Altering the time of vaccination against respiratory pathogens to enhance antibody response and performance of feeder cattle[1]

K. D. Lippolis,* R. F. Cooke,*[2,3] K. M. Schubach,*
A. P. Brandão,*† L. G. T. da Silva,*† R. S. Marques,* and D. W. Bohnert*

*Oregon State University – Eastern Oregon Agricultural Research Center, Burns, OR; and †UNESP – Faculdade de Medicina Veterinária e Zootecnia, Botucatu, Brazil

ABSTRACT: Ninety Angus × Hereford calves were ranked by sex, BW, and age and assigned to 1 of 3 vaccination schemes against the bovine respiratory disease complex: 1) vaccination at weaning (d 0) and a booster at feedlot entry (d 30; CON; $n = 30$), 2) vaccination 15 d before weaning (d −15) and a booster 15 d before feedlot entry (d 15; EARLY; $n = 30$), and 3) vaccination 15 d after weaning (d 15) and a booster 15 d after feedlot entry (d 45; DELAYED; $n = 30$). From d −15 to 7, calves were maintained as a single group on pasture. On d 8, calves were placed into 1 of 18 drylot pens (6 pens/treatment; 5 calves/pen) and fed alfalfa–triticale hay. On d 29, calves were transported 1,440 km in a livestock trailer and unloaded on d 30 at the same feed yard with the same pen arrangement used prior to transport. From d 30 to 75, calves were fed a receiving diet based on alfalfa–triticale hay + corn-based concentrate. Calf BW was recorded on 2 consecutive days (d −15, −14, 0, 1, 28, 29, 75, and 76). Blood samples were collected on d −15, 0, 15, 30, 45, 60, and 75. The EARLY calves had less ($P \leq 0.09$) ADG before weaning (d −15 to −1); however, they had greater ($P \leq 0.01$) ADG during feedlot receiving (d 30 to 75) compared with calves with the other treatments. During preconditioning (d 0 to 29), CON calves had greater ($P \leq 0.04$) DMI compared with EARLY and DELAYED calves. During feedlot receiving, no treatment differences were detected ($P \geq 0.17$) for hay or concentrate DMI, G:F, and morbidity and mortality rates. There were no treatment effects on calf BW at weaning and at the end of the preconditioning or receiving periods ($P \geq 0.65$). Plasma concentrations of antibodies against *Mannheimia haemolytica* were greater ($P \leq 0.05$) in EARLY calves than in CON and DELAYED calves on d 0, greater ($P \leq 0.04$) for CON calves than for EARLY and DELAYED calves on d 15, greater ($P \leq 0.02$) in DELAYED and EARLY calves than in CON calves on d 30, and greater ($P = 0.03$) in EARLY calves than in CON calves on d 75. Plasma concentrations of antibodies against bovine viral diarrhea viruses were greater ($P \leq 0.04$) in EARLY calves than in CON and DELAYED calves on d 15 and greater for EARLY and CON calves than for DELAYED calves on d 30 and 45. Collectively, EARLY calves had greater plasma concentrations of antibodies against the evaluated pathogens at feedlot entry and increased ADG during receiving compared with their CON and DELAYED cohorts. Hence, anticipating initial and booster vaccinations against respiratory pathogens to provide both doses prior to feedlot entry appears to be a valid strategy to enhance cattle health and performance during feedlot receiving.

Key words: feeder cattle, health, performance, respiratory diseases, vaccination

 J. Anim. Sci. 2016.94:3987–3995
doi:10.2527/jas2016-0673

[1]Financial support for this research was provided by USDA-NIFA Oregon (ORE00142). Appreciation is also extended to Zoetis (Florham Park, NJ) and IDEXX (Switzerland AG, Liebefeld-Bern, Switzerland) for product donation.

[2]Corresponding author: reinaldo.cooke@oregonstate.edu.

[3]Reinaldo Cooke is also affiliated as graduate professor to the Programa de Pós-Graduação em Zootecnia/Faculdade de Medicina Veterinária e Zootecnia, UNESP – Univ. Estadual Paulista, Botucatu, SP, Brazil, 18618-970.

Received May 25, 2016.
Accepted July 6, 2016.

INTRODUCTION

The bovine respiratory disease (**BRD**) complex is the most common and costly disease in U.S. feedlots (NASS, 2006), and strategies that mitigate incidence of BRD are warranted for optimal welfare and productivity of feedlot cattle (Duff and Galyean, 2007). An example is the adoption of preconditioning programs that include vaccination against pathogens that cause BRD (Martin et al., 1999; Duff and Galyean, 2007). It is common for preconditioned calves to receive a vaccination against BRD pathogens at weaning and a booster 30 d later at feedlot entry (England et al., 2009). However, weaning and feedlot entry are 2 of the most stressful situations encountered by feeder cattle, and vaccine efficacy can be reduced if administered to highly stressed animals (Blecha et al., 1984). Therefore, altering the time of vaccination against BRD has been investigated to enhance health and performance of feeder cattle.

Richeson et al. (2008) compared vaccination against BRD pathogens on arrival at the feedlot or 14 d later and reported that delaying vaccination increased seroconversion to infectious bovine rhinotracheitis during feedlot receiving. Nevertheless, the majority of BRD cases often occur within the first 14 d on feedlot arrival (Kirkpatrick et al., 2008), and delaying the booster by 2 wk may not provide proper immunological protection against BRD pathogens to newly received feeder calves. In addition, vaccination against BRD pathogens has been shown to reduce cattle DMI, ADG, and G:F (Arthington et al., 2013; Rodrigues et al., 2015). Based on this rationale, we hypothesized that anticipating vaccination and a booster against BRD pathogens by 15 d to provide both doses prior to feedlot entry further enhances cattle health and performance during feedlot receiving. Hence, this experiment compared the effects of anticipating, delaying, or vaccinating against BRD at the time of weaning and feedlot entry on growth, DMI, and plasma antibody parameters of feeder cattle.

MATERIALS AND METHODS

This experiment (d −15 to 75) was conducted at the Oregon State University – Eastern Oregon Agricultural Research Center (Burns station; Burns, OR) and divided into preweaning (d −15 to −1), preconditioning (d 0 to 29), and feedlot receiving (d 30 to 75) phases. All animals were cared for in accordance with acceptable practices and experimental protocols reviewed and approved by the Oregon State University, Institutional Animal Care and Use Committee (number 4738).

