drug will have a reasonable potential for profit. Therefore most drug approvals are sought only for those animal species that are produced in sufficient numbers to support large volume sales, specifically cattle, swine, chickens and turkeys. There is little economic incentive for pharmaceutical firms to generate data necessary to seek FDA/CVM approval of drugs in minor species; hence, very few drugs are available for management of diseases in these minor species. Inequities in drug availability represent serious management and economic problems for producers for minor species. Today, more than half of all commercially led pharmaceutical R&D in the veterinary medical field is focused on developing products for companion animals, and the emphasis on this sector is likely to increase in coming years, as companion animals live longer, and more diseases of old age are diagnosed and treated(2).

The Food and Drug Administration/Center for Veterinary Medicine (FDA/CVM) has been aware that veterinarians and livestock producers were using unapproved drugs for minor species without the safeguards that approved drugs carry. Additionally, little peer-reviewed literature existed to provide veterinarians with sufficient information for rationale extra-label use. Such unapproved drug use could not only cause detrimental effects to the animals being treated, but could also lead to the persistence of drug residues in animal products intended for human consumption. Efforts were and continue to be necessary provide US animal producers with safe and effective means to compete in a global market, while assuring US consumers a safe and wholesome food supply.

In 1976, the FDA/CVM initiated an extensive study of the minor use of animal drugs through the efforts of a minor use/minor species drug committee. This committee, comprised of representatives of the FDA s then Bureau of Veterinary Medicine and Bureau of Foods, the U.S. Department of Agriculture (USDA), the pharmaceutical industry, and animal producer groups identified the scope of the problem as a lack of approved drugs for (1) diseases of minor species and (2) the principle minor diseases of major species. The committee identified the principal diseases for which drugs were not available in the minor species. In summary, private sponsors had supported approvals for the use of minor use drugs as follows: none for rabbits, one for ducks and pheasants (none for other game birds), two for food fish, four for goats and twenty one for sheep. Minor and specialty use needs have continued to accumulate, leaving the producers of these species without the drugs necessary for disease prevention and control. A

definite need has been established for approval of minor use veterinary drugs and the scope of the problem was defined. This need was also affirmed by various grower organizations.

Additionally, the committee recognized that the livestock industry in the United States relies heavily on the judicious use of drugs for the treatment of diseases in food animals. Without these drugs, animal suffering and mortality would greatly increase, as would the cost of producing animal-derived food products. However, before a drug can be marketed for use in a food animal species, it must be shown to be safe to the human consumer of the animal-derived food, and safe and efficacious in the target animal.

The process of generating the safety and efficacy data necessary for FDA/CVM approval of a drug is costly and time-consuming. In 1999, it was estimated that the cost to a pharmaceutical company for research necessary to obtain FDA/CVM approval for a new drug exceeded $20 million, and required 8 to 10 years of concentrated research effort 1. More recently, issues relating to (1) escalating costs in the development of analytical methods, (2) concerns over antimicrobial resistance in human medicine, and (3) increased environmental testing have increased veterinary drug approval costs dramatically2. Drug approvals are generally species and disease specific and additional label claims also come with considerable added expense. Pharmaceutical company estimates place the cost of simply adding a label claim to an FDA/CVM approved drug at $10 to $25 million(3, 4).

In 1982, the IR-4 Animal Drug Program was established as part of the overall IR-4 Minor Use Pesticide Management Program. Since that time the animal portion has been established as a national means of securing approved drugs and as a conduit between the animal industries and the FDA/CVM. In December 1990, the USDA/CSRS requested a peer review of the IR-4 program, including both the pesticide portion and the minor use animal component. A reorganization of the minor use animal drug section was one of the recommendations of the Review Team. This Change was carried out with the development of a separate Minor Use Animal Drug Technical Committee that reported to the IR-4 Administrative Advisors. In 1992, IR-4 Administrative Advisors recommended that with the change from interregional Projects (IRs) to National Research Support Projects (NRSPs), as well as the experience gained under the reorganized IR-4 Project, that the two programs (pesticide and animal) be separated into two projects. In 1993, NRSP-7 was thus created as the Minor Use Animal Drug Program.

Congress has considered bills to promote drug availability for minor species and for minor uses in major species. The Animal Medicinal Drug Uses Clarification Act of 1994 [AMDUCA] and the Animal Drug Approval Act [ADAA] have expanded extra label uses for minor species. The limitations imposed by AMDUCA on extra-label drug use in feeds, however, proved to be a major problem to aquaculture and game bird industries and a guidance document has outlined conditions where limited extra-label use of approved formulations will be permitted under conditions of a valid veterinarian-client-patient relationship. The Minor Use Animal Drug Program is the only organized State/Federal effort to address the inadequate number of FDA/CVM approved drugs available for minor-use species and has been responsible for nearly all of the progress made in the approval of minor-use/minor-species drugs.

Rationale

Priority Established by ESCOP/ESS
The seven ESCOP National Priorities include: (1) Develop new and more competitive crop products and new uses for diverse crops and novel plant species; (2) Develop new products and new uses for animals; (3) Reduce the risks of local and global climatic change on food, fiber, and fuel production; (4) Provide the information and knowledge needed to further improve environmental stewardship; (5) Improve the economic return to agricultural producers; (6) Strengthen our communities and families and (7) Ensure improved food safety and health through agricultural and food systems.

NRSP-7 research addresses three of the seven ESCOP Roadmap Challenges, including Challenge 2, Challenge 5, and Challenge 7. The primary contribution of NRSP-7 is to Ensure improved food safety and health through agricultural and food systems (Challenge 7). Concern over drug residues in our food supply has grown exponentially over the last 10 years. Food producers and veterinarians are under pressure to limit the use of antimicrobials in food animals and employ more prudent oversight over even therapeutic uses. Prior to the initiation of the Program in 1982, private sponsors had supported approvals for the use of minor use drugs as follows: none for rabbits, one for ducks and pheasants (none for other game birds), two for food fish, four for goats and twenty one for sheep. A majority of these approvals represented outdated drugs with insufficient data on the post-treatment residue levels as well as efficacy. In the 31 years of the Program, data supplied by multistate research provided for the modification of 52 label claims to include minor species, an overall average of 1.6 per year. Included in these approvals were one for rabbits, nine for game birds, 16 for fish, lobster and shrimp, 15 for meat and dairy goats, eight for bison and reindeer, one for foxes and two for honey bees.

