Effect of modified-live bovine viral diarrhea virus type 2 vaccine on performance, health, temperature, and behavior response in high-risk beef heifer calves

Brad J. White[1,2], DVM, MS; **Miles E. Theurer**[3], DVM, PhD; **Dan R. Goehl**[1], DVM; **Peggy Thompson**[4], DVM

[1]Precision Animal Solutions, Manhattan, KS 66503
[2]Beef Cattle Institute, Kansas State University, Manhattan, KS 66506
[3]Veterinary Research and Consulting Services, LLC, Hays, KS 67601
[4]Boehringer Ingelheim Vetmedica, Inc, St. Joseph, MO 64157
Corresponding author: Dr. Brad J. White, email: bwhite@vet.k-state.edu

Abstract

The objective of this study was to determine performance, health, vaginal temperature, and behavior differences in calves vaccinated upon feedlot arrival with a multivalent modified-live virus (MLV) vaccine which included bovine viral diarrhea virus (BVDV) type 2 antigen and calves vaccinated with a vaccine which did not include BVDV type 2. Eighty-three beef heifer calves were randomly assigned to receive a multivalent MLV vaccine containing either bovine herpes-virus-1, BVDV type 1, bovine respiratory syncytial virus, and parainfluenza type-3 virus ($n = 42$; 4-WAY), or a MLV vaccine of similar formulation which also contained a BVDV type 2 antigen ($n = 41$; 5-WAY). Performance outcomes were evaluated at 30 and 60 days. Vaginal temperatures were evaluated hourly and daily. Cattle behavior activity was monitored with a real-time location system. Calves in the 5-WAY group had greater average daily gain ($P = 0.026$) at 60 days, excluding dead animals, compared to 4-WAY group. Treatment group was not associated with vaginal temperature. Calves in 5-WAY spent a greater ($P \leq 0.01$) amount of time at the feed bunk on days 0, 2, 3, and 4 compared to 4-WAY. Results of this study indicate no adverse effects from administering an additional strain of BVDV type 2 to high-risk heifers. Behavioral responses indicate a potential advantage to administer 5-WAY vaccine compared to 4-WAY vaccine.

Key words: behavior, bovine respiratory disease, bovine viral diarrhea virus, temperature, vaccination

Résumé

L'objectif de cette étude était de déterminer l'impact de la vaccination sur la performance, la santé, la température vaginale et le comportement des veaux vaccinés à leur arrivée au parc d'engraissement soit avec un vaccin multivalent à virus vivants modifiés incluant un antigène contre le virus de la diarrhée virale bovine du type 2 (BVDV type-2) ou soit avec un vaccin qui n'incluait pas cet antigène. On a alloué au hasard 83 génisses de boucherie dans deux groupes vaccinés avec un vaccin multivalent à virus vivants modifiés incluant soit l'herpès-virus bovin 1, le BVDV type-1, le virus respiratoire syncytial bovin et le virus parainfluenza 3 (n = 42, tétravalent) ou soit un vaccin avec une composition similaire mais qui incluait en plus un antigène contre le BVDV type-2 (n = 41, pentavalent). Les mesures de performance ont été prises au jour 30 et au jour 60. La température vaginale était mesurée à toutes les heures et à chaque jour. Le comportement a été suivi avec un système de localisation en temps réel. Le gain moyen quotidien au jour 60 en excluant les animaux morts était plus élevé dans le groupe pentavalent que dans le groupe tétravalent ($P = 0.026$). Il n'y a pas eu d'effet du traitement sur la température vaginale. Le temps passé près de la mangeoire était plus élevé dans le groupe pentavalent que dans le groupe tétravalent aux jours 0, 2, 3 et 4 ($P < 0.01$). Les résultats de cette étude n'ont pas démontré d'effet négatif de l'ajout d'une souche de BVDV type-2 à la vaccination chez les génisses à haut risque. L'ajustement comportemental suggère un avantage potentiel lié à l'utilisation d'un vaccin pentavalent plutôt que tétravalent.

Introduction

Bovine viral diarrhea virus (BVDV) is an important component of bovine respiratory disease (BRD).[8,14] The virus can cause immunosuppression and lead to development of BRD along with other pathogens.[2,8,14] Bovine viral diarrhea virus is composed of type 1 and type 2 genotypes.[15]

Vaccination of calves to help control and mitigate BRD is a common practice in the industry.[32] The choice of which antigens to include in a vaccination and arrival program is commonly influenced by type of cattle, management strategy, and previous experience with calves from a similar source.[11,23] A survey of beef cattle consulting veterinarians in the United

States and Canada indicated 90.9% of the respondents recommended vaccinating high-risk calves with BVDV type 2 vaccine.[9,25] Meta-analyses of the clinical efficacy of modified-live BVDV vaccines showed reduced morbidity and mortality risk in pathogen challenge studies.[29]

Vaccination of animals has shown to decrease feed intake and elevate body temperature during the initial days after processing.[16,18] These same clinical signs are used to identify calves with BRD, which may inhibit the ability to accurately diagnose morbid animals.[19,37] The objective of this study was to compare potential performance, health, temperature, and behavior benefits in beef calves vaccinated upon arrival with a modified-live viral (MLV) vaccine which included BVDV type 2 antigen, and calves vaccinated upon arrival with a MLV vaccine which did not include BVDV type 2 antigen. Our hypothesis was there would be minimal differences between treatment groups. Conclusions from this study will be important to identify viral antigens to include in vaccination programs.

Materials and Methods

The study was performed at a backgrounding yard in northeast Missouri in 2015. Weather data was collected and downloaded from an online local weather station.[a] Average, minimum, and maximum ambient temperature; as well as average, minimum, and maximum relative humidity recordings were extracted for each day of the study.

Calf arrival protocol

Eighty-three beef heifer calves were enrolled into the study. All calves were group housed in a single, open air, dirt floor pen. Calves were randomly assigned to 1 of 2 vaccine treatment groups using a random number generator.[b] One treatment group was administered 2 mL subcutaneously (SC) of a 4-antigen multivalent MLV vaccine containing bovine herpesvirus-1, BVDV type 1, bovine respiratory syncytial virus, and parainfluenza type-3 virus ($n = 42$; 4-WAY)[c]; the other treatment group was administered 2 mL SC of a 5-antigen multivalent MLV vaccine containing bovine herpesvirus-1, BVDV type 1, BVDV type 2, bovine respiratory syncytial virus, and parainfluenza type-3 virus ($n = 41$; 5-WAY).[d] Calves were processed (trial hour 0; trial day 0) and administered the correct vaccine according to treatment group allocation approximately 24 hours after arrival to the backgrounding yard. At arrival, calves were individually identified with an ear tag, tested for BVDV persistent infection via ear biopsy (antigen capture ELISA), and individual bodyweights (BW) collected. All calves were metaphylactically administered 2.72 mg/ lb of BW gamithromycin[e] (6 mg/kg BW) and 0.09 mg/lb of BW (0.2 mg/kg) of an injectable dewormer[f] SC in the lateral neck based upon average pen weight. Rectal temperatures were collected from each animal at processing.