Animals and Treatments

Ninety Angus × Hereford calves (n = 69; n = 21 heifers) were used in this experiment. All calves were vaccinated against clostridial diseases (Clostrishield 7; Novartis Animal Health, Bucyrus, KS) and the BRD complex (Virashield 6 + Somnus; Novartis Animal Health) at approximately 45 d of age. On d −18 of the experiment, calves were ranked by sex, BW, and age (215 ± 4 kg initial BW and 184 ± 18 d initial age) and assigned to 1 of 3 treatments: 1) vaccination at weaning (d 0) and a booster at feedlot entry (d 30; **CON**; n = 30), 2) vaccination 15 d before weaning (d −15) and a booster 15 d before feedlot entry (d 15; **EARLY**; n = 30), and 3) vaccination 15 d after weaning (d 15) and a booster 15 d after feedlot entry (d 45; **DELAYED**; n = 30). Treatment groups contained 23 steers and 7 heifers each and were balanced for initial calf BW and age. Vaccines administered during the experiment were against *Clostridium* (2 mL, subcutaneously; One Shot Ultra 7; Zoetis, Florham Park, NJ); parainfluenza virus (TSV-2; Zoetis); and infectious bovine rhinotracheitis virus, bovine viral diarrhea virus (**BVDV**) Types 1 and 2, and *Mannheimia haemolytica* (**MH**; 2 mL, s.c.; Bovi-Shield Gold One Shot; Zoetis). Calves not receiving a vaccination were administered 4 mL (s.c.) of sterile saline.

From d −15 to −1, calves were managed as a single group with their respective dams in a semiarid rangeland pasture (Ganskopp and Bohnert, 2009). All dams were multiparous, and dam age during the experiment was 6.2 ± 0.7 yr for CON, 5.8 ± 0.6 yr for DELAYED, and 5.9 ± 0.6 yr for EARLY. Calves were weaned and administered an anthelmintic (subcutaneous injection at 1 mL/50 kg of BW of Dectomax; Zoetis) on d 0. From d 0 to 7, calves were managed as a single group in a meadow foxtail pasture (*Alopecurus pratensis* L.) with ad libitum access to long-stem alfalfa–triticale hay and no concentrate supplementation. On d 8, calves within each treatment were ranked by sex and BW, allocated to 1 of 18 drylot pens (5 calves/pen, 4 steers and 1 heifer; 6 pens/treatment), and fed long-stem alfalfa–triticale hay ad libitum until d 29. Calves were not assigned to the drylot pens immediately after weaning so they could acclimate to the absence of their dams as a single group. On d 29, all calves were loaded into a single double-deck commercial livestock trailer (Legend 50' cattle liner; Barrett LLC, Purcell, OK) and transported 1,440 km. During transport, the driver stopped every 6 h to rest for 60 min but cattle remained in the truck at all times, and total transport time was 24 h. Transport length and duration were selected to elicit the stress challenges of a long haul (Arthington et al., 2008; Cooke et al., 2013). Minimum, maximum, and average environmental temperatures

during transport were −9, 10, and 1°C, respectively, whereas average humidity was 64% and no precipitation was observed. Upon arrival (d 30), calves were unloaded at the same feed yard and with the same pen distribution used prior to transport but allocated to different drylot pens (Cooke et al., 2013). From d 30 to 75, calves were fed long-stem alfalfa–triticale hay ad libitum and offered corn-based concentrate (Table 1) twice daily (0800 and 1600 h), which was offered separately from hay. Water and a commercial mineral mix (Cattleman's Choice; Performix Nutrition Systems, Nampa, ID; contained 14% Ca, 10% P, 16% NaCl, 1.5% Mg, 3,200 mg/kg of Cu, 65 mg/kg of I, 900 mg/kg of Mn, 140 mg/kg of Se, 6,000 mg/kg of Zn, 136,000 IU/kg of vitamin A, 13,000 IU/kg of vitamin D_3, and 50 IU/kg of vitamin E) were offered for ad libitum consumption throughout the experimental period (d −15 to 75).

Table 1. Ingredient composition and nutrient profile of concentrate offered to cattle during the receiving phase[1]

	Concentrate type			
Item	A	B	C	D
DM intake per calf, kg/d	1.20	2.40	4.20	5.40
Ingredient, % DM				
Whole corn	68.7	84.6	87.3	87.7
Soybean meal	27.5	13.5	11.6	11.5
Mineral mix[2]	3.8	1.9	1.1	0.8
Nutrient profile[3] (DM basis)				
TDN,[4] %	82	85	86	86
NEm,[5] Mcal/kg	2.03	2.12	2.14	2.14
NEg,[5] Mcal/kg	1.39	1.45	1.47	1.48
CP, %	21.5	15.6	14.9	14.8

[1]A = offered for 5 d on receiving; B = offered for 10 d after concentrate A; C = offered for 10 d after concentrate B; D = offered for 20 d after concentrate C.

[2]Cattleman's Choice (Performix Nutrition Systems, Nampa, ID) containing 14% Ca, 10% P, 16% NaCl, 1.5% Mg, 3,200 mg/kg of Cu, 65 mg/kg of I, 900 mg/kg of Mn, 140 mg/kg of Se, 6,000 mg/kg of Zn, 136,000 IU/kg of vitamin A, 13,000 IU/kg of vitamin D_3, and 50 IU/kg of vitamin E.

[3]Values obtained via wet chemistry analysis (Dairy One Forage Laboratory, Ithaca, NY).

[4]Calculated according to the equations described by Weiss et al. (1992).

[5]Calculated according to the equations described by NRC (2000).

Sampling

Samples of hay and concentrate ingredients were collected weekly, pooled across all weeks, and analyzed for nutrient content by a commercial laboratory (Dairy One Forage Laboratory, Ithaca, NY). All samples were analyzed by wet chemistry procedures for concentrations of CP (method 984.13; AOAC, 2006), ADF (method 973.18 modified for use in an Ankom 200 fiber analyzer [Ankom Technology Corp., Fairport, NY]; AOAC, 2006), and NDF (Van Soest et al., 1991; modified for use in an Ankom 200 fiber analyzer [Ankom Technology Corp.]). Calculations for TDN used the equation proposed by Weiss et al. (1992), whereas NEm and NEg were calculated with the equations proposed by the NRC (2000). Hay nutritional profile was (DM basis) 59% TDN, 59% NDF, 41% ADF, 1.20 Mcal/kg of NEm, 0.62 Mcal/kg of NEg, and 11.3% CP. Concentrate nutritional profile is described in Table 1.