In addition to adding minor species to label claims, the Program works to ensure food safety through the publication of data on the pharmacokinetics, safety and effectiveness of modern drugs in minor species. Extra-label use of drugs by veterinarians, requires knowledge of the pharmacokinetics, tissue distribution, and sensitivity of the animal to support the decision to treat with an unapproved therapeutic. Regional coordinators in the Program have published 206 peer-reviewed articles supporting veterinarians in their decision to use drugs in an extra-label use manner. This information is also supplied to the FARAD program for online access to veterinarians (http://www.farad.org).

Thus, the linkage to human health includes improving the quality and safety of food, addressing issues of zoonotic diseases that threaten both animal and human health, and assuring safe and efficacious animal health products that do not adversely affect human health.

Additionally, with respect to (ESCOP Roadmap Challenge 5), Improve competitiveness and profitability/economic return to the producer in agriculture, NRSP-7 serves as a critical support component of minor species production systems in the US. Economic survival of these minor species producers depends upon their ability to treat diseases with approved drugs and the knowledge that such treatment will not harm the species or incur illegal drug residues. Production units or farms for minor species typically operate on thin margins. Economic success or even survival depends on optimal health of the crop. Limiting disease with approved

therapeutics allows producers to treat animals with confidence and assurance that the dose selected will perform as intended and will not result in illegal contamination.

The study of ivermectin medicated feed blocks for Cattle Fever Ticks by NRSP-7 is another example in which the program supports improved competitiveness in agriculture. Treatment of cattle within the 852-square mile quarantine zone that runs along the Mexico-Texas border with ivermectin-treated molasses blocks was identified as a minor use in a major species through the efforts of NRSP-7. Additionally, the experience of the Program with the analysis of ivermectin and the drug approval process has enabled NRSP-7 to establish pivotal efficacy and safety data and await only the cooperation of the manufacturers to put the newly documented products to use in the quarantine zone. Since most other treatment options have failed, without these new ivermectin/molasses blocks in use, the entire U.S. cattle industry is at risk if Cattle Tick Fever returns to the United State
(www.angusbeefbulletin.com/extra/2008/dec08/images/.../texas_tick.pdf

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The work on the FDA/CVM approval for progesterone implants for estrus synchronization in sheep by NRSP-7 has enabled sheep farmers to begin producing lambs throughout the year. This in turn allows the producer to supply animals to the market at times other than peak natural breeding periods, improving US sheep farming competitiveness in the US and foreign markets.

NRSP-7 also assists to Develop new products and new uses for animals (Challenge 2). Without NRSP-7, the introduction of many new animal species would not be possible since they are generally high value specialty animals with few, if any, approved therapeutics. The work on the development of the ivermectin/molasses blocks described in the context of Challenge 5 is also consistent with Challenge 2 and is discussed in more detail above. Other options for the containment of the Cattle Fever Tick have failed to contain the tick in the quarantine zone or result in illegal drug residues.

Relevance to stakeholders
Animal producers are the primary stakeholders in the NRSP-7 program, but pharmaceutical companies may be considered significant stakeholders as well. Other groups with interest in minor animal drug use include veterinarians and regulators. The active participation of animal producers and pharmaceutical companies is essential for the success of the program. However, to one degree or another, NRSP-7 involves all stakeholders. NRSP-7 producer stakeholders are represented by the following 58 organizations in 10 categories: American Association of Wildlife Veterinarians, American Association of Zoo Veterinarians, American Farm Bureau, American Feed Industry Association, American Pet Product Manufacturers Association, Inc., American Rabbit Breeders Association, American Sheep Industry Association, American Veterinary Medical Association, Animal Health Institute, Animal Drug Alliance, Arkansas Bait and Ornamental Fish Growers Association, Catfish Farmers of America, Center for Veterinary Medicine, Florida Tropical Fish Farms Association, Inc., Food Animal Concerns Trust, International Association of Aquatic Animal Medicine, International Association of Fish and Wildlife Agencies, North American Deer Farmers Association, North American Gamebird Association, Inc., National Pork Producers Council, National Cattlemen's Beef Association, National Fisheries Institute, National Turkey Federation, Pacific Coast Shellfish Growers Association, and the National Aquaculture Association.

By category, stakeholders include: " Agencies Fish and Wildlife Service, and Animal and Plant Health Inspection Service, and FDA Center for Veterinary Medicine.

" Aquaculture: Marine Fish Dealers, American Tilapia Association, U.S. Trout Farmers Association, American Fisheries Society, World Aquaculture Society, Aquaculture Network Information Center, and Catfish Planet.

" Bees: International Bee Research Association, Iowa State Entomology Index: Beekeeping, and Beekeeper s Home Pages Internet Resources.

" Caprine: American Dairy Goat Association.

" Game Birds: Mississippi State Game Bird Management, Pheasants Forever, Quail World, and North American Gamebird Assiation.

" Institutions: Auburn University (aquaculture and fisheries), Cornell University (aquaculture), Minnesota (avian), and Texas AMU (poultry science).

" Lagamorphs: American Rabbit Breeders Association.

" Ratites: American Emu Association and The American Ostrich Association.

" Reptiles: The Gator Hole and Crocodilian Internet Resources.

" Ungulates: Alpaca Registry, National Bison Association, The White-Tailed Deer Farmer s Network, North American Deer Farmers Association, Deer Hunting Net, and North American Elk Breeders Association.