Cattle performance and health observations

All calves were individually weighed at the time of processing, 30 d after arrival, and again 60 d after arrival. Average daily gain (ADG) was determined by subtracting the BW obtained on arrival (d 0) from the individual BW captured 30 d and 60 d later, and dividing by the number of days between measurements.

An observer blinded to treatment group monitored calves daily for clinical signs of BRD and any other health abnormalities. The remote early disease identification[g] (REDI) system also was utilized to identify morbid animals.[35] The REDI system consists of a real-time location system that monitors animal behavior within the pen, including proximity to areas of interest (feed and water) as well as animal activity and social behavior. These variables are used by the REDI classification engine to determine wellness status of the calf. Any animal identified as morbid with the REDI system was evaluated and diagnosis confirmed by the trained observer prior to treatment.

First-treatment BRD was determined as the percentage of animals identified by the trained observer or REDI system and confirmed by observer and required 1 therapeutic treatment. First-treatment success was determined as the proportion of animals initially treated for BRD that did not require additional therapeutic treatment. Second-treatment BRD was determined as the percentage of animals which required 2 therapeutic treatments for BRD. Second-treatment success was determined as the proportion of calves treated a second time for BRD which did not require any additional therapeutic treatment. Third-treatment BRD was determined as the percentage of animals which required 3 therapeutic treatments for BRD.

A gross necropsy was performed on all calves which died during the study. Mortality risk was determined as the percentage of calves which died divided by the total number of calves in each treatment group. Case fatality risk was defined as the proportion of calves which died which were initially treated for BRD.

Calves were eligible for treatment for BRD 5 days after metaphylaxis or 3 days after previous treatment. For both treatment groups, florfenicol[h] (18 mg/lb BW; 40 mg/kg BW) was used for initial BRD treatment. Treatments were dosed on individual animal BW collected at the chute at time of treatment. Calves requiring a second or third BRD treatment were administered tulathromycin[i] (1.1 mg/lb BW; 2.5 mg/ kg BW) and oxytetracycline[j] (9 mg/lb BW; 20 mg/kg BW), respectively.

Vaginal temperature monitoring

A randomly selected subset of each treatment group (4-WAY, $n = 20$; 5-WAY, $n = 20$) were equipped with a stainless steel temperature logger[k] at time of processing (trial hour 0; 1000 hours). The temperature logger was set to record

vaginal temperatures at 1-hour intervals. The vaginal temperature logger was attached to a controlled insertion drug-releasing device[j] with standard electrical tape. The controlled insertion drug-releasing devices used in this study were previously used and left to soak in disinfectant[m] and water for 21 days prior to the study. Vaginal temperatures were recorded for the first 14 days after vaccination. At conclusion, data from vaginal temperature data loggers were downloaded using a commercial software program[n] and exported into a commercial spreadsheet program.[b]

Behavioral monitoring

A real-time location system[o] was used to continuously monitor behavioral activity throughout the trial on all calves, similar to previously described methods.[26,30,34,35] Calf locations were recorded with a time stamp in the pen, and locations compared to previously identified areas of feed bunk and water tank using a data mining software program.[p] The amount of time at each location of interest was calculated by subtracting the time stamp from the previous recording, and then classifying the calf as being at the previous reading location. The feed and water zones were considered to be within a 4.9 ft (1.5 m) radius of feed bunk and water. The distance traveled for each animal was calculated by evaluating the change in animal position at each time stamp recorded using triangulation calculation. Feeding and watering bouts were determined by the number of times the animal entered and left the area of interest. To be counted as separate bouts, a minimum of 5 seconds was needed between occurrences of events; otherwise the system classified bouts as a single event. Behavior data were collected for the first 27 days of the trial.

Statistical analysis

Data were entered into a commercial software package[q] for analyses to evaluate the effect of the treatment groups. Continuous performance variables (arrival rectal temperature, arrival BW, BW at 30 days, BW at 60 days after arrival, ADG during the first 30 days, and ADG during first 60 days) were evaluated with individual linear models. For both BW and ADG outcomes, separate analyses were performed including and excluding dead animals in the analyses. A binary outcome variable was created for each individual animal for all health events. Potential association of health outcomes (BRD first treatment, first-treatment success, BRD second treatment, second-treatment success, BRD third treatment, and mortality) were evaluated using logistic regression. The BRD first, second, and third treatments and mortality risk were determined as the probability of each calf being diagnosed in each 1 of the categories out of the treatment group population. A P value of ≤ 0.05 was considered significant for all performance and health analyses.

Vaginal temperature data were evaluated hourly for the first 48 hours of the trial, and then daily during the first 14 days of the monitoring period. Biological vaginal temperatures of >90°F (>32.2°C) and <115°F (<46.1°C) were established in order to account for periods in which the vaginal temperature monitoring device was not placed in the animal. Hourly vaginal temperature data for individual calves were averaged for each trial day for daily analysis. Individual linear mixed models were utilized to evaluate potential association of vaginal temperature with trial hour and trial day, treatment group, and potential treatment group and time interaction. All analyses included a random effect for repeated measures on individual animals. A P value of ≤ 0.05 was considered statistically significant for interaction and main effects analyses.

Analysis of behavior data used model effects including treatment group, trial hour and day, and potential treatment group and time interaction. Hourly behavior activities were evaluated for the first 48-hours of the trial similar to the vaginal temperature outcome. Generalized linear mixed models with link logit function were utilized for behavior analyses including all potential effects and removing non-significant ($P > 0.05$) effects 1 at a time until a final model was achieved. Differences between treatment groups within individual hour or day were evaluated with t tests. To account for multiple comparisons, a P value ≤ 0.01 was considered statistically significant for all comparisons within an individual hour or day between treatment groups to decrease the likelihood of Type I error.[28] Hourly data were aggregated into daily events for statistical evaluation by trial day. All analyses included a random effect for repeated measures on individual animals. Feeding and watering bouts were evaluated as count data using Poisson generalized regression models with link log function. Potential differences in behavior activity between treatment groups within an individual hour or day were performed in the same manner used to evaluate vaginal temperatures and behavior outcomes. Hourly and daily distance traveled values were evaluated with linear mixed models in the same manner used to evaluate vaginal temperatures.