Calf BW was recorded on 2 consecutive days (d −15 and −14, d 0 and 1, d 28 and 29, and d 75 and 76), and values from both days were averaged for ADG calculation. Calves were observed daily (0800 to 1000 h and 1600 to 1800 h) for BRD symptoms according to the subjective criteria described by Berry et al. (2004) and received 0.1 mL/kg of BW of Hexasol LA Solution (Norbrook Inc. USA, Overland Park, KS) when symptoms were observed. Concentrate, hay, and total DMI were evaluated daily from d 8 to 75 from each pen by collecting and weighing refusals daily. Samples of the offered and nonconsumed feed were collected daily from each pen and dried for 96 h at 50°C in forced-air ovens for DM calculation. Hay, concentrate, and total daily DMI of each pen were divided by the number of calves within each pen and expressed as kilograms per calf per day. Total BW gain and DMI of each pen from d 30 to 75 were used for receiving G:F calculation.

Blood samples were collected on d −15, 0, 15, 30, 45, 60, and 75 via jugular venipuncture into commercial blood collection tubes (Vacutainer, 10 mL; Becton, Dickinson and Company, Franklin Lakes, NJ) with 158 US pharmacopeia units of freeze-dried sodium heparin for plasma collection. Blood samples were collected prior to treatment administration (d −15 to 45) and prior to concentrate and hay feeding of the day (d 15 to 75).

Blood Analysis

All blood samples were placed immediately on ice, centrifuged (2,500 × *g* for 30 min at 4°C) for plasma harvest, and stored at −80°C on the same day of collection. Plasma was analyzed for concentrations of MH leukotoxin antibodies (Confer et al., 1996; Burciaga-Robles et al., 2010) and BVDV type I and II strains (BVDV Ab ELISA number 99-44000; IDEXX Switzerland AG, Liebefeld-Bern, Switzerland; Gonda et al., 2012), which are 2 of the most common pathogens associated with BRD in cattle (Edwards, 2010). Plasma concentrations of antibodies against these pathogens were evaluated based on day of the experiment (d −15 to 75) or based on equivalent days relative to the vaccination and booster.

Table 2. Performance parameters of calves assigned to 1 of 3 vaccination schemes against respiratory pathogens at 1) vaccination at weaning (d 0) and a booster at feedlot entry (d 30; CON; $n = 30$), 2) vaccination 15 d before weaning (d −15) and a booster 15 d before feedlot entry (d 15; EARLY; $n = 30$), and 3) vaccination 15 d after weaning (d 15) and a booster 15 d after feedlot entry (d 45; DELAYED; $n = 30$)[1]

Item	EARLY	CON	DELAYED	SEM	*P*-value
BW, kg					
Before weaning (d −15)	215	215	215	4	0.99
Weaning (d 0)	220	225	223	4	0.76
Final preconditioning (d 29)	228	234	231	4	0.65
Final feedlot receiving (d 75)	275	273	271	4	0.78
ADG, kg/d					
Before weaning (d −15 to −1)	0.38[a]	0.65[b]	0.55[b]	0.08	0.04
Preconditioning (d 0 to 29)	0.26	0.30	0.26	0.07	0.88
Feedlot receiving (d 30 to 75)	1.04[a]	0.87[b]	0.88[b]	0.04	0.01

[a,b]Means with different superscripts differ ($P \leq 0.05$).

[1]Vaccines administered were against *Clostridium* (2 mL, subcutaneously; One Shot Ultra 7; Zoetis, Florham Park, NJ); parainfluenza virus (TSV-2; Zoetis); and infectious bovine rhinotracheitis virus, bovine viral diarrhea Types 1 and 2 viruses, and *Mannheimia haemolytica* (2 mL, s.c.; Bovi-Shield Gold One Shot; Zoetis). Calves not receiving a vaccination were administered 4 mL (s.c.) of sterile saline.

Statistical Analysis

Calf was considered the experimental unit. Quantitative data were analyzed using the MIXED procedure of SAS (SAS Inst. Inc., Cary, NC), and binary data were analyzed using the GLIMMIX procedure of SAS and Satterthwaite approximation to determine the denominator degrees of freedom for tests of fixed effects. The model statement for BW, ADG, G:F, and morbidity and mortality rates contained the effects of treatment, sex, and the resultant interaction. The model statement for DMI and plasma variables contained the effects of treatment, sex, day, and all resultant interactions. Data were analyzed using calf (pen × treatment × sex). Nevertheless, DMI and G:F data used pen(treatment) as random variable and did not include sex in the fixed model because DMI was recorded from each pen. G:F that used pen(treatment) as random variable and did not include sex in the fixed model because DMI was recorded from each pen. The specified term for the repeated statements was day, and the subject for DMI and plasma variables were, respectively, pen(treatment) or calf(pen × treatment × sex). The covariance structure used was first-order autoregressive, which provided the smallest Akaike information criterion and, hence, the best fit for all variables analyzed. Although calves were not managed in pens from d −15 to 7, pen was included in random and repeated statements to ensure equal statistical structure across the experimental period. Results are reported as least squares means and were separated using PDIFF. Significance was set at $P \leq 0.05$ and tendencies were determined if $P > 0.05$ and ≤ 0.10. Results are reported according to main effects if no interactions were significant or according to the highest-order interaction detected.

RESULTS AND DISCUSSION

Performance Traits

During the preweaning phase, a treatment effect was detected ($P = 0.04$) for ADG (Table 2). Calves assigned to EARLY had decreased ($P \leq 0.05$) ADG compared with calves assigned to CON and tended ($P = 0.09$) to have decreased ADG compared with DELAYED calves, whereas ADG was similar ($P = 0.35$) between CON and DELAYED calves. This outcome is supported by Arthington et al. (2013), who observed reduced ADG in heifers vaccinated for MH and *Clostridium* compared with unvaccinated heifers. However, treatment differences in ADG were not sufficient to impact calf weaning BW, which were similar ($P = 0.76$) across treatments (Table 2).

During the preconditioning phase, a treatment × day interaction was detected ($P = 0.03$) for hay DMI, which was less for EARLY and DELAYED calves compared with CON calves from d 15 to 18 (Fig. 1). Supporting our findings, Rodrigues et al. (2015) also reported that DMI was reduced due to vaccination against BRD pathogens for 72 h and returned to levels similar to those of nonvaccinated cohorts 4 d after vaccination. Moreover, overall preconditioning hay DMI was greater ($P \leq 0.04$) for CON calves compared with EARLY and DELAYED calves and similar ($P = 0.86$) between EARLY and DELAYED calves (Table 3; treatment effect, $P = 0.05$). It is important to note that hay DMI was not evaluated during the initial 7 d of preconditioning and that CON calves received a vaccination at weaning on d 0. Hence, hay DMI was evaluated after the expected decrease in DMI caused by vaccination to CON calves, which helps explaining the treatment effect detected for overall preconditioning hay DMI. Nevertheless, such difference