These stakeholders provide input to NRSP-7 as to their individual drug needs and support through the contribution of animals, facilities for drug testing, commercial drugs, data, and analytical methodology. Stakeholder needs Veterinary medicine has a key role in protecting the health and productivity of several billion farm animals worldwide, ensuring the quality of the food they yield, and in protecting the health of approximately one billion companion animals. But despite the large number of animals treated with veterinary pharmaceuticals, the human healthcare market is about 35 times larger than the combined market for all non-human species, which had a global value in 2012 of $21.1 billion. This figure can be divided among three main modalities: veterinary pharmaceuticals, biologicals and medicated feed additives (MFAs). 63% of the $21.1 billion veterinary health market in 2011 is accounted for by pharmaceuticals ($13.3 billion), 25% by biologicals ($5.27 billion) and 12% by medicinal feed additives ($2.5 billion). Food animal healthcare comprised $12.45 billion of the total 2011 market; companion animal healthcare comprised $8.64 billion (http://finance.yahoo.com/news/global-veterinary-health-products-market-193000008.html). Moreover, this animal market is dominated by a large number of products that generate small revenues, and so the balance between the amount of R&D investment required relative to the likely return on this investment is a particularly crucial issue in veterinary drug development.

Minor species represent an excellent example of this diverse market. Agricultural production of fish, game birds, sheep, goats, ratites bees and deer in the United States is critically important to numerous regional economies in the United States. This diverse aggregation of minor species represents approximately $4.8 billion in state and local US farm revenues annually. Additionally, processing and export of minor species food and fiber products represents an additional $36.6 billion of revenue. Individually, however, these minor species represent drug markets too small to provide a sufficient return on the high cost of developing a new drug application.

Prior to NRSP-7, the FDA/CVM had approved the use of drugs for minor species as follows: none for rabbits, one for ducks and pheasants (none for other game birds), two for food fish, four for goats and twenty one for sheep (most of which have been withdrawn). Minor and specialty use needs have continued to accumulate, leaving the producer of these species without the drugs

necessary for disease prevention and control. The Minor Use Animal Drug Program has received 352 Animal Drug Requests submitted by animal producers, researcher investigators at federal, state, and university laboratories, veterinarians, and animal industry personnel for approval of a specific drug for the control of a certain disease in an animal industry. Of these requests, more than 40 have been identified as priority projects for NRSP-7.

Measuring stakeholder use Animal produces who use unapproved drugs for the treatment of livestock face the liability of illegal drug residues as well as the risk of ineffective dosages. Before the Minor Use Animal Drug Program, these producers had little choice, but to use unapproved drugs when faced with outbreak situations. Without these drugs, animal suffering and mortality would greatly increase, as would the cost of producing animal-derived food products. The FDA/CVM is aware that veterinarians and livestock producers were using unapproved drugs without the safeguards that approved drugs carry. Because there is widespread use of unapproved drugs in minor species and the level of use is small, approval of drugs for the minor use needs does not generally result in a measurable increase in sales to the pharmaceutical company. Thus, it is not possible to achieve a measure of stakeholder use of NRSP-7 data and drug approvals through increases in drug sales. One major exception to this situation is in the area of aquaculture. Increases in sales and usage of NRSP-7 developed drug approvals can be monitored through medicated feed records and pharmaceutical company shipment records.

The current development of valid metrics to measure stakeholder use of NRSP-7 information involve more use of the NRSP-7 website. Surveys, technical conferences with various partner groups can be conducted through the internet. Other avenues to increase information on stakeholder use include inviting stakeholder representatives to technical committee meetings, providing closer contact during monthly conference calls between semi-annual technical committee meetings.

Implementation

Objectives

1. 1. Identify the animal drug needs for minor species and minor uses in major species.
2. 2. Generate and disseminate data for the safe, effective, and legal use of drugs intended for use in minor animal species.
3. 3. Facilitate FDA/CVM approvals of drugs for minor species and minor uses.

Projected Outcomes

1. To date 354 drug requests have been submitted by stakeholders to the Minor Use Animal Drug Program for the development of data in support of the submission of a New Animal Drug Allowance (NADA). Through a prioritization process that has included (i) constraints imposed by concerns of antimicrobial resistance, (ii) limitations of availability of certain expensive or rare animal species, (iii) appropriate efficacy models, and (iv) high risk/benefit liabilities and lack of economic incentive for certain pharmaceutical manufacturers, the number of highest priority projects has been estimated at 40. Added to

our current active projects, the backlog of projects represents a research commitment stretching over several decades.

2. Currently there are nine active research projects involving five animal species and seven different drugs. Ruminant species remain the predominant group with a majority of Public Master Files (53%) as well. In 31 years, data supplied by the Program provided for the modification of 52 label claims to include minor species, an overall average of 1.6 per year. Included in these approvals were one for rabbits, nine for game birds, 16 for fish, lobster and shrimp, 15 for meat and dairy goats, eight for bison and reindeer, one for foxes and two for honey bees.
3. Additionally, NRSP-7 has published 206 articles in peer-reviewed journals, averaging 6.6 per year over the term of the program. For the last five years, however, publications have nearly doubled to 10.6 per year. Thus, although FDA/CVM drug approvals have waned due to increasing costs, the Program has increased its efforts to supply critical data needs to minor species producers. The data generated by the Program is also shared with the Food Animal Residue Avoidance Database (http://www.farad.org) program to further increase visibility.
4. The work on the FDA/CVM approval for progesterone implants for estrus synchronization in sheep by NRSP-7 has enabled sheep farmers to begin producing lambs throughout the year. This in turn allows the producer to supply animals to the market at times other than peak
5. The study of ivermectin medicated feed blocks for Cattle Fever Ticks by NRSP-7 is another example in which the program impacts improved competitiveness in agriculture. Treatment of cattle within the 852-square mile quarantine zone that runs along the Mexico-Texas border with ivermectin-treated molasses blocks was identified as a minor use in a major species through the efforts of NRSP-7. Over several years, the Program has established pivotal efficacy and safety data and approval of this use awaits only the cooperation of the manufacturers to put the newly documented products to use in the quarantine zone. Since most other treatment options have failed, without these new ivermectin/molasses blocks in use, the entire U.S. cattle industry is at risk if Cattle Tick Fever returns to the United States.

Management, Budget, and Business Plan

1. Organizational structure - NRSP-7 is composed of a Technical Committee and four Administrative Advisors representing state experiment station directors. These Administrative Advisors provide liaison among the directors of the state experiment stations, USDA/CSREES, FDA/CVM, various animal organizations, and others coordinating the efforts of this program.

