RESEARCH ABSTRACT

SWINE HEALTH

Title: A study to assess the correlation between plasma, oral fluid and urine concentrations of flunixin meglumine with the tissue residue depletion profile in finishing age swine – **NPB #13-210**

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Scientific Abstract:

The United States is the world's leading exporter of pork. In recent years, several of these pork export destination countries have heightened monitoring for meat drug residues. In order to maintain a safe, healthy food supply and preserve trade relations, the swine industry must assess the impact of these improved tissue residue testing methods on drug residue detection in meat. This study investigated the use of flunixin, a commonly used anti-inflammatory drug labeled for use as an adjunctive therapy for swine respiratory disease. This project explored the usefulness of plasma, oral fluid (OF) and urine concentrations of flunixin to predict the residue depletion profile of flunixin in edible tissues of finishing age swine. This project also assessed the potential for untreated pigs to acquire flunixin residues following comingled housing with flunixin treated pigs.

Twenty crossbred finishing pigs were housed in groups of three treated and one untreated control pig. Treated pigs were administered flunixin meglumine as a single dose on one occasion at 2.2 mg/kg intramuscularly according to product label. Samples for plasma flunixin determination were obtained at 0, 1, 3, 6, 12, 24, 36 and 48 hours after treatment. Necropsy and collection of urine, OF, muscle, liver, kidney, and injection site were conducted in groups at 1, 4, 8, 12 and 16 days post treatment. flunixin levels were analyzed by liquid chromatography/tandem mass spectrometry.

A physiologically-based pharmacokinetic (PBPK) model was developed that correlated measured flunixin concentrations in the plasma, OF, urine, liver, kidneys, and muscle. The regression coefficient was $R^2 = 0.91$, suggesting high overall goodness-of-fit. This indicates that the PBPK model could be parameterized with plasma, urine, and OF flunixin concentrations that could assist with predicting tissue residues and withdrawal periods in pigs especially when sampled at earlier time points ($\leq$24 h) with a high confidence of accuracy. Thus, oral fluids and urine together with this PBPK model could potentially be a less invasive and more easily administered ante mortem biological monitoring tools for assessing tissue residue potential. Although flunixin was not detected in pen-level OF on day 8 post-treatment, OF samples collected at 1, 4 and 12 days after administration were positive for parent flunixin. Furthermore, the 5-hydroxy metabolite of flunixin (5-OH) was also present in all the OF samples except those collected on Day 8. Further studies are needed to refine OF collection for drug analysis.

The potential for environmental residue contamination was also demonstrated in this study. Urine samples in untreated control pigs (no flunixin administration) tested positive for flunixin out to four days post-exposure to flunixin treated pigs. However, flunixin concentrations in the muscle, liver, kidney, and injection sites from these same untreated pigs were below the limit of detection of the assay at every time point after exposure.

Given the relationship between plasma, urine and oral fluid flunixin concentrations and drug concentrations in body tissue demonstrated in this study, the PBPK model developed as part of this research may be applied as an adjunct to current testing methods. Furthermore, comingling flunixin treated and untreated pigs could result in positive urine tests but does not appear to be a significant risk factor in positive tissue residue tests.