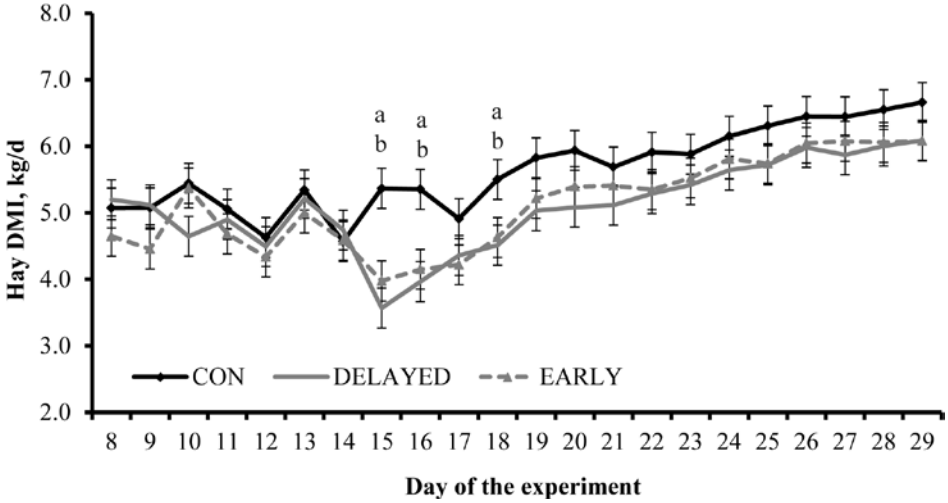

Figure 1. Hay DMI during preconditioning in calves assigned to 1 of 3 vaccination schemes against respiratory pathogens at 1) vaccination at weaning (d 0) and a booster at feedlot entry (d 30; CON; $n = 30$), 2) vaccination 15 d before weaning (d −15) and a booster 15 d before feedlot entry (d 15; EARLY; $n = 30$), and 3) vaccination 15 d after weaning (d 15) and a booster 15 d after feedlot entry (d 45; DELAYED; $n = 30$). Vaccines administered were against *Clostridium* (2 mL, subcutaneously; One Shot Ultra 7; Zoetis, Florham Park, NJ); parainfluenza virus (TSV-2; Zoetis); and infectious bovine rhinotracheitis virus, bovine viral diarrhea Types 1 and 2 viruses, and *Mannheimia haemolytica* (2 mL, s.c.; Bovi-Shield Gold One Shot; Zoetis). Calves not receiving a vaccination were administered 4 mL (s.c.) of sterile saline. A treatment × day interaction was detected ($P < 0.01$). Within days, letters indicate ($P \leq 0.05$) [a]CON vs. DELAYED and [b]CON vs. EARLY.

was not sufficient to impact ($P \geq 0.65$) preconditioning ADG or final preconditioning BW (Table 2).

During the feedlot receiving phase, no treatment effects were detected ($P \geq 0.22$) for hay, concentrate, and total DMI (Table 3). A treatment effect was detected ($P = 0.01$) for feedlot receiving ADG, which was greater ($P \leq 0.01$) for EARLY calves compared with DELAYED and CON calves and similar ($P = 0.87$) between DELAYED and CON calves (Table 2). Yet no treatment differences were detected ($P \geq 0.16$) for receiving G:F (198.5, 193.4, and 175.0 g/kg of G:F for EARLY, CON, and DELAYED calves, respectively; SEM = 8.6) and final receiving BW (Table 2). Rodrigues et al. (2015) also reported that vaccination against BRD pathogens did not impact concentrate intake, despite differences detected in hay DMI. Supporting our findings, Arthington et al. (2013) did not detect differences in total DMI in feeder heifers vaccinated or not against BRD pathogens but did observe an ADG decrease in vaccinated heifers.

These results support our hypothesis that anticipating vaccination against BRD pathogens, in a manner such that both injections are administered prior to feedlot entry, improve receiving performance of feeder cattle. The vaccines administered herein contained a freeze-dried preparation of modified-live virus strains, a product from whole cultures of inactivated MH, and a proprietary (Zoetis) adjuvant formulation. The viral fraction and adjuvant contained in the vaccines used herein assist in recruiting leukocytes to the site of vaccine delivery, which, in turn, synthesize proinflammatory cytokines and elicit a systemic acute-phase response (Carroll and Forsberg, 2007). These responses are known to impair animal performance via several metabolic mechanisms, including fever, reduced appetite, and impaired tissue anabolism (Johnson, 1997; Rodrigues et al., 2015). Nevertheless, the negative impact of vaccination on ADG of EARLY calves during the preweaning phase cannot be fully elucidated as calf DMI was not assessed. Moreover, the greater ADG in EARLY calves during feedlot receiving did not result from increased DMI, suggesting that vaccination against BRD pathogens impacts cattle performance beyond feed intake modulation (Arthington et al., 2013).

Table 3. Feed intake parameters (kg/d; DM basis) of calves assigned to 1 of 3 vaccination schemes against respiratory pathogens at 1) vaccination at weaning (d 0) and a booster at feedlot entry (d 30; CON; $n = 30$), 2) vaccination 15 d before weaning (d −15) and a booster 15 d before feedlot entry (d 15; EARLY; $n = 30$), and 3) vaccination 15 d after weaning (d 15) and a booster 15 d after feedlot entry (d 45; DELAYED; $n = 30$)[1]

Item	EARLY	CON	DELAYED	SEM	*P*-value
Preconditioning (d 8 to 29)					
Hay	5.08[a]	5.60[b]	5.03[a]	0.16	0.05
Feedlot receiving (d 31 to 75)					
Hay	4.10	3.67	3.98	0.16	0.22
Concentrate	3.72	3.71	3.71	0.07	0.99
Total	7.81	7.39	7.69	0.18	0.28

[a,b]Means with different superscripts differ ($P \leq 0.05$).

[1]Vaccines administered were against *Clostridium* (2 mL, subcutaneously; One Shot Ultra 7; Zoetis, Florham Park, NJ); parainfluenza virus (TSV-2; Zoetis); and infectious bovine rhinotracheitis virus, bovine viral diarrhea Types 1 and 2 viruses, and *Mannheimia haemolytica* (2 mL, s.c.; Bovi-Shield Gold One Shot; Zoetis). Calves not receiving a vaccination were administered 4 mL (s.c.) of sterile saline.