Results

Environmental conditions each day the trial heifers were exposed are displayed in Table 1. All calves were negative for BVDV based on the antigen capture ELISA at arrival. Calves in the 5-WAY treatment group had greater BW and ADG at 60 days, excluding the dead animals in the analyses ($P = 0.008$ and $P = 0.026$, respectively), compared to calves in the 4-WAY group (Table 2). Gross necropsy results determined BRD was the cause of death in all calves which died during the study. Case fatality risk tended to be greater in the 5-WAY treatment group ($P = 0.053$) compared to the 4-WAY group (Table 3). No other performance or health outcomes evaluated were significantly different between treatment groups.

A total of 9 calves (4-WAY, $n = 4$; 5-WAY, $n = 5$) had missing vaginal temperature readings throughout the 14-day observational period because the controlled insertion drug-

Table 1. Environmental conditions by trial day.

Day	Avg temperature, °F	Maximum temperature, °F	Minimum temperature, °F	Avg humidity, %	Maximum humidity, %	Minimum humidity, %
0	54	69	39	52	93	25
1	60	71	48	62	87	33
2	70	82	57	57	72	42
3	70	80	60	78	100	54
4	70	80	60	77	100	48
5	72	82	62	69	94	45
6	72	80	64	72	100	51
7	65	68	62	96	100	83
8	65	71	59	85	100	68
9	68	77	59	90	100	69
10	60	68	53	70	94	52
11	56	66	46	54	87	32
12	56	68	44	60	93	40
13	58	64	55	85	100	67
14	70	77	62	91	100	65
15	72	80	64	89	100	65
16	71	80	62	76	100	51
17	58	69	46	70	100	52
18	49	57	41	71	88	55
19	47	53	41	83	100	67
20	55	69	41	70	100	40
21	62	75	50	61	88	29
22	64	77	50	65	100	38
23	70	80	59	83	100	56
24	71	78	64	81	100	57
25	70	77	64	79	100	61
26	70	78	62	75	94	47
27	68	80	57	80	100	48

Table 2. Model-adjusted least square means (± SE) of performance parameters in beef heifer calves vaccinated with 4-WAY or 5-WAY modified-live virus vaccine upon arrival.

Performance and health parameters	4-WAY*			5-WAY†			P value
Average arrival rectal temperature, °F	103.4	±	0.18	103.4	±	0.18	0.835
Arrival weight, lb	477.9	±	6.63	483.7	±	6.71	0.540
Average body wt at 30 d, lb‡	550.2	±	7.8	569.8	±	8.2	0.088
Average body wt at 30 d, lb§	537.1	±	22.08	514.2	±	22.3	0.468
Average body wt at 60 d, lb‡	614.4	±	9.5	652.1	±	10.0	0.008
Average body wt at 60 d, lb§	599.8	±	25.3	588.5	±	25.6	0.755
ADG during first 30 d, lb‡	2.42	±	0.21	2.80	±	0.21	0.219
ADG during first 30 d, lb§	2.37	±	0.22	2.53	±	0.22	0.618
ADG during first 60 d, lb‡	2.28	±	0.15	2.77	±	0.16	0.026
ADG during first 60 d, lb§	2.23	±	0.17	2.50	±	0.17	0.270

*4-WAY = Pyramid 4, Boehringer Ingelheim Animal Health, St. Joseph, MO
†5-WAY = Pyramid 5, Boehringer Ingelheim Animal Health, St. Joseph, MO
‡Dead animals excluded in analyses
§Dead animals included in analyses

Table 3. Model-adjusted least square means (± SE) of health parameters in beef heifer calves vaccinated with 4-WAY or 5-WAY modified-live virus vaccine upon arrival.

Performance and health parameters	4-WAY*			5-WAY†			P value
BRD 1st treatment, %	45.2	±	7.7	26.8	±	6.9	0.080
First treatment success, %	57.9	±	11.3	27.3	±	13.4	0.100
BRD 2nd treatment, %	19.0	±	6.1	19.5	±	6.2	0.957
Second treatment success, %	25.0	±	15.3	50.0	±	17.7	0.298
BRD 3rd treatment, %	14.3	±	5.4	9.7	±	4.6	0.525
Mortality, %	2.4	±	2.4	9.8	±	4.6	0.145
Case fatality risk, %	5.3	±	5.1	36.4	±	14.5	0.053

*4-WAY = Pyramid 4, Boehringer Ingelheim Animal Health, St. Joseph, MO

†5-WAY = Pyramid 5, Boehringer Ingelheim Animal Health, St. Joseph, MO

releasing device attached to the data loggers slipped out, or animals had values outside of the biological temperature values established before analyses. Vaginal temperatures were collected for a minimum of 19 hours after processing for all 9 of these calves, with the majority of the vaginal temperatures being collected on them for the first 3 days of the study. Observations from all recordings within the biological temperature cutoffs were included in all statistical analyses.

There was not a significant treatment-by-trial-hour interaction ($P = 0.92$), and treatment group was not significantly ($P = 0.91$) associated with vaginal temperature during the initial 48-hour monitoring period. Trial hour was significantly associated ($P < 0.01$) with vaginal temperature during the initial 48-hour monitoring period (Figure 1A). There was not a significant treatment-by-day interaction ($P = 0.70$) with vaginal temperature. Treatment group was not significantly ($P = 0.95$) associated with vaginal temperature for the average daily analysis, but trial day was significantly ($P < 0.01$) associated with vaginal temperature (Figure 1B).

Due to equipment malfunction, behavior data were first collected beginning on trial hour 12 of the study. Data were consistently recorded for all animals after the initial 12-hour monitoring period. Observations for behavior data on the day of death for all calves that died during the trial were removed prior to analyses as the exact time of death of those animals was unknown.

There was a significant interaction ($P < 0.01$) between treatment group and trial hour for the amount of time calves spent within 4.9 ft (1.5 m) of the feed bunk and water (Figures 2A and 2B, respectively). Calves in the 5-WAY group spent more time near the feed bunk on trial hours 13 to 20, 32, 34 to 38, 42, 44, and 48 compared to calves in the 4-WAY treatment group; however, calves in the 5-WAY treatment group spent less time at the feed bunk on hours 24, 26, 39 to 41, and 43 compared to calves in the 4-WAY treatment group (Figure 2A). Calves in the 5-WAY treatment group also spent a greater amount of time near the water on trial hours 14, 24, 25, 28, 35, 37, 43, and 44, and a lesser amount of time near the water on hours 12, 13, 15, 17, 18, 20, 21, 30, 31, 38 to 40, and 47 compared to 4-WAY treatment group (Figure 2B).

