RESEARCH REPORT
PUBLIC HEALTH/WORKER SAFETY

Title: Determining the necessity of preventive use of antimicrobials at tail-docking and castration including comparison with alternatives – **NPB #17-124**

Investigator: Dr. Chris Rademacher, DVM

Institution: Iowa State University College of Veterinary Medicine

Co-investigators: Drs. Locke Karriker, Justin Brown, Anna Forseth

Date Submitted: 12/7/2018

Industry Summary: As the FDA continues to receive pressure to reduce antibiotic use in livestock species, there will be additional scrutiny on antibiotic usage. In particular, the routine application of antibiotics to animals that may be deemed as preventive use will be examined more thoroughly. To justify the current practice of antibiotic usage at the time of piglet litter processing, scientifically validated data must be collected that demonstrates the improvement of animal health and well-being. Conducting these evaluations within commercial swine production facilities increases the likelihood of direct applicability of research findings to the swine producer.

The primary objective was to evaluate the potential benefit of antibiotic use in a preventive manner compared to not using antibiotics at the time of piglet processing. The deliverable from this objective was to demonstrate value of antibiotic use over no antibiotic use when given around the time of piglet processing in terms of percent pre-weaning mortality (post-application), average daily gain (ADG) from processing to weaning as well as additional clinical parameters. A second deliverable was to compare three different classes of antibiotics against the use of no antibiotics to identify differences in value between each antibiotic class. Nine hundred and sixty piglets (n=960) from four commercial sow farms (approximate herd size of

4,000 sows) within the same production system, with differing health statuses, were enrolled in the study and data collection occurred June-July 2017. Two hundred and forty piglets from each farm were assigned to one of four treatment groups: beta-lactam (procaine penicillin G - 15,000 IU/lb.), macrolide (Draxxin 25 - 2.5 mg/kg), tetracycline (oxytetracycline - 19.8 mg/kg), or saline control (2cc/piglet). At the time of processing, treatments were administered via intramuscular injection in the post-auricular region using a 20-gauge x 0.5-inch needle. The outcomes measured from processing to weaning included percent mortality, wound healing, complete blood cell counts (CBC), average daily gain (ADG), and navel size. Scoring of castration and tail-docking wounds occurred two days post-processing, seven days post-processing and at the time of weaning.

Data analysis did not reveal statistically significant ($p< 0.05$) differences of antibiotic treated and non-treated animals on growth (ADG), pre-weaning mortality, castration or tail docking wound scores, navel size or infective leukograms (CBC). There was a gender difference that was statistically significant ($p< 0.05$) with the barrows (castrated males) having a 2.1 mm larger umbilicus at weaning in comparison to gilts. Data analysis did not reveal statistically significant differences ($p< 0.05$) for growth (ADG), mortality, or castration and tail docking wound score between the three antibiotic classes evaluated within this study. There were statistically significant differences between the farms ($p< 0.05$) for growth (ADG), with the highest health status farm having the highest ADG, but no statistically significant farm treatment interaction was noted on any of the farms. Comparing the different antibiotic treatments when analyzing CBC results for infective leukograms did not reveal any statistically significant differences ($p< 0.05$).

Industry Takeaways

- Macrolide, tetracyclines and beta-lactam antibiotics given at processing (1-4 days of age) to sow litter piglets did not change % mortality or ADG from processing until weaning when compared to piglets who did not receive antibiotics at processing.
- Macrolide, tetracyclines and beta-lactam antibiotics given at processing (1-4 days of age) to sow litter piglets did not change wound healing scores, navels scores or infectious leukograms (defined by CBC) when compared to piglets who did not receive antibiotics at processing.
- No statistically significant differences ($p<.05$) were noted between barrows and gilts when evaluating ADG, % mortality, or wound healing scores were evaluated.

This study begins to take a closer look at the necessity of preventive antibiotic use given at the time of processing due to the presence of open wounds from tail docking and castration of males. Differences between using antibiotics, any of the three classes, and not using antibiotics

were not appreciated on production parameters nor indicators of infection as defined by the ability of pigs to heal wounds or by evaluating blood parameters (CBC). This research was conducted on four commercial farms of varying health status and the same result was observed on each of the four farms. Differences were appreciated between farms on ADG independent of the treatment, which may indicate that there were health differences between the farms. Study treatments were completed on sow litter piglets only and did not include any piglets from gilt litters. The range in processing times were from 1-4 days of age and did not include any litters that were within 24 hours. One limitation of this study was the lack of a ceftiofur class antibiotics in the treatment evaluation. Ceftiofur class antibiotics are commonly prescribed by veterinarians for preventive use based upon farm diagnostics demonstrating the presence of a pathogen that is susceptible to this drug. The results from this study suggest that veterinarians and producers should examine and discuss the necessity of antibiotic use at processing within herds that have a high health status.