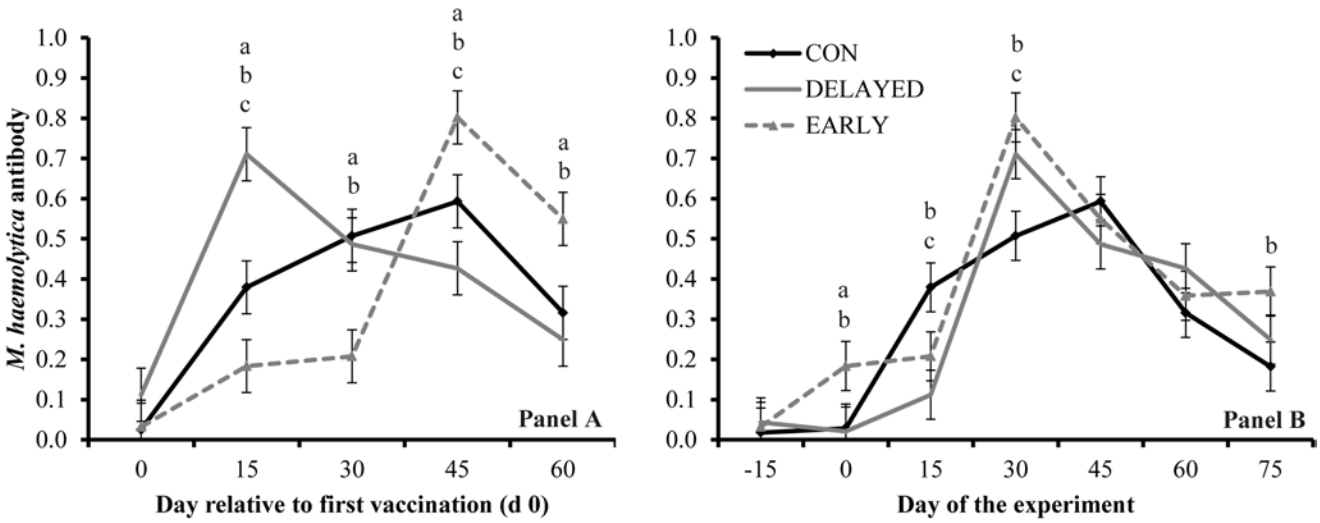

Figure 2. Plasma concentrations of antibodies against *Mannheimia haemolytica* (ng/antibody bound) in calves assigned to 1 of 3 vaccination schemes against respiratory pathogens at 1) vaccination at weaning (d 0) and a booster at feedlot entry (d 30; CON; $n = 30$), 2) vaccination 15 d before weaning (d −15) and a booster 15 d before feedlot entry (d 15; EARLY; $n = 30$), and 3) vaccination 15 d after weaning (d 15) and a booster 15 d after feedlot entry (d 45; DELAYED; $n = 30$). Vaccines administered were against *Clostridium* (2 mL, subcutaneously; One Shot Ultra 7; Zoetis, Florham Park, NJ); parainfluenza virus (TSV-2; Zoetis); and infectious bovine rhinotracheitis virus, bovine viral diarrhea Types 1 and 2 viruses, and *Mannheimia haemolytica* (2 mL, s.c.; Bovi-Shield Gold One Shot; Zoetis). Calves not receiving a vaccination were administered 4 mL (s.c.) of sterile saline. Panel A reports values relative to the day of the first vaccination (d 0) and revaccination (d 30) within each treatment, and Panel B reports values during the experimental period (d −15 to 75). Treatment × day interactions were detected ($P < 0.01$). Within days, letters indicate ($P \leq 0.05$) [a]EARLY vs. DELAYED, [b]EARLY vs. CON, and [c]DELAYED vs. CON.

Health Variables

A treatment × day interaction was detected ($P < 0.01$) for plasma concentrations of antibodies against MH when data were analyzed based on days relative to the initial vaccination and the booster (Fig. 2a). Plasma MH antibody concentrations were less ($P \leq 0.03$) in EARLY calves compared with CON and DELAYED calves 15 and 30 d after the initial vaccination and also greater ($P < 0.01$) for DELAYED vs. CON calves 15 d after the initial vaccination. Conversely, EARLY calves had greater ($P \leq 0.02$) MH antibody concentrations compared with CON and DELAYED calves 15 and 30 d after the booster, which was also greater ($P = 0.05$) for CON vs. DELAYED calves 15 d after the booster. No further treatment differences were detected ($P \geq 0.33$). Circulating concentrations of neutralizing antibodies provide an indication of immune protection, disease prevention, and vaccine efficacy in cattle (Howard et al., 1989; Bolin and Ridpath, 1990; Callan, 2001). Supporting our hypothesis, delaying vaccination against BRD pathogens to avoid the stress of weaning enhanced their initial MH antibody response, whereas anticipating vaccination by 15 d impaired such response. This latter outcome was unexpected but can be associated with a potential decrease in nutrient intake of EARLY calves, as suggested by treatment differences in preweaning ADG (Table 2; Arthington et al., 2013; Rodrigues et al., 2015), to levels that impaired antibody production by their adaptive immune system (Galyean et al., 1999; Downey et al., 2013; Moriel et al., 2015).

Antibody response to the MH booster among treatments, however, was the opposite of the response to the initial vaccination. A booster vaccination against MH is not required, although this is a common practice in commercial feedlots due to the frequent lack of health history in high-risk receiving cattle (Edwards, 2010). Yet one of the immunological purposes of a booster vaccination is to provide repeated antigen exposure in calves that lacked an adequate immune response to the initial vaccination (Edwards, 2010). Hence, it seems plausible that EARLY calves benefited from and likely a required booster against MH due to their inadequate MH antibody response to the initial vaccination. Conversely, the same outcome was not observed in DELAYED calves due to their elevated MH antibody response to the initial vaccination, given that existing circulating antibodies can bind to antigen provided by the booster vaccine and prevent its recognition and subsequent antibody production by the adaptive immune system (Zimmerman et al., 2006; Downey et al., 2013).