There was a significant interaction ($P < 0.01$) between treatment group and day for time calves spent within 4.9 ft (1.5 m) of feed bunk and water (Figures 3A and 3B, respectively). Calves in the 5-WAY treatment group spent a greater amount of time at the feed bunk on trial day 0, 2, 3, and 4, more time near the water on day 5, 12, and 16, and less time near the water on day 0, 24, and 27 compared to 4-WAY calves. Analyses of the feeding and watering bouts determined a significant interaction ($P < 0.01$) between treatment group and trial day (Figures 3C and 3D, respectively). Calves in the 5-WAY treatment group had greater feeding bouts on day 0, 4, and 5, and greater watering bouts on day 1, 5, 8, 10, 12, 16, 17, 20, 21, and 22, compared to calves in the 4-WAY treatment group.

There was not a significant interaction present between treatment group and trial hour and day for distance traveled ($P = 0.28$ and $P = 0.27$, respectively). Treatment group was not associated with distance traveled during the initial 48-hour monitoring period or daily monitoring period ($P = 0.35$ and $P = 0.12$, respectively). Trial hour and day were both associated with distance traveled ($P < 0.01$; Figure 4).

Discussion

Results of this study indicate no adverse effects from administering both BVDV type 1 and type 2 strains (5-WAY vaccine) compared to using a vaccine (4-WAY vaccine) containing only BVDV type 1 antigen to high-risk feeder heifers. The study was performed in a commercial backgrounding operation using management typically practiced in the beef industry, resulting in great external validity. The use of the different modalities to remotely monitor body temperature and behavior in beef calves augment previous literature evaluating health and well-being of animals.[26]

Performance outcomes were evaluated including and excluding dead animals in analyses. Mortality risk was not significantly different between the treatment groups, but a numerical difference was present. Mortality risk is 1 of the primary drivers of net economic returns in calves.[6,17,31] The decision to include mortality estimates into the outcomes
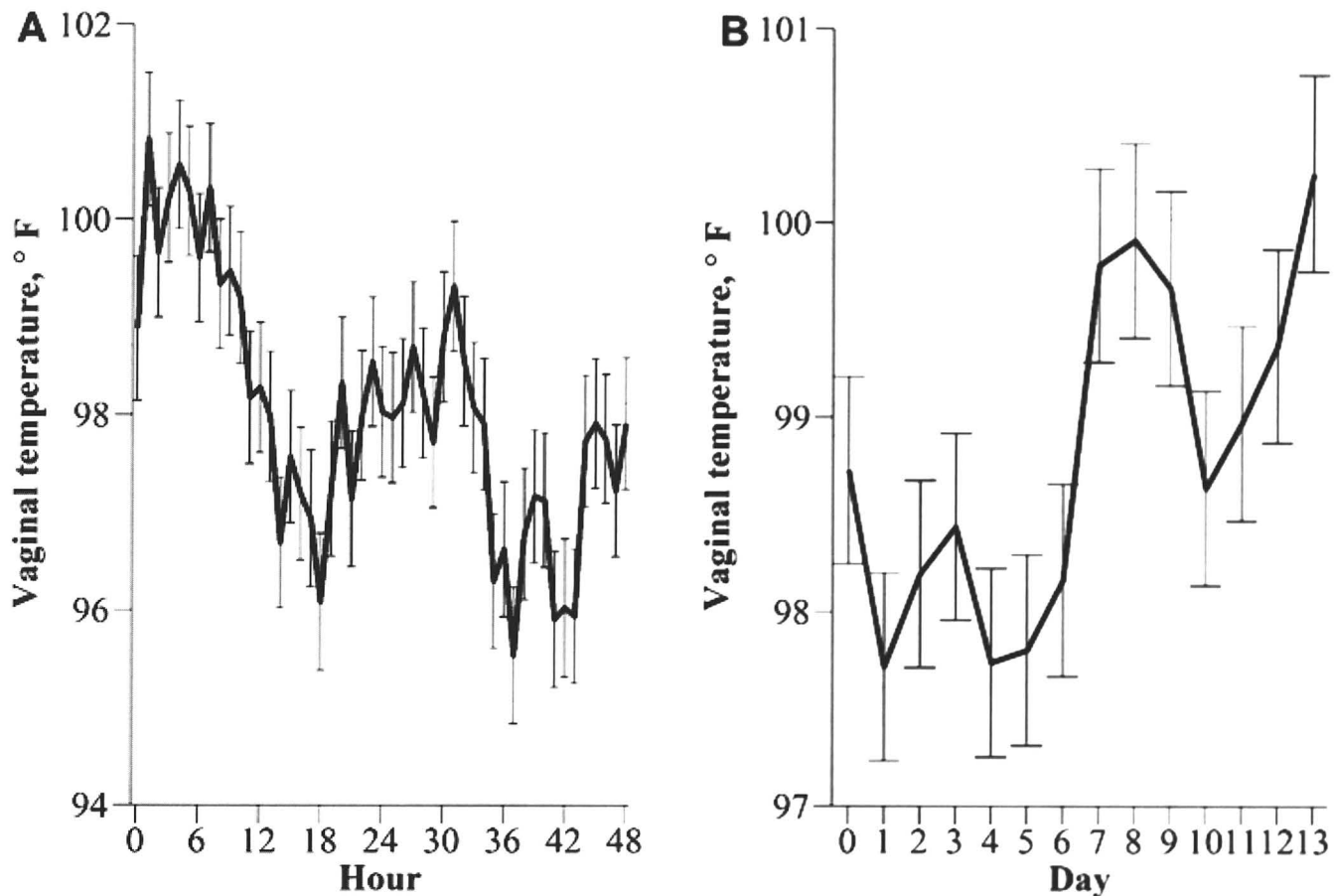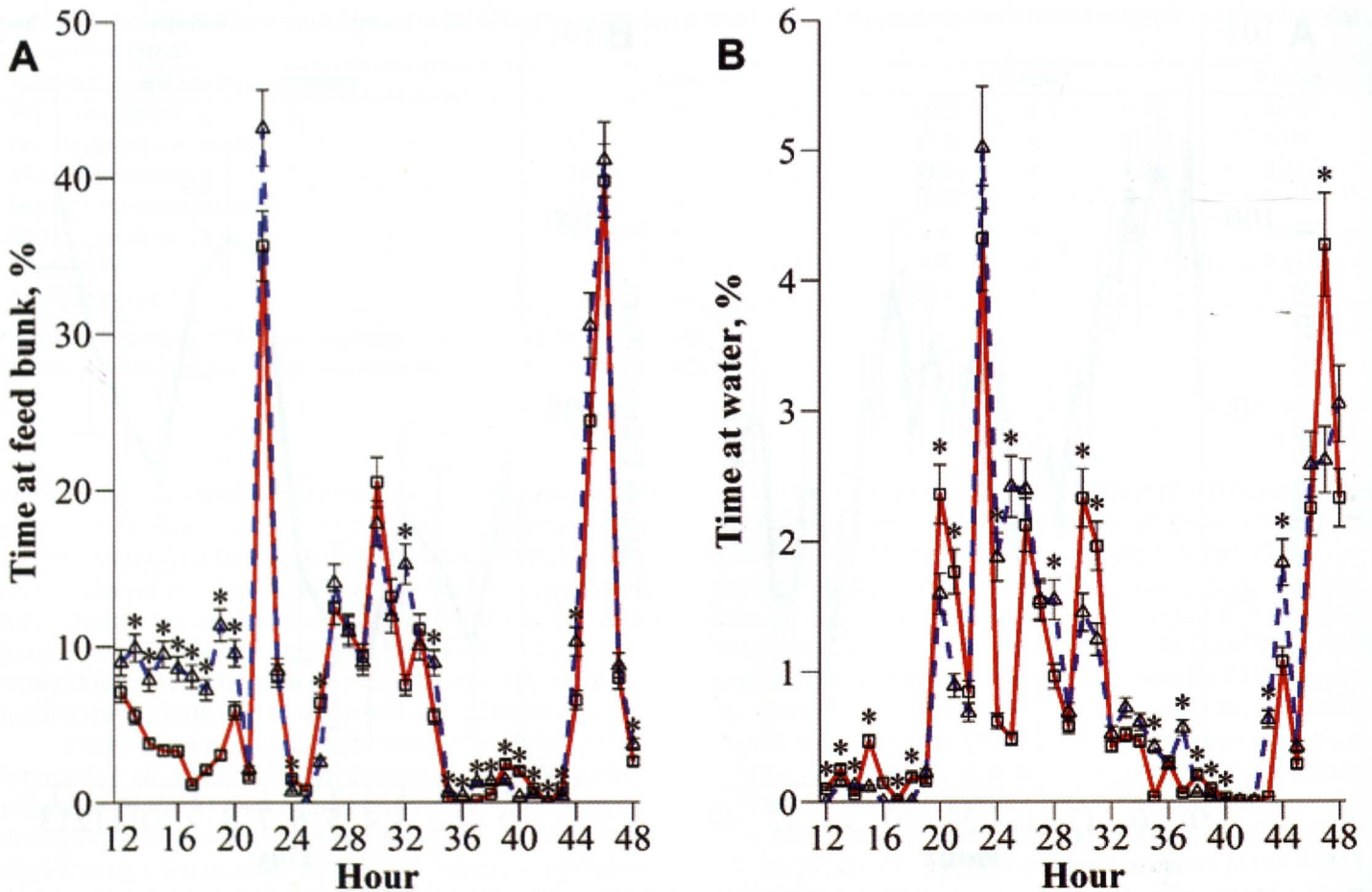
Figure 1. Model-adjusted least squares mean (±SE) vaginal temperature by trial hour (A) during initial 48-hour monitoring period and by trial day (B) in beef heifer calves vaccinated with 4-WAY or 5-WAY modified-live virus vaccine upon arrival. Model included effects for repeated measures on individual calves and trial hour or trial day. Trial hour 0 was when calves were initially processed (1000 hours). The treatment by time interaction was not significant for either the hour or day evaluations (P = 0.92 and P = 0.70, respectively). Treatment group was not significant for either hour or day evaluation of vaginal temperatures (P = 0.91 and P = 0.95, respectively). Trial hour and trial day were both significantly ($P < 0.01$) associated with vaginal temperature.