Keywords: processing, antibiotics, preventive use, castration, tail docking

Scientific Abstract: The perception of overuse of antibiotics in production animal species is an on-going concern and has been implicated as contributing to the growing problem of antibiotic resistance in humans. One of the primary areas of concern is the routine application of antibiotics in food producing animal species. In order to validate the current practice of antibiotic use when processing litters, scientifically validated data must be collected that demonstrates the usage of antibiotics at processing improves animal health and well-being. The objective of this study was to evaluate the potential benefit of antibiotics given concurrently with processing procedures (castration and/or tail docking) performed at 1-4 days of age. Live animal work involved 960 piglets (n=960) on four different commercial sow farms within the same production system of varying health statuses. Animals were enrolled in the study and data collection occurred June-July 2017. Two hundred and forty piglets from each farm were assigned to one of four treatment group: beta-lactam (procaine penicillin G - 15,000 IU/lb.), macrolide (Draxxin 25 - 2.5 mg/kg), tetracycline (oxytetracycline - 19.8 mg/kg), or saline control (2cc/piglet). At the time of processing, treatments were administered via intramuscular injection in the post-auricular region using a 20-gauge x 0.5-inch needle. The outcomes measured from processing to weaning included percent mortality, wound healing, complete blood cell counts (CBC), average daily gain (ADG), and navel size. Scoring of castration wounds and tail-docking wounds occurred two days post-processing, seven days post-processing and at weaning. Data analysis did not reveal statistically significant differences ($p < 0.05$) on growth (ADG), % mortality, or castration or tail docking wound scores between the three antibiotic classes evaluated during this study or in comparison to the untreated pigs. There were statistically significant differences between the farms ($p < 0.05$) for growth (ADG), with the

highest health status farm having the highest ADG, but no statistically significant farm by treatment interaction was noted on any of the farms. Comparing treatments and analyzing CBC results, there did not appear to be any statistically significant differences ($p < 0.05$).
Data analysis did not reveal statistically significant ($p < 0.05$) differences between navel size of antibiotic treated and non-treated animals, between castration or tail docking wound scores of antibiotic treated and non-treated animals. A statistically significant ($p<0.05$) gender associated navel size difference was observed with males (barrows; castrated males) having a 2.1 mm larger umbilicus at weaning in comparison to females (gilts).

Introduction: Recently, the Food and Drug Administration (FDA) released a five-year blue print detailing how the agency plans to build upon their current programs to advance antibiotic stewardship in veterinary settings. The perception of overuse of antibiotics in production animal species was specifically addressed within this document and described as contributing to the growing problem of antibiotic resistance. Those routine uses of mass antibiotic medication will come under scrutiny and demands peer reviewed scientific evidence to justify the continued use of this preventive measure within production animal medicine. The concurrent administration of injectable antibiotics at the time of processing has been a long-standing use of medically important antibiotics within the swine industry. Processing is generally defined as the process of docking the tails and performing open castration on the male piglets, resulting in open wounds that can be contaminated by bacteria present in the environment. Processing typically occurs early in the life of the piglet, generally between 1-5 days of age. The primary objective of this study was to evaluate the preventive use of antibiotics applied at the time of processing compared to pigs that were not given antibiotics. A secondary objective was to evaluate if there were differences between the three different classes of antibiotics, each with unique mechanisms of action, selected for use in this study.

Objectives:

- The primary objective was to evaluate the potential benefit of antibiotics used in a preventive manner compared to not using antibiotics during processing procedures. The deliverable from this objective is to demonstrate value of antibiotic use versus not using any antibiotic during the processing procedures in terms of percent pre-weaning mortality, average daily gain (ADG), infective leukograms (Complete Blood Count; CBC), wound healing scores and navel size, from the time of processing to weaning.
- A secondary objective was to compare three different classes of antibiotics to evaluate differences between treatment utilizing the same parameters outlined in the primary objective.