The organizational structure of the Minor Use Animal Drug program follows:

Administrative Advisory Committee The Administrative Advisory Committee is composed of one appointee by Experiment Station Directors from each of the four regions (North Central, Northeast, Southern, and Western). The chair of the committee is selected internally. The role of the Administrative Advisory Committee is to provide liaison among the directors of the agricultural experiment stations in the four regions, colleges of veterinary medicine, the USDA/CSREES, the FDA/CVM, various animal organizations, and with those coordinating the

efforts of this program. This committee will establish and set policy consistent with the mission of this project. This committee will also advise on budget and administrative matters relating to this program.

Technical Committee The Technical Committee is composed of the following representatives: " National Animal Drug Coordinator (Chair) " Regional Animal Drug Coordinators representing each of the four regions (North Central, Northeast, Southern, and Western) " Administrative Advisory Committee Chair (non-voting) " USDA/CSREES Representative (non-voting) " FDA/CVM liaison to NRSP-7 (non-voting)

In addition to the above committee, the FDA/CVM has a Minor Use Animal Drug Committee that meets with the Technical Committee generally once a year at the semi-annual meetings of the Technical Committee. This FDA/CVM committee consists of representatives from the Division of Therapeutic Drugs for Food Animals, Antimicrobial Drugs Branch, Methods Validation and Analytical Branch, Companion and Wildlife Drugs Branch, and the Environmental Sciences Staff. The National Animal Drug Coordinator is salaried on a part-time basis and maintains an office. The Regional Animal Drug Coordinators are not compensated by salary except for secretarial or technical services.

Cooperating Agencies and Principal Leaders:

US Department of Agriculture/CRESS Dr. Gary Sherman USDA/CRESS Representative Dr. Gary Jensen USDA/CRESS Representative

US Food and Drug Administration/Center for Veterinary Medicine Dr. Meg R. Oeller FDA/CVM Liaison Dr. Amy Omer FDA/CVM Liaison Dr. Dorothy Bailey FDA/CVM Liaison

Administrative Advisors Dr. John Baker (Chair) Michigan AES Dr. Margaret E. Smith New York AES Dr. Frances D. Galey Wyoming AES Dr. Philip H. Elzer Louisiana AES

National Coordinator Dr. John G. Babish New York

Regional Coordinators Dr. Lisa Tell California AES Dr. Paul R. Bowser New York AES Dr. Rodman G. Getchell (elect) Dr. Thomas Vickroy Florida AES Dr. Ronald W. Griffith Iowa AES

2. Funding activities In the past, Research for the Minor Use Animal Drug Program was funded through a USDA special research grant administered by CSREES in cooperation with the NRSP-7 Technical Committee. Currently, however, NRSP-7 has been dependent on off-the-top Regional Research funds allocated to the Minor Use Program. Support for NRSP-7 also comes from pharmaceutical companies, and universities in the form of in kind contributions for Regional Coordinators. The program also receives significant in-kind support from several other sources including the institutions conducting the research (state agriculture experiment stations, colleges of veterinary medicine, federal laboratories), animal producer groups through contributions of animals for research, and pharmaceutical companies. Perhaps the most significant of this in-kind support comes through the cooperation of the pharmaceutical companies that provide access to their proprietary data package prepared for the drug approval in

a major species, estimated at $20 - $100 million (http://www.ahi.org/about-animal-medicines/industry-statistics/). In addition, the pharmaceutical sponsors complete the approval package by adding the new use of the drug to their current label, and often contribute to the program in the form for drug research, as well as direct financial aid. Without the generous support of the pharmaceutical manufactures, this program would not be possible.

The Regional Animal Coordinators are not compensated by salary for time contributed to the Minor Use Animal Drug Program. In two cases, secretarial and/or technical support services are budgeted from the Program. Funding of $20,000 is provided for the National Drug Coordinator s part-time salary (30%) and the maintenance of an office.

From 1982 through 2009, government funding was awarded from appropriated, line item USDA funds averaging $423,121 per year. Hatch funding, provided in four of the last five years, has averaged $336 K or a 21% decrease in funding that represents approximately 40% of the total cost of the funding the Program and represents amounts used for direct funding of required research. Congressional sequestration budget have further reduced these amounts over the last two years. The non-federal funds and sources provided for NRSP-7 since 1982 have totaled over $9.4 million.

A total of $13.5 million has been granted through Federal funding and an additional 60 percent, on average, has been obtained through nonfederal funds during the 31-year term of the NRSP-7 program. Average federal expenditures per completed research for a drug approval or publication of the 33 Public Master Files was $410 K. The total expenditure (federal plus non-federal) per completed research for a drug approval or publication of a Public Master File was $696K. This figure represents a 75% increase in the average cost per Public Master File of $398,000 computed for the last five-year renewal. Reasons for the increased approval costs for all include the higher standard of reporting expected by FDA/CVM, increased cost of improved analytical methods and the associated equipment, and the cost of performing bridging assays for validating new analytical techniques. With these increased cost over the last five years, the projected cost per Public Master File is approximately $3.5 million.

Even with the estimated increased cost per drug approval in recent years, the NRSP-7 program continues to demonstrate remarkable efficiency and cost effectiveness. Compared to an average investment of the pharmaceutical industry of $10 to $25 million for adding a label claim to an existing veterinary drug, information generated for additional label claims by the NRPS-7 program costs only approximately 15 to 35% of pharmaceutical industry costs (http://www.ahi.org/about-animal-medicines/industry-statistics/).

3. Research Research projects are initiated by requests, usually from researchers or animal producers, to the program s regional coordinators to address a particular minor use animal drug need. These requests, known as ADRs (Animal Drug Requests), are prioritized according (i) to financial and regulatory feasibility, (ii) to importance to the animal industry, and the pharmaceutical manufacturer s commitment to the minor use animal drug approval. Once a request is accepted as a research project, study protocols are developed and reviewed by FDA/CVM. All research projects are conducted in accordance with FDA s Good Laboratory Practices regulations. This process is outlined schematically in attached Figure 1.