depends on the preference of an individual to make Type I or Type II errors, and the probability of true differences existing. If it is thought that a difference in mortality risk truly exists between treatment groups, then evaluation should be performed on outcomes which include dead animals in the analyses; however, if the belief is that no difference truly exists in mortality risk between treatment groups, then evaluation should be performed on outcomes with dead animals excluded from analyses. Information about probability of a true difference existing should to be considered in order to adequately evaluate outcomes.[22] Both outcomes are provided in this report to allow the reader to utilize the results based upon their own conclusions.

Analysis of averaged daily vaginal temperatures revealed similar results to hourly evaluation. The significant association between trial hour and trial day and vaginal temperature is most likely due to changes in environmental conditions and diurnal temperature patterns in cattle.[5,27]

Vaginal temperature has been positively correlated with rectal temperature in dairy and beef animals.[1,24,33] There was no evidence in the present study to suggest 1 treatment group had greater vaginal temperatures. Vaginal temperature has been shown to increase in beef heifers for 1 day after vaccination with a multivalent modified-live virus vaccine containing the same antigens as the 5-WAY vaccine treatment group in this study compared to non-vaccinated control animals.[18] Adjuvants may be different for each of the products evaluated, which could alter the response of the animal to the vaccine.[21] Pens was the experimental unit in previous studies, where individual animal was the appropriate experimental unit based on study design in the current study.[18,36]