Materials and Methods: All live animal procedures were pre-approved by the Iowa State University Institutional Animal Care and Use Committee (IACUC). Four commercial breeding herd farms (approximately 4.000 sows per farm) within the same production system were utilized for the purposes of this study. Each study location adhered to the guidelines listed in the approved IACUC protocol. In order to stratify the potential effects of breeding herd health status during the trial, the study was replicated across all four commercial breeding farms concurrently. To evaluate the difference between processed males (testicles and tails removed) and females (only tails removed), each farm had 30 litters selected with at least 4 males and 4 females present within each litter, allowing all four treatments to be applied within the same litter. Each study farm had 60 pigs per treatment (30 males and 30 females) for a total enrollment of nine hundred and sixty pigs (n=960). Piglets were randomized in terms of treatment within each litter during the trial allotment procedures. Once the pigs were allotted to a treatment, they were weighed, ear tagged, processed and then the appropriate treatment was applied as described. Treatment 1 (n=240 pigs): oxytetracycline (oxytetracycline dihydrate) given by intramuscular injection (IM) in the post-auricular region of the neck (20-gauge x 0.5-inch needle) as a single dosage of 19.8 mg oxytetracycline/kg body weight (9.0 mg/lb.. body weight) at the time of processing. Treatment 2 (n=240 pigs): Draxxin 25 (tulathromycin injectable) given by IM in the post-auricular region of the neck (20-gauage x 0.5-inch needle) as a single dosage at a dosage of 2.5 mg/kg (1 mL/22 lb.) body weight at the time of processing. Treatment 3 (n=240 pigs): Penicillin G (procaine penicillin G) given by IM in the post-auricular region of the neck (20-gauage x 0.5-inch needle) as a single dosage at a dosage of 15,000 I.U/lb. body weight at the time of processing. Treatment 4 (n=240 pigs): sterile hypertonic saline (2cc per pig) given by IM in the post-auricular region of the neck (20-gauage x 0.5-inch needle) at the time of processing. The dose of each treatment was determined by the approximate weight of the animals at the time of injection. Outcomes measured from the time of the processing event (1-5 days of age) until weaning were percent mortality, weight gain (ADG=average daily gain), visual wound score, infective leukogram (CBC), and observation of other clinical signs (i.e. diarrhea, cough, lameness, swollen joints, hernia, abscess). Mortality was measured by tracking the number of pigs in each treatment that were found dead, euthanized or missing during the study (from processing to weaning) and dividing that number by the total number of pigs in each treatment at the time of enrollment to yield a percent mortality. Weight gain (ADG) was calculated based on the difference in weights from the weight of each pig at enrollment and weights prior to weaning. This difference in weight was divided by the number of days the pigs were on trial. In order to account for differences in weaning age (lactation length), all wean weights were adjusted to 21 day wean weights using NSIF guidelines for 21 day litter weight adjustment and ADG was computed from this standard weight (Adjusted 21-day litter weight = wt[2.218 - .0811(age) + .0011(age2)]). Weights were attained by purchasing a new, portable scale (capable of measuring from 0-30 pounds) for each farm. Pigs were secured to a rope

gently placed around the back leg, just below the hock and then attached to the scale. The final pig weight was recorded after the weight of the bucket had been subtracted out. Visual wound scores were assessed at days 2, 7 and again at the time of weaning. Wounds were evaluated on a 3-point scale: 1-exudate or blood, 2-swollen/reddened, 3-no swelling, redness, exudate, or blood. CBCs were completed at 2 days (48 hours) post processing as an indication of systemic infection due to an infected castration or tail docking wound. A blood sample was collected for each piglet at approximately 48 hours, labeled with the piglet ID and submitted to the Iowa State University Veterinary Diagnostic Lab for CBC examination. CBC results were analyzed based on looking for the presence or absence of an inflammatory leukogram, which is defined as a profile that contained a neutrophilia and concurrent lymphopenia. Other clinical signs such as diarrhea, cough, lameness, swollen joints, hernia, and/or abscesses were assessed on a daily basis by the farm staff and were noted in a log that was kept for each litter. Farms were allowed to administer antibiotic treatments to the sow or piglets during the study. If the sows or pigs were treated prior to enrollment, then those litters were not selected. If treatment to either the sow or piglet occurred after enrollment in the study, then it was noted in the logbook so it could be accounted for during analysis. Due to anecdotal reports of increased numbers of hernias in the grow-finish phase in pigs raised without antibiotics given at the time of piglet processing, navel size (width) was measured at weaning using calipers (in millimeters) to identify differences in treatments.

Data analysis was completed using the SAS® software (SAS, Cary, NC). For ADG, navel and CBC parameters, a generalized linear mixed model was used with ADG or navel as the outcome variables and treatment, gender, processing age, farm, tail infection and start weight as fixed effects. The sow was used as a random effect. For mortality and wound healing parameters, PROC GLIMMIX was used with mortality or healing as the outcome variables. Treatment, gender, processing age, farm, tail infection and start weight were fixed effects and sow was used as a random effect.