Research Planned for Upcoming Year - To date 354 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. Through a prioritization process that has included (1) constraints imposed by concerns of antimicrobial resistance, (2) limitations of availability of certain expensive or rare animal species, (3) appropriate efficacy models, and (4) high risk/benefit liabilities and lack of economic incentive for certain pharmaceutical manufacturers, the number of highest priority projects has been estimated at approximately 40. Of these, the Program has been actively working on nine projects.

Over the last five years the total Federal plus non-Federal cost for NRSP-7 to provide the data necessary to support a single label claim has risen to approximately $3.5 million. This increase is due to (1) more sophisticated analytical procedures for residue analysis, (2) the need to conduct all studies under Good Laboratory Practices and auditing of projects, and (3) more expensive environmental assessments. Federal costs per Public Master File are estimated at roughly half this amount or $1.75 million. With NRSP-7 total level of funding of approximately $300,00 per year and cost per drug approval of $1.75 million, the expected time for achieving a drug approval is 5.6 years. Thus, it is anticipated that NRSP-7 will achieve one approval over the next five years.

This level of progress falls critically below the needs and expectations of our stakeholders and it is the objective of the Program to use the next year to evaluate the continued viability of the program in the face of continuing escalating costs and dwindling funding.

Over the next year, the Program will work to organize on several fronts to establish the potential for increased funding. First, the Program will work to obtain more grants from the FDA/CVM Minor Use grant program. Since the inception of the MUMS program at the FDA/CVM, NRSP-7 has taken advantage of this funding for several projects, but can increase this number in the upcoming year. This year I-010536 Strontium Chloride for otolith marking study has applied for MUMS funding to supplement the Program s Hatch Funding.

Second, NRSP-7 will critically review the current nine active projects with the goal of completing two or three of the most visible. Projects likely to be completed in the coming year include I-006013 Erythromycin in Salmonids, I-011389 CIDR implants for goats, I-010062 Fenbendazole in pheasants, and I-012056 Ivermectin block for Cattle Tick Fever.

Third, USDA/NIFA has been exploring ways to consolidate related programs. This has been successfully implemented for a subset of programs related to plant protection, and task forces are currently working toward consolidation of selected water programs. Early-phase discussions concerning possible consolidation of animal protection and production programs, including NRSP-7, are now underway.

Fourth, the Program will continue communications with the IR-4 Pesticide program liaison Dr. Malamud-Roam to further assess critical pesticide approvals for animals. Finally, the Program will solicit funding from companies interested in developing markets for natural alternatives to antibiotic growth promoters. For example, Dr. John P. Maye of S. S. Steiner, New York, NY, has developed data on the growth promoting and antibacterial properties of hops alpha acids. In US

patent 7,090,873 he has demonstrated the growth promoting properties of these alpha acids on cattle. Dr. Maye has contacted the Program for interest in developing these applications for both major and minor species.

4. FDA/CVM approval A successful research project is submitted to FDA s Center for Veterinary Medicine for review and inclusion in a Public Master File. The availability of the data for use on a label claim is announced through publication of the Public Master File in the Federal Register. A pharmaceutical sponsor may then reference, at no cost, the data in the Public Master File to support a new animal drug application for the minor use. The final step in the process is FDA/CVM approval of this application for the pharmaceutical sponsor, so that the product may be labeled and sold for minor use.

5. Assessment of outcomes Productivity - In the 31 years of the Program, data supplied by the Program provided for the modification of 52 label claims to include minor species, an overall average of 1.6 per year. Included in these approvals were one for rabbits, nine for game birds, 16 for fish, lobster and shrimp, 15 for meat and dairy goats, eight for bison and reindeer, one for foxes and two for honey bees.

Additionally, NRSP-7 has published 206 articles in peer-reviewed journals, averaging 6.6 per year over the term of the program. For the last five years, however, publications have nearly doubled to 10.6 per year. Thus, although FDA/CVM drug approvals have waned due to increasing costs, the Program has increased its efforts to supply critical data needs to minor species producers. The data generated by the Program is also shared with the Food Animal Residue Avoidance Database (http://www.farad.org) program to further increase visibility.

Currently there are nine active research projects involving five animal species and seven different drugs. Ruminant species remain the predominant group with a majority of Public Master Files (53%).

NRSP-7 has also provided information on therapeutics in minor species use through peer-reviewed publications, workshops and presentations to stakeholders and at professional meetings. Use of the Internet to optimize communications with stakeholders and program participants continues to improve in this rapidly changing medium. Moreover, NRSP-7 is the only initiative that generates information on the safe and effective use of therapeutics in minor species. Through NRSP-7, producers and veterinarians have the necessary information to reduce pain and suffering in commercially important minor species.

Completion of original objectives - A primary objective of NRSP-7 was to identify the animal drug needs for minor species and minor uses in major species. The Minor Use Animal Drug Program has received over 354 Animal Drug Requests submitted by researcher investigators at federal, state, and university laboratories, veterinarians, and animal industry personnel for approval of a specific drug for the control of a certain disease in an animal industry. Of these drug requests, the NRSP-7 Technical Committee has identified 40 of high priority. While in one sense NRSP-7 has completed one of our original objectives, withdrawal of available products, antimicrobial resistance, disease prevalence, husbandry practices, and the changing business

relationships in the veterinary pharmaceutical industry preclude considering our current list of projects and potential projects as final.

Integration

Program facilitation and coordination exists among animal producers, pharmaceutical manufacturers, FDA/CVM, USDA/CSREES, other government agencies, state agricultural experiment stations, and schools of veterinary medicine. Animal producers have provided the majority of drug requests and they frequently supply animals and facilities for target animal safety and residue depletion studies. Pharmaceutical companies participate through the sharing of analytical methodology and providing commercial drug product for testing. The major contribution of the pharmaceutical manufacturer is, however, is the cost borne for the approval of drugs for a major species, estimated at approximately $20 - $100 million and the cost of adding a label claim at $10 to $25 million (http://www.ahi.org/about-animal-medicines/industry-statistics/).