Behavioral activity of animals is routinely monitored to assess animal health and well-being.[3,13] The REDI system continuously monitors animal activity without interfering with the natural behavior pattern of animals.[4,26] Differences in feeding behavior between treatment groups during the
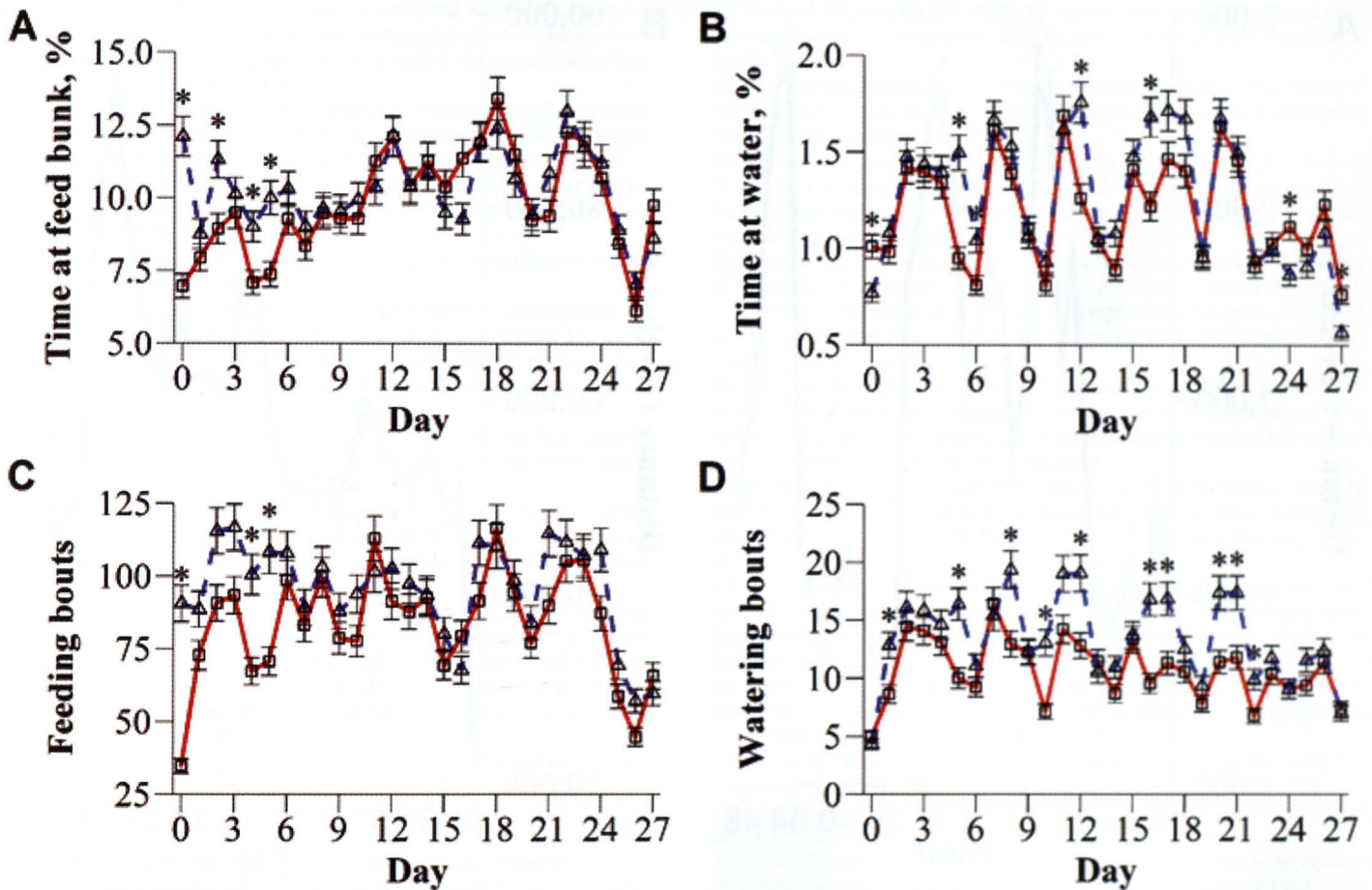
Figure 2. Model-adjusted least squares mean (±SE) percent of time calves spent within 4.9 ft (1.5 m) of the feed bunk (A) and water (B) by treatment group (4-WAY modified-live virus [solid red line with squares]; 5-WAY modified-live virus [dashed blue line with triangles] vaccine) and trial hour during initial 48-hour monitoring period. Model included effects for repeated measures on individual calves. Trial hour 0 was when calves were initially processed (1000 hours). Interaction between treatment group and trial hour was significant (*P* < 0.01). Significant differences (*P* ≤ 0.01) between treatment group within trial hour denoted by *.

initial hours and days were unexpected. Feeding activity on day 0 was consistent with patterns identified during the initial 48-hour evaluation, as trial hours 12 to 23 represent the same data used for day 0. The behavioral monitoring system used in the present study only monitors the percentage of time and frequency of bouts in pen locations, and does not measure the amount of feed or water consumed. As a result, we cannot confirm the cattle were actually consuming feed and water during the periods of time spent at the respective locations. Previous research has indicated morbid animals spend less time at the feed bunk, and have decreased growth performance compared to clinically healthy animals.[7,20,28,38]

The water behavioral activity evaluated during the initial 48 hours and daily evaluation was highly variable, similar to published literature.[20,28,30] While differences were detected between treatment groups on individual hour and day, more research is warranted to determine biological significance of water behavioral activity in beef calves. The distance calves traveled in this study appears to be greatly variable when

evaluated on an hour and daily basis. The lesser distance traveled on trial d 0 was most likely attributable to fewer hours included in trial d 0 (equipment malfunction) compared to the other trial days. More research is needed to evaluate deviations in animal behavior to identify methods to determine animal health and well-being status.[10]

There were limitations in this study. First, calves in both treatment groups were group-housed throughout the trial. Individual cattle activity may influence the behavior of other animals housed in the pen, and group housing could increase exposure to circulating pathogens in the entire pen. In aggregate, this would create a pen effect or the lack of ability to measure the full potential benefits of herd immunity. The pen effect of group housing would be expected to potentially minimize differences among treatment groups, but in this study differences in feeding and watering behavior were detected on multiple hours and days between treatment groups. A more complete description of the effect of vaccine could be accomplished by further research where pen, not individual

Figure 3. Model-adjusted least squares mean (±SE) percent of time calves spent within 4.9 ft (1.5 m) of the feed bunk (A) and water (B) by treatment group (4-WAY modified-live virus [solid red line with squares]; 5-WAY modified-live virus [dashed blue line with triangles] vaccine) and trial day. Model-adjusted mean (±SE) number of feeding bouts (C) and number of watering bouts (D) by treatment group (4-WAY and 5-WAY vaccine) and trial day. Models included effects for repeated measures on individual calves. Interaction between treatment group and trial day significant ($P < 0.01$) for all models included. Significant differences ($P \leq 0.01$) between treatment group within trial day denoted by *.

animal, is the experimental unit. A second limitation is that a non-vaccinated control group was not utilized to evaluate the effect of vaccine, as this was not the objective of the study. Additional field research is needed comparing clinically relevant outcomes in vaccinated and non-vaccinated calves.[12,29]

Conclusions

Results of this study indicate no adverse effects from administering BVDV type 2 vaccine to high-risk beef heifers. Vaginal temperature monitoring appears to be an effective modality to continuously capture body temperatures in research settings. The post-vaccination feeding behavior response suggests potential advantages to using a 5-antigen multivalent MLV vaccine (bovine herpesvirus-1, BVDV type 1, BVDV type 2, bovine respiratory syncytial virus, and parainfluenza type-3 virus) relative to a 4-antigen multivalent MLV vaccine (bovine herpesvirus-1, BVDV type 1, bovine respiratory syncytial virus, and parainfluenza type-3 virus).

Larger scaled field research studies with multiple replicates are needed to better define the usefulness of a vaccine containing BVDV type 1 and type 2 antigens compared to BVDV type 1 alone.

