Painful processing procedures in piglets such as tail docking, castration and teeth clipping are an emerging animal welfare concern. We hypothesized that transmammary delivery of a non-steroidal anti-inflammatory drug, firocoxib, would reduce pain associated with processing in piglets. The first study compared the pharmacokinetics, efficacy, safety and tissue residue concentrations of four doses of firocoxib (0.5, 1.0, 1.5, or 2.0 mg/kg) administered to sows and delivered to nursing piglets prior to processing. Sixteen sows, 5±2 d postpartum, were randomly assigned to one of four treatment groups. On d 0 sows received a single intramuscular dose of firocoxib at 7±1 h before piglet surgical castration, tail docking, and teeth clipping (males) or sham handling (females). Firocoxib, cortisol and prostaglandin E2 (PGE2) concentrations were determined from selected samples collected from sows and three piglets/litter (two barrows and one gilt) at 0, 2, 4, 6, 8, 12, 24, 48, 72, 96, and 120 h after drug administration. On d 21, piglets were weighed and all animals were euthanized and necropsied. Tissues were collected from 3 piglets/litter for histological examination and drug residue analysis. Mean (±SEM) peak plasma firocoxib concentrations (C_max) were 107.90±15.18, 157.50±24.91, 343.68±78.89, and 452.83±90.27 ng/mL in sows receiving 0.5, 1.0, 1.5, and 2.0 mg/kg firocoxib, respectively, and 9.53±1.21, 31.04±6.79, 53.30±11.1, and 44.03±7.47 ng/mL in their respective piglets. Mean plasma terminal half-life values ranged from 26 to 31 h in sows and 30 to 48 h in piglets. Barrows nursing sows that received 2.0 mg/kg firocoxib had a lower mean plasma cortisol concentration at 1±1 h after processing compared to barrows nursing sows that received 1.0 mg/kg (P=0.0416) and 0.5 mg/kg of firocoxib (P=0.0397). Piglets nursing sows that received 1.5 mg/kg firocoxib had consistently the lowest concentrations of circulating PGE2 suggesting inhibition of the cyclooxygenase enzyme by firocoxib. From
processing to weaning, litters of sows receiving 2.0 mg/kg firocoxib gained more weight than litters of sows that received 0.5 mg/kg (P=0.008) or 1.0 mg/kg (P=0.005). No signs of NSAID toxicity were observed on examination of the kidney, liver, stomach and small intestine and concentrations of firocoxib and the descyclopropylmethyl metabolite were below the limit of detection (0.01 µg/g) in all tissues examined from sows and piglets. These findings indicate that maternal delivery of firocoxib to suckling piglets before tail docking and castration may safely reduce processing-induced stress and enhance production by increasing weaning weights. The second study evaluated changes in cranial skin and ocular temperature, assessed using infrared thermography (IRT), and gait, assessed using a pressure mat, as biomarkers of pain in piglets after transmammary delivery of firocoxib prior to processing. Eight postpartum sows (n=2 sows per replicate for 4 replicates), nursing approximately eight piglets per litter (male and female; 5 days old; minimum BW = 1.8 kg) were enrolled in the study. Replicates were conducted in January, February, July and August 2019. Sows were randomly assigned to 1 of 2 treatment groups (n = 4 sows (32 piglets)/ group). Group 1 received 1.5 mg/kg Firocoxib intramuscularly (IM) in the right side of the neck at the time of study commencement. Group 2 served as a control and received a placebo injection consisting of physiological saline at a similar injection volume as sows in the firocoxib group. Treatments were administered at 6±1 h before piglet surgical castration, tail docking, and ear notching (males) or tail docking and ear nothing (females). IRT images were captured at 1 h, 2 h, 4 h, 7 h, 24 h, 30 h, 36 h and 48 h after processing. The effect of castration on piglet gait was assessed by briefly removing piglets from their pen and allowing them to walk across a pressure mat at 0.5, 7 h, 24 h, 36 h and 48 h post-processing. IRT and pressure mat data were analyzed using commercial software. Statistical analysis was conducted with the piglet as the experimental unit. Female piglets had significantly greater cranial skin temperatures compared to male piglets (P=0.0473). Cranial skin temperature was also significantly lower in piglets that were nursing sows that received firocoxib compared to control piglets at 2 h (P=0.0108) and 4 h (P=0.0316). However, cranial skin temperatures in piglets that were nursing sows that received firocoxib were higher than piglets nursing placebo-treated sows at 36h (P=0.0086) and 48h (P=0.0375) after processing. It is noteworthy that skin temperatures of piglets nursing the firocoxib-treated sows were higher than the control piglets in January and February but this effect was less evident in July and August. Ocular temperatures in piglets that were nursing sows that received firocoxib were higher than piglets nursing placebo-treated sows at 1h (P=0.0207), 30h (P=0.0011) and 36 h (P=0.0024) after processing. Ocular temperatures of piglets nursing the firocoxib-treated sows were also higher than the control piglets in August (P<0.0018). These observations suggest that season should be considered when infrared thermography is used to assess changes in ocular temperature after processing. Furthermore, compared to cranial skin temperatures, ocular temperature assessment may be more robust for assessing pain during warm seasons compared to cool seasons. Piglets nursing sows that received the placebo demonstrated a significantly greater increase in force applied to the front limbs at 7 h after processing compared to piglets nursing sows medicated with firocoxib (P=0.0127). We hypothesize that pain associated with castration results in a shift in force from the hind limbs to the front limbs of piglets to distribute weight away from the surgical site. In conclusion, these studies identified a candidate dose of firocoxib for transmammary delivery by dose-titration and demonstrated the feasibility and target animal safety of administering firocoxib by the transmammary route to piglets prior to processing. Furthermore, the results of these
experiments demonstrated that at higher doses, transmammary firocoxib mitigated pain associated with processing as illustrated by a dose-dependent reduction in plasma cortisol concentrations, an increase in cranial and ocular temperatures at later time points after processing and a reduction in processing-induced changes in gait in treated compared to control piglets. These findings address current animal welfare concerns related to pain associated with processing in piglets and will have an immediate and significant impact on the sustainability of U.S. swine production systems. The results of this study support the use of transmammary firocoxib to mitigate pain associated with processing and thus help to maintain consumer confidence in pork production practices and keep American agriculture competitive as pain management expectations evolve.