CgFARAD™ NEWSLETTER

WINTER 2024

In this edition of our newsletter, we highlight some of the research and related projects in which are co-directors have been involved.

Seminar on Prudent Drug Use in Food Animals

CgFARAD™ hosted an inaugural virtual seminar on research related to prudent drug use. The half-day event was held on August 2, 2023. The seminar attracted 86 participants from the U.S. and Canada. There was an excellent line-up of presentations from six graduate students and three lead researchers. The topics and speakers are noted below (the session was not recorded).

- **"Impact of a regulation restricting critical antimicrobial usage on prevalence of antimicrobial resistance in E. coli isolates from fecal and manure pit samples on dairy farms in Québec, Canada"** – Maud de Lagarde, DVM, DACVIM, PhD., Adjunct Professor, Faculté de médecine vétérinaire, Université de Montréal
- "**Quantifying Antimicrobial Use on Canadian Dairy Farms**" – Landon M. C. Warder, BScH (BIOM-NANS), Ph.D. Candidate, Department of Health Management, Atlantic Veterinary College, University of Prince Edward Island
- **"Revisiting the Use of Chlortetracycline in Feed"** – Michael D. Apley, DVM, PhD, DACVCP, Frick Professor of Clinical Sciences, Kansas State University College of Veterinary Medicine
- **"Developments in diagnostic tools to inform antimicrobial stewardship"** – Jennifer Abi Younes, Ph.D. Candidate, Department of Large Animal Clinical Sciences, University of Saskatchewan
- "**Characterizing bacteremia in neonatal calves with diarrhea**" – Luiza Stachewski Zakia, DVM, DVSc, DACVIM (LA), PhD Student, Department of Population Medicine, University of Guelph
- **"Why so different? Comparing international strategies to manage risks of veterinary drug residues in food"** – Al Chicoine, DVM, MSc, Diplomate ACVCP, Assistant Professor, Department of Veterinary Biomedical Sciences, University of Saskatchewan, Western College of Veterinary Medicine
- **"Comparison of the intestinal pharmacokinetics of two different florfenicol dosing regimens and its impact on the prevalence and phenotypic resistance of E. coli and Enterococcus over time"** – Jennifer Halleran, DVM, PhD, DACVIM-LAIM, Assistant Professor in Ruminant Medicine, Dept of Population Health and Pathobiology, NC State College of Veterinary Medicine
- **"Beta-lactamase genes distribution in Enterobacteriaceae from the food animal surveillance programs in the United States"** – Md Kaisar Rahman, Ph.D. Student, One Health Sciences, Texas Tech University School of Veterinary Medicine, Amarillo Texas
- **"Simulation models to inform antimicrobial use decisions in the feedlot"** – Cheryl Waldner DVM PhD FCAHS, Professor, Department of Large Animal Clinical Sciences & NSERC/Beef Cattle Research Council Senior Industrial Research Chair, University of Saskatchewan

The concept is to provide an opportunity for graduate students to showcase what they are working on and introduce them to other students and lead researchers in the field. This may spark some ideas for further studies or collaborative research. We will aim to host an annual session.

Dexamethasone Depletion in Lactating Dairy and Beef Cattle

Trisha Dowling, DVM, MSc, DACVIM & DACVCP and Ron Johnson, DVM, PhD, DACVCP, co-directors of the CgFARAD™

Dexamethasone is a synthetic glucocorticoid approved in Canada in both dairy and beef cattle for a variety of therapeutic uses, including inflammatory conditions, bovine ketosis and parturient udder edema. In Canada, dexamethasone is approved as an oral powder or injectable solution supplied by multiple pharmaceutical companies. Approved labels have varying dosage regimens for dexamethasone sodium phosphate injectable products ranging from 0.044 mg/kg daily IM or IV to 5-20 mg per animal IM or IV. Dexamethasone is also used extra-label at varying dosage regimens. Despite the common use of dexamethasone and its widespread availability, product labels in Canada do not provide withdrawal times for meat or milk, which may be misinterpreted by product users as a "zero withdrawal time". The European Union's (EU) maximum residue limits (MRLs) for dexamethasone in cattle are 2 ppb for liver, 0.75 ppb for muscle, 0.75 ppb for kidney and 0.3 ppb for milk,2 while the CODEX Alimentarius MRLs are 2 ppb for liver, 1 ppb for muscle, 1 ppb for kidney and 0.3 µg/L for milk. Recently, the list of MRLs for Veterinary Drugs in Foods in Canada was amended to include dexamethasone at 1 ppb for muscle and kidney, 2 ppb for liver and 0.3 ppb for milk (https://www.canada.ca/en/health-canada/programs/consultation-proposal-maximum-residue-limits-veterinary-drugs-foods-mrl-2023-1/document.html). The Canadian Food Inspection Agency uses sensitive Multi-Residue Methods for dexamethasone, and no dispensation has been granted for detection of dexamethasone residues in Canadian cattle. Highlighting this, Ontario data provided by the Ontario Ministry of Agriculture, Food and Rural Affairs (Troy Jenner, Manager, Food Safety Science Unit, OMAFRA) reports that since May 2019, in Ontario-licensed abattoirs, there has been a dexamethasone violation rate of approximately 1.11% in cattle carcasses (steers, cull dairy cows, heifers, and male veal calves) selected for residue testing through monitoring and surveillance programs, with steers and cull dairy cow making up the majority of test positives. This suggests that the presumed zero withdrawal time followed by Canadian producers results in detectable dexamethasone residues at slaughter.