Endnotes

[a]Weather Underground, http://www.wunderground.com, Maywood, MO
[b]Microsoft Office Excel, Microsoft Corp, Redman, WA
[c]Pyramid 4, Boehringer Ingelheim, St. Joseph, MO
[d]Pyramid 5, Boehringer Ingelheim, St. Joseph, MO
[e]Zactran, Merial Limited, Duluth, GA
[f]Cydectin, Boehringer Ingelheim, St. Joseph, MO
[g]REDI; Precision Animal Solutions, LLC, Canton, MO
[h]Nuflor, Merck Animal Health, Whitehouse Station, NJ
[i]Draxxin, Zoetis, Florham Park, NJ
[j]Biomycin 200, Boehringer Ingelheim, St. Joseph, MO
[k]HOBO U12, Onset Computer Corporation, Bourne, MA
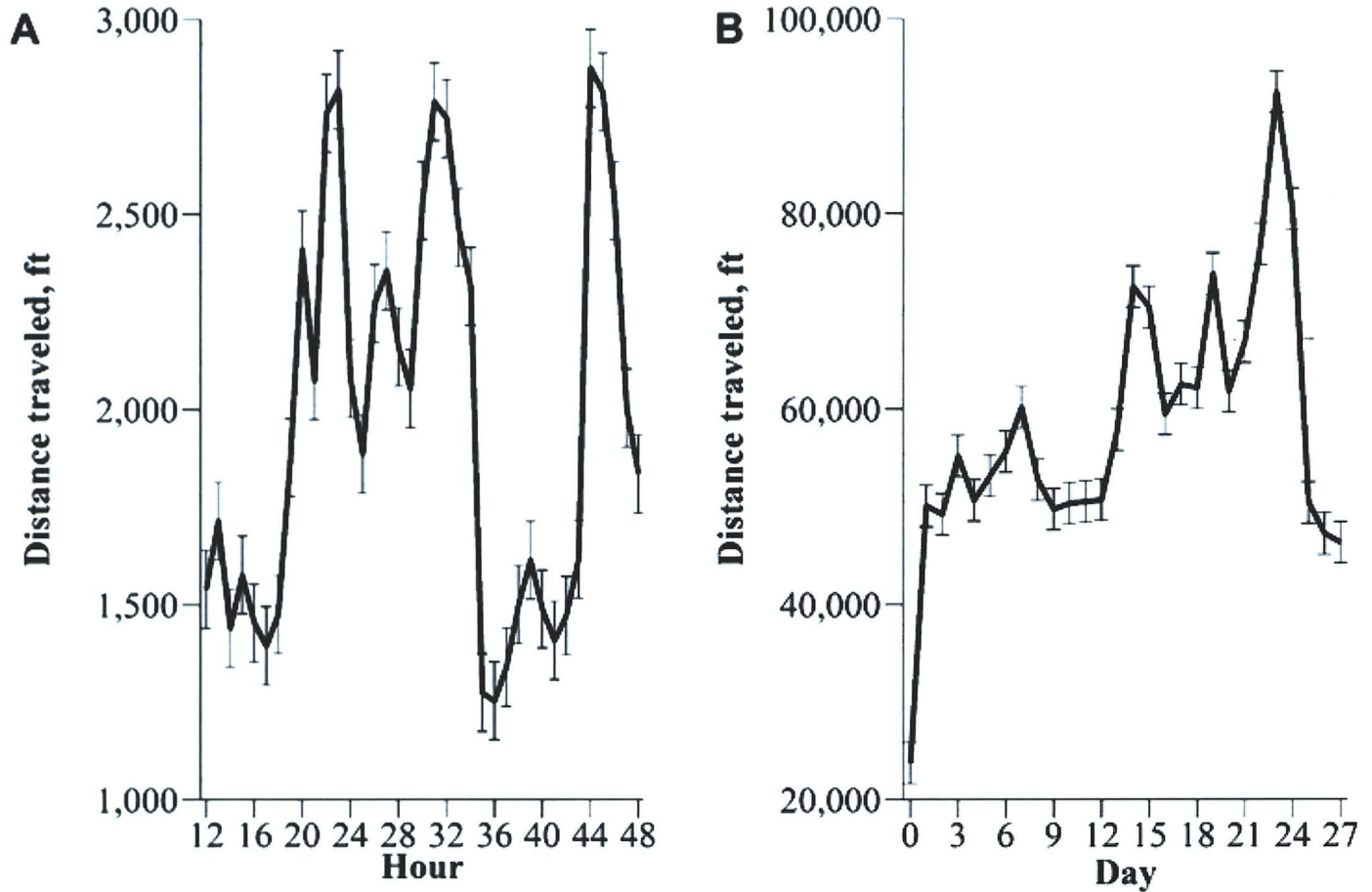
Figure 4. Model-adjusted least squares mean (±SE) distance traveled by trial hour (A) during initial 48-hour monitoring period and by trial day (B) in beef heifer calves vaccinated with 4-WAY or 5-WAY modified-live virus vaccine upon arrival. Model included effects for repeated measures on individual calves and trial hour or trial day. Trial hour 0 was when calves were initially processed (1000 hours). The treatment by time interaction was not significant for either the hour or day evaluations (P = 0.28 and P = 0.27, respectively). Treatment group was not significant for either hour or day evaluation of distance traveled (P = 0.35 and P = 0.12, respectively). Trial hour and trial day were both significantly (P < 0.01) associated with distance traveled.

References

1. Burdick NC, Carroll JA, Dailey JW, Randel RD, Falkenberg SM, Schmidt TB. Development of a self-contained, indwelling vaginal temperature probe for use in cattle research. *J Theor Biol* 2012; 37:339-343.

2. Chase CC, Elmowalid G, Yousif AA. The immune response to bovine viral diarrhea virus: a constantly changing picture. *Vet Clin North Am Food Anim Pract* 2004; 20:95-114.

3. Gonyou HW. Why the study of animal behavior is associated with the animal welfare issue. *J Anim Sci* 1994; 72:2171-2177.

4 Grignard L, Boissy A, Boivin X, Garel JP, Le Neindre P. The social environment influences the behavioural responses of beef cattle to handling. *Appl Anim Behav Sci* 2000; 68:1-11.

5. Hanzlicek GA, White BJ, Mosier D, Renter DG, Anderson DE. Serial evaluation of physiologic, pathological, and behavioral changes related to disease progression of experimentally induced *Mannheimia haemolytica* pneumonia in postweaned calves. *Am J Vet Res* 2010; 71:359-369.

6. Irsik M, Langemeier M, Schroeder T, Spire M, Roder JD. Estimating the effects of animal health on the performance of feedlot cattle. *Bov Pract* 2006; 40:65-74.

7. Jackson KS, Carstens GE, Tedeschi LO, Pinchak WE. Changes in feeding behavior patterns and dry matter intake before clinical symptoms associated with bovine respiratory disease in growing bulls. *J Anim Sci* 2016; 94:1644-1652.

8. Larson RL. Bovine viral diarrhea virus-associated disease in feedlot cattle. *Vet Clin North Am Food Anim Pract* 2015; 31:367-380.

9. Lee TL, Terrell SP, Bartle SJ, Reinhardt CD, Apley MD, Rethorst D, Thomson DU. Current feedlot cattle health and well-being program recommendations in the United States and Canada: the 2014 feedlot veterinary consultant survey. *Bov Pract* 2015; 49:124-131.