Since the beginning of the Minor Use Animal Drug Program, The FDA/CVM has supplied a full-time liaison to coordinate the drug approval process. In the last four years, they have added two additional staff positions to support the Program. The four regional coordinators are associated with colleges of veterinary medicine or experiment stations. These coordinators have full responsibility for supervising the development of all data entering the Public Master Files. Regional Coordinators also present and publish results of their studies. USDA/CSREES provides two full time liaison who, along with the Administrative Advisors and Technical Committee, oversee the prioritization of drug requests as well as project planning and implementation. Persons serving as Administrative Advisors are provided by the agricultural experiment stations from the four regions of the United States. The fundamental need for NRSP-7 to operate as a functionally integrated program has existed since its inception and NRSP-7 has spent 31 years cultivating the relationships necessary for optimal efficiency.

Outreach, Communications and Assessment

Public Master Files and New Animal Drug Allowances (NADAs) - The goal of the outreach and communication plan of NRSP-7 is to provide stakeholder access to information regarding program goals, accomplishments and impacts through a variety of channels. One form of outreach consists of the publication of the efficacy, target animal safety and drug residue depletion data generated as a Public Master File in the Federal Register and as a New Animal Drug Allowance (NADA) or Abbreviated New Animal Drug Allowance (ANADA). Publication in the Federal Register places the required studies in the public domain and a New Animal Drug Allowance provides the producer stakeholder the availability of the drug for the claimed minor use. Table 2 lists the 33 Public Master Files and 52 New Animal Drug Allowances developed from data generated by NRSP-7 (see attached Table 2).

Approvals and projects that have changed the outlook of two industries include the approvals of lincomycin hydrochloride water-soluble powder and tylosin tartrate powder for control of American Foulbrood in honey bees. These approvals represent a significant therapeutic addition to an industry working to reverse the declining honey bee population. Although the use of these

products will not substantially increase sales of these drugs, due to the small quantities required. The potential effect on the industry is important. Secondly, the ivermectin/molasses block formulation study currently being conducted in Texas for the control of Cattle Tick Fever, has the potential of averting a major threat to the U.S. cattle population. Several efficacy studies have supported the use of this novel formulation in cattle tick control. NRSP-7 labs in the Southern Region have worked with producers to assure a uniform distribution of ivermectin in the molasses blocks, insuring that cattle will receive uniform dosing.

Presentations and publications - Presentations, abstracts, publications and doctoral dissertations represent yet another form of communication to the stakeholders. Over the last 32 years, NRSP-7 has produced 206 peer-reviewed publications. Notably, while drug approvals have become more costly and time consuming to obtain over the last five years, NRSP-7 has nearly doubled its publication rate from 6.4 per year to 10.6 per year for the last five years. A liting of these publications follows this report. Website - The Technical Committee has worked to develop the NRSP-7 website (www.NRSP7.org) as a communication tool for dissemination of information generated by the program. The site provides for the submission of Animal Drug Requests (ADR's), operational information and monitoring of project progress by Technical Committee members, access to the MUMS (Minor Use Minor Species) program and links to a variety of stakeholders' websites. The use of the Internet to optimize communications with stakeholders and program participants continues to improve in this rapidly changing medium. Since inception in 1999, the NRSP-7 website has been visited 11,950 times for an average of 4.1 hits per day, an increase of 30% over the last review period. NRSP-7 believes that this represents a significant degree of interaction with stakeholders as well as the public at large.

Sharing NRSP-7 information with FARAD Another form of dissemination of NRSP-7 data is the publication of drug pharmacokinetic and residue depletion studies through FARAD (Food Animal Residue Avoidance Database). FARAD is a computer-based decision support system designed to provide livestock producers, extension specialists, and veterinarians with practical information on how to avoid drug, pesticide and environmental contaminant residue problems.

The FARAD website (www.FARAD.org) provides: " Current label information including withdrawal times of all drugs approved for use in food- producing animals in the United States. " Official tolerances for drug and pesticides in tissues, eggs and milk. " Database with approximately 43,000 scientific articles and entries with data on residues, pharmacokinetics and the fate of chemicals in food animals.

By supplying FARAD with information developed on minor use animal drug residue depletion and pharmacokinetics, NRSP-7 affords the stakeholder yet another conduit for obtaining critical information to avoid illegal and potentially hazardous drug residues in food animals.

Steps to improve communications Several changes have been incorporated in an effort to enhance communication both within the program and with stakeholders. First, monthly teleconferences are held by the Technical Committee to discuss potential projects, interactions with stakeholders and progress in studies. Second, stakeholders have been invited to be active non-voting participants in the annual spring teleconferences. The nature of the participation is ad

hoc and representatives from different stakeholder groups are invited on a rotating basis, without representation from a single or specific group "assigned" to the committee.

Informatics will be better utilized to increase/improve communication with NRSP-7 participants and stakeholders. Improvements to web usage include posting pdf versions of publications and or dissertations that have been supported through NRSP7 funds as well as links to other appropriate pages (partners, producer and/or pharmaceutical company websites). Existing brochures and any newly developed media information packages should likewise be posted. Stakeholders can be surveyed using the web site monitoring capabilities.

Projected Participation NRSP-7 functions through the coordination of efforts among animal producers, pharmaceutical manufacturers, Food and Drug Administration/Center for Veterinary Medicine, United States Department of Agriculture/Cooperative State Research, Education, and Extension Service, universities, State Agricultural Experiment Stations and veterinary medical colleges throughout the country. Working relationships between the Program and both the FDA/CVM and NIFA/CSRESS have been and should continue to be excellent. Also, USDA/ARS has been participating with NRSP-7 in the Cattle Fever Tick studies in Texas. Participation has also been forthcoming from game bird growers that have donated birds for safety and efficacy studies. Pharmaceutical companies have also provided analysis of feeds and tissues samples in selected studies. When the pharmaceutical companies could not provide analysis, they have provided expertise in the development of analytical methods for the tissue residue studies in minor species.

Peer-reviewed publications over the last five years: 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.

16. Topic Popovic, N., Howell, T., Babish, J. G., and Bowser, P. R. (2012) Cross-sectional study of hepatic CYP1A and CYP3A enzymes in hybrid striped bass, channel catfish and Nile tilapia following oxytetracycline treatment, Res Vet Sci 92, 283-291.