A treatment × day interaction was also detected ($P < 0.01$) for plasma concentrations of antibodies against MH when data were analyzed based on day of the experiment (Fig. 2b). Calves assigned to EARLY had greater ($P \leq 0.05$) MH antibody concentrations compared with calves assigned to CON and DELAYED on d 0 of the experiment, given that only EARLY calves were vaccinated prior to weaning. On d 15 of the experiment, CON calves had the greatest ($P \leq 0.04$) antibody concentrations due to their improved MH antibody response to the initial vaccination compared with EARLY calves and

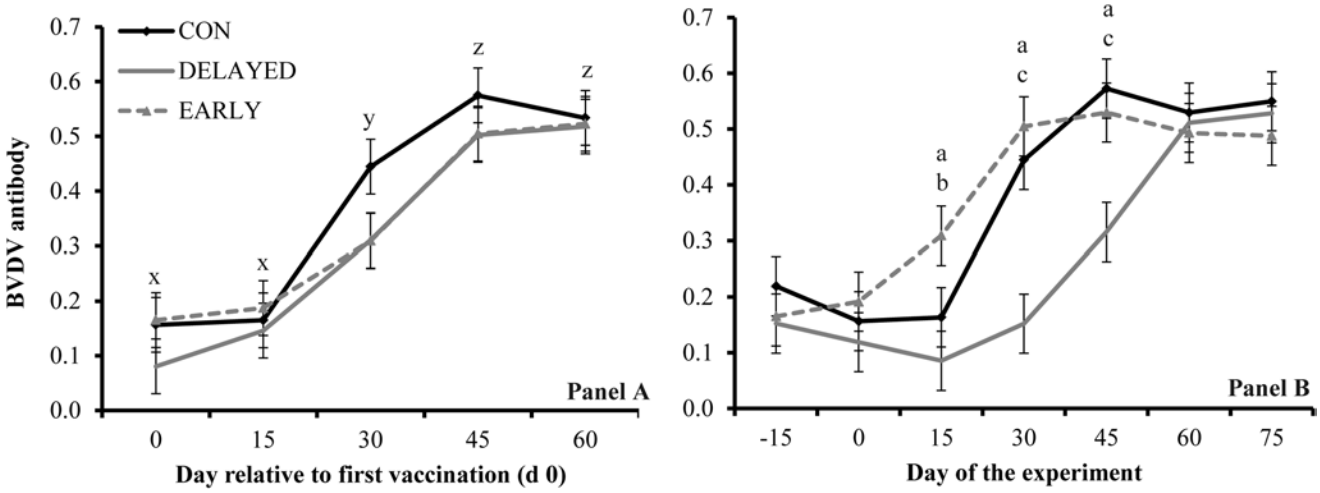

Figure 3. Plasma concentrations of antibodies against bovine viral diarrhea virus (BVDV; sample:positive control ratio as in Gonda et al. [2012]) in calves assigned to 1 of 3 vaccination schemes against respiratory pathogens at 1) vaccination at weaning (d 0) and a booster at feedlot entry (d 30; CON; n = 30), 2) vaccination 15 d before weaning (d −15) and a booster 15 d before feedlot entry (d 15; EARLY; n = 30), and 3) vaccination 15 d after weaning (d 15) and a booster 15 d after feedlot entry (d 45; DELAYED; n = 30). Vaccines administered were against *Clostridium* (2 mL, subcutaneously; One Shot Ultra 7; Zoetis, Florham Park, NJ); parainfluenza virus (TSV-2; Zoetis); and infectious bovine rhinotracheitis virus, bovine viral diarrhea Types 1 and 2 viruses, and *Mannheimia haemolytica* (2 mL, s.c.; Bovi-Shield Gold One Shot; Zoetis). Calves not receiving a vaccination were administered 4 mL (s.c.) of sterile saline. Panel A reports values relative to the day of the first vaccination (d 0) and revaccination (d 30) within each treatment, and Panel B reports values during the experimental period (d −15 to 75). A day effect was detected in Panel A ($P < 0.01$). x–zMeans with different letters differ ($P < 0.01$). A treatment × day interaction was detected ($P < 0.01$) for Panel B only, and within days, letters indicate ($P \leq 0.05$) [a]EARLY vs. DELAYED, [b]EARLY vs. CON, and [c]DELAYED vs. CON.

the fact that DELAYED calves were yet to be vaccinated. On d 30 of the experiment, MH antibody concentrations were greater ($P \leq 0.02$) in DELAYED and EARLY calves compared with CON calves. On d 75 of the experiment, MH antibody concentrations were greater ($P = 0.03$) in EARLY calves compared with CON calves. No further treatment differences were detected ($P \geq 0.20$). These results indicate that both EARLY and DELAYED calves had greater plasma concentrations of antibodies against MH at feedlot entry (d 30 of the experiment) compared with CON calves, suggesting improved immune protection against this pathogen (Callan, 2001) despite differences detected for MH antibody response to the initial and booster vaccinations (Fig. 2a).

No treatment differences were detected ($P = 0.33$) when plasma concentrations of antibodies against BVDV were analyzed based on equivalent days relative to the vaccination and booster (Fig. 3a). This outcome suggests that, contrarily to MH, treatments did not impact BVDV antibody response to the initial or booster vaccination. It is important to note that increased plasma concentration of antibodies against BVDV were only detected 30 d after the initial vaccination (day effect, $P < 0.01$; Fig. 3a). Richeson et al. (2009) also reported a similar interval between vaccination against BVDV and substantial increases in serum BVDV titers, whereas Rodrigues et al. (2015) did not detect such increase within 14 d after vaccination. Hence, the interval between vaccination and synthesis of BVDV antibodies (>15 d) likely prevented benefits of DELAYED calves over CON calves because the immunological consequences of stress endure for up to 15 d (Purdy et al., 2000). Similarly, the antibody response to the initial BVDV vaccination in EARLY calves was not impaired by the decrease in preweaning ADG, given that this outcome was observed at least 15 d before the increase in plasma BVDV antibodies in these calves.

A treatment × day interaction was detected ($P < 0.01$) for plasma concentrations of antibodies against BVDV when data were analyzed based on day of the experiment (Fig. 3b). On d 15, EARLY calves had greater ($P \leq 0.04$) antibody concentrations compared with CON and DELAYED calves. On d 30 and 45, BVDV antibody concentrations were greater ($P \leq 0.01$) in EARLY and CON calves compared with DELAYED calves. No further treatment differences were detected ($P \geq 0.28$). These outcomes can be directly attributed to lack of differences in BVDV antibody response (Fig. 3a), treatment design, and interval between vaccination and increased plasma concentrations of BVDV antibodies. Therefore, EARLY and CON calves had greater plasma concentrations of antibodies against BVDV, suggestive of improved immune protection against this pathogen (Callan, 2001), at feedlot entry compared with DELAYED calves.