10. Moya D, Silasi R, McAllister TA, Genswein B, Crowe T, Marti S, Schwartz-kopf-Genswein KS. Use of pattern recognition techniques for early detection of morbidity in receiving feedlot cattle. *J Anim Sci* 2015; 93:3623-3638.

11. Nickell JS, White BJ. Metaphylactic antimicrobial therapy for bovine respiratory disease in stocker and feedlot cattle. *Vet Clin North Am Food Anim Pract* 2010; 26:285-301.

12. Perino LJ, Hunsaker BD. A review of bovine respiratory disease vaccine field efficacy. *Bov Pract* 1997; 31: 59-66.

13. Portillo TA. Pen riding and evaluation of cattle in pens to identify compromised individuals. *Proceedings*. 47th Annu Conf Am Assoc Bov Pract 2014; 5-8.

14. Ridpath J. The contribution of infections with bovine viral diarrhea viruses to bovine respiratory disease. *Vet Clin North Am Food Anim Pract* 2010; 26:335-348.

15. Ridpath JF. Bovine viral diarrhea virus. In: Mahy BWJ, van Regenmortel MHV, ed. *Encyclopedia of virology.* 3rd ed. Oxford: Academic Press, 2008; 374-380.

16. Rodrigues MC, Cooke RF, Marques RS, Cappellozza BI, Arispe SA, Keisler DH, Bohnert DW. Effects of vaccination against respiratory pathogens on feed intake, metabolic, and inflammatory responses in beef heifers. *J Anim Sci* 2015; 93:4443-4452.

17. Schroeder TC, Albright ML, Langemeier MR, Mintert J. Factors affecting cattle feeding profitability. *J Am Soc Farm Man Rural Appras* 1993; 57:58-54.

18. Sharon KP, Duff GC, Paterson JA, Dailey JW, Carroll JA, Marceau EA. Effects of timing of a modified-live respiratory viral vaccination on performance, feed intake, antibody titer response, and febrile response of beef heifers. *Prof Anim Sci* 2013; 29:307-312.

19. Smith RA, Stokka GL, Radostits O, Griffin D. Health and production management in beef feedlots In: Radostits O, ed. *Herd health: food animal production medicine.* 3rd ed. Philadelphia, PA: WB Saunders Company, 2001; 592-595.

20. Sowell BF, Branine ME, Bowman JG, Hubbert ME, Sherwood HE, Quimby W. Feeding and watering behavior of healthy and morbid steers in a commercial feedlot. *J Anim Sci* 1999; 77:1105-1112.

21. Spickler AR, Roth JA. Adjuvants in veterinary vaccines: modes of action and adverse effects. *J Vet Intern Med* 2003; 17:273-281.

22. Sterne JA, Smith DG. Sifting the evidence-what's wrong with significance tests? *Brit Med J* 2001; 322:226-231.

23. Stokka G, Goldsmith TJ. Feedlot vaccination: does it really matter? *Vet Clin North Am Food Anim Pract* 2015; 31:185-196.

24. Suthar V, Burfeind O, Maeder B, Heuwieser W. Agreement between rectal and vaginal temperature measured with temperature loggers in dairy cows. *J Dairy Res* 2013; 80:240-245.

25. Terrell SP, Thomson DU, Wileman BW, Apley MD. A survey to describe current feeder cattle health and well-being program recommendations made by feedlot veterinary consultants in the United States and Canada. *Bov Pract* 2011; 45:140-148.

26. Theurer ME, Amrine DE, White BJ. Remote noninvasive assessment of pain and health status in cattle. *Vet Clin North Am Food Anim Pract* 2013; 29:59-74.

27. Theurer ME, Anderson DE, White BJ, Miesner MD, Larson RL. Effects of weather variables on thermoregulation of calves during periods of extreme heat. *Am J Vet Res* 2014; 75:296-300.

28. Theurer ME, Anderson DE, White BJ, Miesner MD, Mosier DA, Coetzee JF, Lakritz J, Amrine DE. Effect of *Mannheimia haemolytica* pneumonia on behavior and physiologic responses of calves during high ambient environmental temperatures. *J Anim Sci* 2013; 91:3917-3929.

29. Theurer ME, Larson RL, White BJ. A systematic review and meta-analysis of commercially available vaccine effectiveness against bovine herpes virus, bovine viral diarrhea virus, bovine respiratory syncytial virus, and parainfluenza-type 3 virus in cattle for bovine respiratory disease complex. *J Am Vet Med Assoc* 2015; 246:126-142.

30. Theurer ME, White BJ, Coetzee JF, Edwards LN, Mosher RA, Cull CA. Assessment of behavioral changes associated with oral meloxicam administration at time of dehorning in calves using a remote triangulation device and accelerometers. *BMC Vet Res* 2012; 8:48.

31. Theurer ME, White BJ, Larson RL, Schroeder TC. A stochastic model to determine the economic value of changing diagnostic test characteristics for identification of cattle for treatment of bovine respiratory disease. *J Anim Sci* 2015; 93:1398-1410.

32. USDA. Part III: Trends in health and management practices on U.S. feedlots, 1994–2011. In: APHIS, ed. *National animal health monitoring system.* Fort Collins, CO: Animal and Plant Health Inspection Service, Veterinary Services, 2013.

33. Vickers LA, Burfeind O, von Keyserlingk MA, Veira DM, Weary DM, Heuwieser W. Technical note: Comparison of rectal and vaginal temperatures in lactating dairy cows. *J Dairy Sci* 2010; 93:5246-5251.

34. White BJ, Anderson DE, Renter DG, Larson RL, Mosier DA, Kelly LL, Theurer ME, Robert BD, Walz ML. Clinical, behavioral, and pulmonary changes in calves following inoculation with *Mycoplasma bovis. Am J Vet Res* 2012; 73:490-497.

35. White BJ, Goehl DR, Amrine DE. Comparison of a remote early disease identification (REDI) system to visual observations to identify cattle with bovine respiratory diseases. *Int J Appl Res Vet M* 2015; 13:23-30.

36. White BJ, Larson RL. Systematic evaluation of scientific research for appropriateness of data analysis to improve clinical decision making. *J Am Vet Med Assoc* 2015; 247:759-762.

37. White BJ, Renter DG. Bayesian estimation of the performance of using clinical observations and harvest lung lesions for diagnosing bovine respiratory disease in post-weaned beef calves. *J Vet Diagn Invest* 2009; 21:446-453.

38. Wolfger B, Schwartzkopf-Genswein KS, Barkema HW, Pajor EA, Levy M, Orsel K. Feeding behavior as an early predictor of bovine respiratory disease in North American feedlot systems. *J Anim Sci* 2015; 93:377-385.