17. Tell, L. A., Stephens, K., Teague, S. V., Pinkerton, K. E., and Raabe, O. G. (2012) Study of nebulization delivery of aerosolized fluorescent microspheres to the avian respiratory tract, Avian Dis 56, 381-386.

18. Romanet, J., Smith, G. W., Leavens, T. L., Baynes, R. E., Wetzlich, S. E., Riviere, J. E., and Tell, L. A. (2012) Pharmacokinetics and tissue elimination of tulathromycin following subcutaneous administration in meat goats, Am J Vet Res 73, 1634-1640.

19. Mehl, M. L., Tell, L., Kyles, A. E., Chen, Y. J., Craigmill, A., and Gregory, C. R. (2012) Pharmacokinetics and pharmacodynamics of A77 1726 and leflunomide in domestic cats, J Vet Pharmacol Ther 35, 139-146.

20. Lee, K. A., Tell, L. A., and Mohr, F. C. (2012) Inflammatory markers following acute fuel oil exposure or bacterial lipopolysaccharide in mallard ducks (Anas platyrhynchos), Avian Dis 56, 704-710.

21. Leclere, M., Magdesian, K. G., Cole, C. A., Szabo, N. J., Ruby, R. E., Rhodes, D. M., Edman, J., Vale, A., Wilson, W. D., and Tell, L. A. (2012) Pharmacokinetics and preliminary safety evaluation of azithromycin in adult horses, J Vet Pharmacol Ther 35, 541-549.

22. Leavens, T. L., Tell, L. A., Clothier, K. A., Griffith, R. W., Baynes, R. E., and Riviere, J. E. (2012) Development of a physiologically based pharmacokinetic model to predict tulathromycin distribution in goats, J Vet Pharmacol Ther 35, 121-131.

23. Hope, K. L., Tell, L. A., Byrne, B. A., Murray, S., Wetzlich, S. E., Ware, L. H., Lynch, W., Padilla, L. R., and Boedeker, N. C. (2012) Pharmacokinetics of a single intramuscular injection of ceftiofur crystalline-free acid in American black ducks (Anas rubripes), Am J Vet Res 73, 620-627.

24. Dechant, J. E., Rowe, J. D., Byrne, B. A., Wetzlich, S. E., Kieu, H. T., and Tell, L. A. (2012) Pharmacokinetics of ceftiofur crystalline free acid after single and multiple subcutaneous administrations in healthy alpacas (Vicugna pacos), J Vet Pharmacol Ther.

25. Cornwell, E. R., Anderson, G. B., Wooster, G. A., Getchell, R. G., Groocock, G. H., Casey, J. W., Bain, M. B., and Bowser, P. R. (2012) Low prevalence of Cyprinid Herpesvirus 3 Found in common carp (Cyprinus carpio carpio) collected from nine locations in the Great Lakes, J Wildl Dis 48, 1092-1096.

26. Clothier, K. A., Leavens, T., Griffith, R. W., Wetzlich, S. E., Baynes, R. E., Riviere, J. E., and Tell, L. A. (2012) Tulathromycin assay validation and tissue residues after single and multiple subcutaneous injections in domestic goats (Capra aegagrus hircus), J Vet Pharmacol Ther 35, 113-120.

27. Bowser, P. R., Casey, J. W., Casey, R. N., Quackenbush, S. L., Lofton, L., Coll, J. A., and Cipriano, R. C. (2012) Swimbladder Leiomyosarcoma in Atlantic salmon (Salmo salar) in North America, J Wildl Dis 48, 795-798.

28. Young, G., Smith, G. W., Leavens, T. L., Wetzlich, S. E., Baynes, R. E., Mason, S. E., Riviere, J. E., and Tell, L. A. (2011) Pharmacokinetics of tulathromycin following subcutaneous administration in meat goats, Res Vet Sci 90, 477-479.

29. White, S. D., Bourdeau, P., Bruet, V., Kass, P. H., Tell, L., and Hawkins, M. G. (2011) Reptiles with dermatological lesions: a retrospective study of 301 cases at two university veterinary teaching hospitals (1992-2008), Veterinary dermatology 22, 150-161.

30. Tell, L. A., Brooks, J. W., Lintner, V., Matthews, T., and Kariyawasam, S. (2011) Antimicrobial susceptibility of Arcanobacterium pyogenes isolated from the lungs of white-tailed deer (Odocoileus virginianus) with pneumonia, J Vet Diagn Invest 23, 1009-1013.

31. Strunk, A., Imai, D. M., Osofsky, A., and Tell, L. A. (2011) Dysgerminoma in an eastern rosella (Platycercus eximius eximius), Avian Dis 55, 133-138.

32. Leavens, T. L., Tell, L. A., Clothier, K. A., Griffith, R. W., Baynes, R. E., and Riviere, J. E. (2011) Development of a physiologically based pharmacokinetic model to predict tulathromycin distribution in goats, J Vet Pharmacol Ther.

33. Kline, Y., Clemons, K. V., Woods, L., Stevens, D. A., and Tell, L. A. (2011) Pharmacokinetics of voriconazole in adult mallard ducks (Anas platyrhynchos), Medical mycology 49, 500-512.

34. Hawkins, M. G., Taylor, I. T., Byrne, B. A., Armstrong, R. D., and Tell, L. A. (2011) Pharmacokinetic-pharmacodynamic integration of orbifloxacin in Japanese quail (Coturnix japonica) following oral and intravenous administration, J Vet Pharmacol Ther 34, 350-358.

35. Goetting, V., Lee, K. A., and Tell, L. A. (2011) Pharmacokinetics of veterinary drugs in laying hens and residues in eggs: a review of the literature, J Vet Pharmacol Ther 34, 521-556.

36. Dore, E., Angelos, J. A., Rowe, J. D., Carlson, J. L., Wetzlich, S. E., Kieu, H. T., and Tell, L. A. (2011) Pharmacokinetics of ceftiofur crystalline free acid after single subcutaneous administration in lactating and nonlactating domestic goats (Capra aegagrus hircus), J Vet Pharmacol Ther 34, 25-30.