No treatment effects were detected ($P > 0.05$) for morbidity or mortality data during the preconditioning or feedlot receiving phases (Table 4), despite treatment differences being detected for plasma concentrations of MH and BVDV antibodies. Morbidity during the receiving period was not as prevalent compared with values from research conducted at commercial

Table 4. Health responses of calves assigned to 1 of 3 vaccination schemes against respiratory pathogens at 1) vaccination at weaning (d 0) and a booster at feedlot entry (d 30; CON; $n = 30$), 2) vaccination 15 d before weaning (d −15) and a booster 15 d before feedlot entry (d 15; EARLY; $n = 30$), and 3) vaccination 15 d after weaning (d 15) and a booster 15 d after feedlot entry (d 45; DELAYED; $n = 30$)[1,2]

Item	EARLY	CON	DELAYED	SEM	*P*-value
Morbidity, %					
Preconditioning, % (d 0 to 30)	27.9	34.5	32.3	9.5	0.88
Feedlot receiving, % (d 31 to 75)	2.1[a]	16.5[b]	9.3[ab]	5.3	0.17
Mortality, %	0.0	4.4	4.4	4.5	0.73
Preconditioning, % (d 0 to 30)	–	–	–	–	–
Feedlot receiving, % (d 31 to 75)	0.0	4.4	4.4	4.5	0.73

[a,b]Means with different superscripts differ ($P \leq 0.05$).

[1]Vaccines administered were against *Clostridium* (2 mL, subcutaneously; One Shot Ultra 7; Zoetis, Florham Park, NJ); parainfluenza virus (TSV-2; Zoetis); and infectious bovine rhinotracheitis virus, bovine viral diarrhea Types 1 and 2 viruses, and *Mannheimia haemolytica* (2 mL, s.c.; Bovi-Shield Gold One Shot; Zoetis). Calves not receiving a vaccination were administered 4 mL (s.c.) of sterile saline.

[2]Calves were observed daily for morbidity according to the subjective criteria described by Berry et al. (2004) and received 0.1 mL/kg of BW of Hexasol LA Solution (Norbrook Inc. USA, Overland Park, KS) when symptoms were observed.

receiving yards (Snowder et al., 2006; Marques et al., 2016), which may have hindered proper assessment of this variable. This outcome can be associated with the fact that although calves were subjected to the stress of weaning and long transportation (Arthington et al., 2008; Cooke et al., 2013), they returned to the same facility with the same pen members and were not exposed to calves from other sources in a novel environment (Step et al., 2008). Yet it is important to note that morbidity was less ($P = 0.05$) in EARLY calves compared with CON cohorts during the feedlot receiving phase (Table 4), despite the lack of main treatment effect ($P = 0.17$) for this variable. According to the results observed herein and the G*power 3 software (Faul et al., 2007), at least 50 calves/treatment were needed to yield a significant ($P \leq 0.05$) main treatment effect for receiving morbidity. Hence, additional research with greater treatment replication and inclusion of commingling stress is warranted to further investigate how the treatments evaluated herein impact morbidity and mortality rates in high-stress feedlot receiving scenarios.

Overall Conclusions

Collectively, the EARLY treatment resulted in increased plasma concentrations of antibodies against MH and BVDV at feedlot entry and increased ADG during feedlot receiving compared with the CON and DELAYED treatments. Moreover, treatment effects on plasma BVDV and MH antibodies at feedlot entry should not be associated with increased antibody response in EARLY calves but with a greater interval between vaccinations and feedlot entry. Further research is warranted to validate these outcomes in high-stress feedlot receiving scenarios where morbidity and mortality are traditionally greater, as observed herein, including evaluation of antibodies against other BRD pathogens and calf performance until slaughter. Nevertheless, anticipating the vaccination and booster against BRD pathogens to provide both doses prior to feedlot entry appears to be a valid strategy to enhance cattle health and performance during feedlot receiving.

LITERATURE CITED

AOAC. 2006. Official methods of analysis. 18th ed. AOAC Inc., Arlington, VA.

Arthington, J. D., R. F. Cooke, T. D. Maddock, D. B. Araujo, P. Moriel, N. Dilorenzo, and G. C. Lamb. 2013. Effects of vaccination on the acute-phase protein response and measures of performance in growing beef calves. J. Anim. Sci. 91:1831–1837. doi:10.2527/jas.2012-5724

Arthington, J. D., X. Qiu, R. F. Cooke, J. M. B. Vendramini, D. B. Araujo, C. C. Chase Jr., and S. W. Coleman. 2008. Effects of preshipping management on measures of stress and performance of beef steers during feedlot receiving. J. Anim. Sci. 86:2016–2023. doi:10.2527/jas.2008-0968

Berry, B. A., A. W. Confer, C. R. Krehbiel, D. R. Gill, R. A. Smith, and M. Montelongo. 2004. Effects of dietary energy and starch concentrations for newly received feedlot calves: II. Acute-phase protein response. J. Anim. Sci. 82:845–850.

Blecha, F., S. L. Boyles, and J. G. Riley. 1984. Shipping suppresses lymphocyte blastogenic responses in Angus and Brahman × Angus feeder calves. J. Anim. Sci. 59:576–583.

Bolin, S. R., and J. F. Ridpath. 1990. Range of viral neutralizing activity and molecular specificity of antibodies induced in cattle by inactivated bovine viral diarrhea virus-vaccines. Am. J. Vet. Res. 51:703–707.

Burciaga-Robles, L. O., D. L. Step, C. R. Krehbiel, B. P. Holland, C. J. Richards, M. A. Montelongo, A. W. Confer, and R. W. Fulton. 2010. Effects of exposure to calves persistently infected with bovine viral diarrhea virus type 1b and subsequent infection with *Mannheima haemolytica* on clinical signs and immune variables: Model for bovine respiratory disease via viral and bacterial interaction. J. Anim. Sci. 88:2166–2178. doi:10.2527/jas.2009-2005

Callan, R. J. 2001. Fundamental considerations in developing vaccination protocols. Bovine Pract. 34:14–22.

Carroll, J. A., and N. E. Forsberg. 2007. Influence of stress and nutrition on cattle immunity. Vet. Clin. North Am. Food Anim. Pract. 23:105–149.

Confer, A. W., S. H. Nutt, S. M. Dabo, R. J. Panciera, and G. L. Murphy. 1996. Antibody responses to outer membrane proteins of *Pasteurella haemolytica* A:3. Am. J. Vet. Res. 57:1452–1457.

Cooke, R. F., T. A. Guarnieri Filho, B. I. Cappellozza, and D. W. Bohnert. 2013. Rest stops during road transport: Impacts on performance and acute-phase protein responses of feeder cattle. J. Anim. Sci. 91:5448–5454. doi:10.2527/jas.2013-6357

Downey, E. D., R. G. Tait Jr., M. S. Mayes, C. A. Park, J. F. Ridpath, D. J. Garrick, and J. M. Reecy. 2013. An evaluation of circulating bovine viral diarrhea virus type 2 maternal antibody level and response to vaccination in Angus calves. J. Anim. Sci. 91:4440–4450. doi:10.2527/jas.2012-5890

Duff, G. C., and M. L. Galyean. 2007. Board-invited review: Recent advances in management of highly stressed, newly received feedlot cattle. J. Anim. Sci. 85:823–840. doi:10.2527/jas.2006-501

Edwards, T. A. 2010. Control methods for bovine respiratory disease for feedlot cattle. Vet. Clin. North Am. Food Anim. Pract. 26:273–284. doi:10.1016/j.cvfa.2010.03.005

England, J., R. Ellis, and P. Cuneo. 2009. Vaccination and imunization: vaccination programs for cattle operations. In: Cattle producer's handbook. 3rd ed. Agric. Publ. Distribution, University of Idaho, Moscow, ID. p. 605/1-605/3.