Previous depletion studies in milk suggested a withdrawal period of 72 h after IM dexamethasone injection. However, these studies had low animal numbers per study groups and employed less sensitive and/or specific analytical methods (enzyme immunoassay and radioimmunoassay) than liquid chromatography/mass spectrophotometry (LC-MS) assays used by regulatory authorities. With respect to tissue residues in cattle, only two studies could be found. In the first study, 3 milk fed calves were administered short acting sodium phosphate ester in combination with the long-acting phenylpropionate ester of dexamethasone and they were slaughtered 24 hours after IM injection. Using an immunoassay, dexamethasone residues ranged from 4.1-32.8 ppb in liver, 0.8-4.5 ppb in muscle and 2.4-15.0 ppb in kidney. The second study used 10 calves that received an oral formulation of dexamethasone for 20 days and 10 calves that received dexamethasone 21-disodium phosphate 2 mg/kg of IM q 12 h for 3 days. Both groups were slaughtered thirty days after the last dose. Tissue samples analyzed by liquid LC-MS measured dexamethasone residues at concentrations of 0.4-1.0 ppb in liver, 0.4-0.6 ppb in kidney and 0.2-0.6 ppb in muscle. All tissue concentrations were below the respective EU and CODEX MRL values. From two studies with only single slaughter time points, it is impossible to predict a depletion profile for dexamethasone treated cattle.

The CgFARAD™ (www.cgfarad.usask.ca) is a Canadian service providing expert mediated veterinary pharmacology advice for residue avoidance to veterinarians. Since its beginning in 2002, the service has received numerous requests for withdrawal advice in lactating dairy cattle and beef cattle for both on label and extra-label use of injectable dexamethasone prescribed by licenced Canadian veterinarians. A search of the CgFARAD™ database records revealed the most common uses for dexamethasone that resulted in requests to the CgFARAD™ were for analgesia and anti-inflammatory activity (mainly associated with calving trauma), followed by adjunct treatment of atypical interstitial pneumonia and other respiratory conditions, induction of abortion, and treatment of ketosis (dairy cattle). The CgFARAD™ has provided conservative withdrawal recommendations of 10 days for meat and 96 hours for milk for most on label uses of injectable dexamethasone, with extended extra-label withdrawal recommendations depending on dosage regimens used and the condition being treated. The most common dosing regimen requested to the CgFARAD™ for withdrawal recommendations in both lactating dairy cattle and beef cattle is 0.05 mg/kg IM once daily for 3 consecutive days.

With support from the Dairy Farmers of Ontario, Beef Farmers of Ontario, and Ontario Ministry of Agriculture, Food, and Rural Affairs (OMAFRA), the CgFARAD™ personnel in conjunction with researchers from the Western College of Veterinary Medicine and the Ontario Veterinary College recently conducted residue depletion studies for this dosage regimen in beef and dairy cattle. The results of the study are published in the Journal of Veterinary Pharmacology and Therapeutics September, 2023: https://doi.org/10.1111/jvp.13409.

Egg Residue Depletion of Oral and Topical Formulations of Fluralaner (Braveto™) in Laying Hens

Trisha Dowling, DVM, MSc, DACVIM & DACVCP, co-director of CgFARAD™ and Dr Karen Schwean-Lardner, B. Sc. (Agr), M. Sc., Ph. D., Professor of Poultry Science, University of Saskatchewan

Dermanyssus gallinae, the poultry red mite, is a blood-sucking ectoparasite that affects the health, welfare and productivity of commercial layers but also hens in hobby flocks. D. gallinae harms poultry either directly through blood-feeding or indirectly as a potential vector for numerous pathogens. This mite has a very fast reproductive rate and parasite burdens of ≥ 150,000 mites per bird are reported. While infestations/dermatitis occur in commercial farm workers, in “backyard” poultry operations the mite is a threat to people as well as to domestic fowl other than poultry and to companion animals, including dogs, cats and horses.

In 2017, the European Union (EU) approved the isoxazoline ectoparasiticide fluralaner for the treatment and control of D. gallinae in chickens. Fluralaner is approved to be administered by two oral doses of 0.5 mg/kg via drinking water, seven days apart. While the safety and efficacy of the Exzolt™ product has been well established in laying hens, once approved in Canada the manufacturer will sell it in one litre containers with enough fluralaner to treat 10,000 birds. This will prevent the use of the labeled product in backyard flocks. The fluralaner products approved for dogs (an oral tablet) and cats (a topical solution) showed potential as a suitable alternative for such small flocks.

In a study carried out at the University of Saskatchewan’s Poultry Centre, 36 laying hens were treated with either the dog oral fluralaner product or the cat topical fluralaner product at 1.4 mg/kg for two doses 7 days apart. The

higher than the label dose for the poultry product was due to the limitations on accurately measuring small amounts of the dog or cat product. Eggs were collected for 30 days after the first administration and were analyzed by the Canadian Food Inspection Agency's Centre for Veterinary Drug Residues. While the administration of the dog oral product did result in residues above the proposed Maximum Residue Limit (MRL) of 1300 ppb, the cat topical product did not exceed the proposed MRL at any time. Therefore, the cat topical product shows promise for treatment of mites on backyard hens with no need to discard eggs once the proposed MRL is legally accepted in Canada. The next step will be to repeat the cat topical application of fluralaner in an efficacy study with red mites on hens.

Funded by Egg Farmers of Canada and the Canadian Food Inspection Agency.

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