Results: Data analysis did not reveal statistically significant differences ($p < 0.05$) on growth (ADG), % mortality, or castration or tail docking wound scores between the three antibiotic classes evaluated during this study or in comparison to the untreated pigs (Table 1). There were statistically significant differences between the farms ($p < 0.05$) for growth (ADG), with the highest health status farm having the highest ADG, but no statistically significant farm by treatment interaction was noted on any of the farms. Comparing treatments and analyzing CBC results, there did not appear to be any statistically significant differences ($p < 0.05$).
Data analysis did not reveal statistically significant ($p < 0.05$) differences between navel size of antibiotic treated and non-treated animals, between castration or tail docking wound scores of antibiotic treated and non-treated animals. A statistically significant ($p<0.05$) gender associated

navel size difference was observed with males (barrows; castrated males) having a 2.1 mm larger umbilicus at weaning in comparison to females (gilts).

Anecdotal reports indicating that the most meaningful impact of antibiotic treatment on the measured outcomes of percent mortality and ADG can be observed in the smallest pigs within a litter. To assess these reports, the smallest 25% of pigs (by enrollment weight) and the smallest 25% of litters were analyzed using the same statistical model. Once again, data analysis did not reveal statistically significant ($p < 0.05$) ADG or percent mortality differences between the three antibiotic classes evaluated or compared to negative controls.

Table 1. Production Parameters by treatment.

Parameter	Macrolide (Draxxin)	Oxytetracycline (LA-200)	Beta-Lactam (Pen G)	No antibiotic (saline)	p-value
ADG (lb./day)	.52	.50	.50	.50	.32
Mortality (%)	5.0	5.0	5.8	5.4	.89

Discussion: This study begins to take a closer look at the necessity of preventive antibiotics given at the time of piglet processing. Antibiotics have been used in a preventive manner in the past due to the presence of open wounds from tail docking of all pigs and castration of the males. In this evaluation, no differences between using antibiotics and not using antibiotics were appreciated, both on production parameters or indicators of infection, as defined by ability of the pigs to heal wounds or by evaluating blood parameters indicating infection (CBC). There were also no differences between the three antibiotic classes that were evaluated using the same parameters. The size of the pig did not appear to change the nature of these results, even though it is a paradigm that the smallest pigs are the ones that would benefit most from the preventive use of antibiotics at processing. These results were surprising, as the closely held paradigm regarding the importance of concurrent antibiotic administration at the time of processing contradicts the data collected by this study. This evaluation was completed on four commercial breeding farms of varying health status and the same results were observed on each of the four farms. Differences were appreciated between farms on ADG, independent of the treatment, which may indicate that there were health differences between the farms. The farms had the same genetic base, feeding programs, similar facilities and management, leaving health as one of the more uncontrolled variables. The study pigs were born into a clean environment that was washed and disinfected approximately every 21 days, thereby reducing the chances of environmental contamination. The lack of any evidence of infection from the CBC results and in wound healing scores seems to reinforce the fact there appeared to be a lack of infection, helping to explain the lack of any differences in mortality and growth. One of the primary reasons for the concurrent administration of antibiotics at processing is to reduce the incidence of umbilical hernias that occur later in life. One potential contributing cause for

umbilical herniation is ascending umbilical infections occurring shortly after birth leading to incomplete abdominal connective tissue closure around the umbilical ring. These umbilical hernias are not usually visible until the pigs enter the finishing period of their growth cycle. This study unfortunately did not follow the pigs after they were weaned. An estimate of umbilical infection was attempted by measuring the size of the navel, but significant differences between treatment were not seen. It was noted that castrated males (barrows) had a 2.1mm larger navel diameter at weaning compared to the females (gilts), which could be due to the anatomical differences between the genders rather than any treatment effect. All study treatments were completed on sow litter piglets only and did not include any piglets from gilt litters. It is generally accepted that gilt litters tend to have higher rate of disease. One limitation of this study was the lack of a ceftiofur class antibiotic in treatment evaluation. Ceftiofur class antibiotics are commonly prescribed by veterinarians for preventive use based upon farm diagnostics demonstrating the presence of a pathogen that is susceptible to this drug. The results from this study suggest that veterinarians and producers should examine and discuss the necessity of antibiotic use at processing within herds that have a high health status.