Faul, F., E. Erdfelder, A. G. Lang, and A. Buchner. 2007. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav. Res. Methods 39:175–191. doi:10.3758/BF03193146

Galyean, M. L., L. J. Perino, and G. C. Duff. 1999. Interaction of cattle health/immunity and nutrition. J. Anim. Sci. 77:1120–1134.

Ganskopp, D. C., and D. W. Bohnert. 2009. Landscape nutritional patterns and cattle distribution in rangeland pastures. Appl. Anim. Behav. Sci. 116:110–119. doi:10.1016/j.applanim.2008.10.006

Gonda, M. G., X. Fang, G. A. Perry, and C. Maltecca. 2012. Measuring bovine viral diarrhea virus vaccine response: Using a commercially available ELISA as a surrogate for serum neutralization assays. Vaccine 30:6559–6563. doi:10.1016/j.vaccine.2012.08.047

Howard, C. J., M. C. Clarke, and J. Brownlie. 1989. Protection against respiratory infection with bovine virus diarrhea virus by passively acquired antibody. Vet. Microbiol. 19:195–203. doi:10.1016/0378-1135(89)90066-7

Johnson, R. W. 1997. Inhibition of growth by pro-inflammatory cytokines: An integrated view. J. Anim. Sci. 75:1244–1255.

Kirkpatrick, J. G., D. L. Step, M. E. Payton, J. B. Richards, L. F. McTague, J. T. Saliki, A. W. Confer, B. J. Cook, S. H. Ingram, and J. C. Wright. 2008. Effect of age at the time of vaccination on antibody titers and feedlot performance in beef calves. J. Am. Vet. Med. Assoc. 233:136–142. doi:10.2460/javma.233.1.136

Marques, R. S., R. F. Cooke, M. C. Rodrigues, B. I. Cappellozza, C. K. Larson, P. Moriel, and D. W. Bohnert. 2016. Effects of organic or inorganic Co, Cu, Mn, and Zn supplementation to late-gestating beef cows on productive and physiological responses of the offspring. J. Anim. Sci. 94:1215–1226. doi:10.2527/jas.2015-0036

Martin, S. W., E. Nagy, D. Armstrong, and S. Rosendal. 1999. The associations of viral and mycoplasmal antibody titers with respiratory disease and weight gain in feedlot calves. Can. Vet. J. 40:560–570.

Moriel, P., L. F. A. Artioli, M. H. Poore, A. W. Confer, R. S. Marques, and R. F. Cooke. 2015. Increasing the metabolizable protein supply enhanced growth performance and led to variable results on innate and humoral immune response of preconditioning beef steers. J. Anim. Sci. 93:4473–4485. doi:10.2527/jas.2015-9238

National Agricultural Statistics Service (NASS). 2006. Cattle death loss. National Agricultural Statistics Service, Agricultural Statistics Board, USDA, Washington, DC.

NRC. 2000. Nutrient requirements of beef cattle. 7th ed. Natl. Acad. Press, Washington, DC.

Purdy, C. W., R. W. Loan, D. C. Straus, R. E. Briggs, and G. H. Franks. 2000. Conglutinin and immunoconglutinin titers in stressed calves in a feedlot. Am. J. Vet. Res. 61:1403–1409. doi:10.2460/ajvr.2000.61.1403

Richeson, J. T., P. A. Beck, M. S. Gadberry, S. A. Gunter, T. W. Hess, D. S. Hubbell, and C. Jones. 2008. Effects of on-arrival versus delayed modified-live virus vaccination on health, performance, and serum infectious bovine rhinotracheitis titers of newly-received beef calves. J. Anim. Sci. 86:999–1005. doi:10.2527/jas.2007-0593

Richeson, J. T., E. B. Kegley, M. S. Gadberry, P. A. Beck, J. G. Powell, and C. A. Jones. 2009. Effects of on-arrival versus delayed clostridial or modified live respiratory vaccinations on health, performance, bovine viral diarrhea virus type I titers, and stress and immune measures of newly received beef calves. J. Anim. Sci. 87:2409–2418. doi:10.2527/jas.2008-1484

Rodrigues, M. C., R. F. Cooke, R. S. Marques, B. I. Cappellozza, S. A. Arispe, D. H. Keisler, and D. W. Bohnert. 2015. Effects of vaccination against respiratory pathogens on feed intake, metabolic and inflammatory responses in beef heifers. J. Anim. Sci. 93:4443–4452. doi:10.2527/jas.2015-9277

Snowder, G. D., L. D. Van Vleck, L. V. Cundiff, and G. L. Bennett. 2006. Bovine respiratory disease in feedlot cattle: Environmental, genetic, and economic factors. J. Anim. Sci. 84:1999–2008. doi:10.2527/jas.2006-046

Step, D. L., C. R. Krehbiel, H. A. DrPra, J. K. Cranston, R. W. Fulton, J. G. Kirkpatrick, D. R. Gill, M. E. Payton, M. A. Montelongo, and A. W. Confer. 2008. Effects of commingling beef calves from different sources and weaning protocols during a forty-two-day receiving period on performance and bovine respiratory disease. J. Anim. Sci. 86:3146–3158. doi:10.2527/jas.2008-0883

Van Soest, P. J., J. B. Robertson, and B. A. Lewis. 1991. Methods for dietary fiber, neutral detergent fiber, and nonstarch polysaccharides in relation to nutrition animal. J. Dairy Sci. 74:3583–3597. doi:10.3168/jds.S0022-0302(91)78551-2

Weiss, W. P., H. R. Conrad, and N. R. St. Pierre. 1992. A theoretically-based model for predicting total digestible nutrient values of forages and concentrates. Anim. Feed Sci. Technol. 39:95–110. doi:10.1016/0377-8401(92)90034-4

Zimmerman, A. D., R. E. Boots, J. L. Valli, and C. C. L. Chase. 2006. Evaluation of protection against virulent bovine viral diarrhea virus type 2 in calves that had maternal antibodies and were vaccinated with a modified-live vaccine. J. Am. Vet. Med. Assoc. 228:1757–1761. doi:10.2460/javma.228.11.1757