37. Cornwell, E. R., Eckerlin, G. E., Getchell, R. G., Groocock, G. H., Thompson, T. M., Batts, W. N., Casey, R. N., Kurath, G., Winton, J. R., Bowser, P. R., Bain, M. B., and Casey, J. W. (2011) Detection of viral hemorrhagic septicemia virus by quantitative reverse transcription polymerase chain reaction from two fish species at two sites in Lake Superior, J Aquat Anim Health 23, 207-217.

38. Cornwell, E. R., Cinelli, M. J., McIntosh, D. M., Blank, G. S., Wooster, G. A., Groocock, G. H., Getchell, R. G., and Bowser, P. R. (2011) Epizootic Nocardia infection in cultured weakfish, Cynoscion regalis (Bloch and Schneider), J Fish Dis 34, 567-571.

39. Clothier, K. A., Leavens, T., Griffith, R. W., Wetzlich, S. E., Baynes, R. E., Riviere, J. E., and Tell, L. A. (2011) Pharmacokinetics of tulathromycin after single and multiple subcutaneous injections in domestic goats (Capra aegagrus hircus), J Vet Pharmacol Ther 34, 448-454.

40. Clothier, K. A., Leavens, T., Griffith, R. W., Wetzlich, S. E., Baynes, R. E., Riviere, J. E., and Tell, L. A. (2011) Tulathromycin assay validation and tissue residues after single and multiple subcutaneous injections in domestic goats (Capra aegagrus hircus), J Vet Pharmacol Ther.

41. Young, G., Smith, G. W., Leavens, T. L., Wetzlich, S. E., Baynes, R. E., Mason, S. E., Riviere, J. E., and Tell, L. A. (2010) Pharmacokinetics of tulathromycin following subcutaneous administration in meat goats, Res Vet Sci.

42. Tell, L. A., Clemons, K. V., Kline, Y., Woods, L., Kass, P. H., Martinez, M., and Stevens, D. A. (2010) Efficacy of voriconazole in Japanese quail (Coturnix japonica) experimentally infected with Aspergillus fumigatus, Medical mycology 48, 234-244.

43. Rowe, J. D., Tell, L. A., Carlson, J. L., Griffith, R. W., Lee, K., Kieu, H., Wetzlich, S., and Hallford, D. (2010) Progesterone milk residues in goats treated with CIDR-G((R)) inserts, J Vet Pharmacol Ther 33, 605-609.

44. Hope, K. M., Casey, R. N., Groocock, G. H., Getchell, R. G., Bowser, P. R., and Casey, J. W. (2010) Comparison of quantitative RT-PCR with cell culture to detect viral hemorrhagic septicemia virus (VHSV) IVb infections in the Great Lakes, J Aquat Anim Health 22, 50-61.

45. Clothier, K. A., Jordan, D. M., Loynachan, A. T., and Griffith, R. W. (2010) Safety evaluation of tulathromycin use in the caprine species: tulathromycin toxicity assessment in goats, J Vet Pharmacol Ther 33, 499-502.

46. Bain, M. B., Cornwell, E. R., Hope, K. M., Eckerlin, G. E., Casey, R. N., Groocock, G. H., Getchell, R. G., Bowser, P. R., Winton, J. R., Batts, W. N., Cangelosi, A., and Casey, J. W. (2010) Distribution of an invasive aquatic pathogen (viral hemorrhagic septicemia virus) in the Great Lakes and its relationship to shipping, PLoS One 5, e10156.

47. Spitsbergen, J. M., Blazer, V. S., Bowser, P. R., Cheng, K. C., Cooper, K. R., Cooper, T. K., Frasca, S., Jr., Groman, D. B., Harper, C. M., Law, J. M., Marty, G. D., Smolowitz, R. M., St Leger, J., Wolf, D. C., and Wolf, J. C. (2009) Finfish and aquatic invertebrate pathology resources for now and the future, Comp Biochem Physiol C Toxicol Pharmacol 149, 249-257.

48. Rowe, J. D., Tell, L. A., and Wagner, D. C. (2009) Animal safety report on intravaginal progesterone controlled internal drug releasing devices in sheep and goats, J Vet Pharmacol Ther 32, 303-305.

49. Nguyen, K. Q., Hawkins, M. G., Taylor, I. T., Wiebe, V. J., and Tell, L. A. (2009) Stability and uniformity of extemporaneous preparations of voriconazole in two liquid suspension vehicles at two storage temperatures, Am J Vet Res 70, 908-914.

50. Kosoff, R. E., Chen, C. Y., Wooster, G. A., Getchell, R. G., Bowser, P. R., Clifford, A., Craig, J. L., Lim, P., Wetzlich, S. E., Craigmill, A. L., and Tell, L. A. (2009) Florfenicol residues in three species of fish after 10-day oral dosing in feed, J Aquat Anim Health 21, 8-13.

51. Davis, J. L., Smith, G. W., Baynes, R. E., Tell, L. A., Webb, A. I., and Riviere, J. E. (2009) Update on drugs prohibited from extralabel use in food animals, J Am Vet Med Assoc 235, 528-534.

52. Bowser, P. R., Kosoff, R. E., Chen, C. Y., Wooster, G. A., Getchell, R. G., Craig, J. L., Lim, P., Wetzlich, S. E., Craigmill, A. L., and Tell, L. A. (2009) Florfenicol residues in Nile tilapia after 10-d oral dosing in feed: effect of fish size, J Aquat Anim Health 21, 14-17.

Projected Participation

Budget Requests Summary

Literature Cited

1. Ringer, R. K., Miller, L. R., and Saylor, W. W. (1999) Minor-use animal drug program--a national agricultural program to approve animal drugs for minor species and uses, J Am Vet Med Assoc 214, 1636-1637.

2. Lathers, C. M. (2003) Challenges and opportunities in animal drug development: a regulatory perspective, Nature reviews. Drug discovery 2, 915-918.

3. Pfizer. Personal Communication (2013).

4. AHI. Animal Health Institue Statistics.