Objectives

To assess the association between a commercially available vaccine against \textit{Moraxella bovis} and cumulative incidence of infectious bovine keratoconjunctivitis (IBK) from processing to weaning (primary objective) and body weight at weaning (secondary objective).

Design

Randomized blinded controlled trial.

Animals

214 calves (≥ 2 months of age) born in the spring of 2015 at an Iowa State University cow-calf research unit with no visible lesions or scars on either eye.

Procedures

Calves were randomly allocated to receive SC administration of a single dose of a commercial vaccine against \textit{M. bovis} (112 enrolled and 110 analyzed) or saline (0.9% NaCl) solution (111 enrolled and 104 analyzed). Calves were monitored for signs of IBK from treatment to weaning, and body weight at weaning was recorded. People involved in calf enrollment and outcome assessment were blinded to treatment group assignment. Cumulative incidence of IBK and weaning weight were compared between vaccinated and unvaccinated calves; the effect measure was the risk ratio and mean difference, respectively.

Results

IBK was detected in 65 (59.1%) vaccinated calves and 62 (59.6%) unvaccinated calves (unadjusted risk ratio, 0.99; 95% confidence interval, 0.79 to 1.24) during the study period. No significant difference in weaning weights was identified between vaccinated and unvaccinated calves (unadjusted effect size, 4.40 kg [9.68 lb]; 95% confidence interval, –3.46 to 12.25 kg [–7.61 to 26.95 lb]).

Conclusions and Clinical Relevance

Results suggested that the commercially available \textit{M. bovis} vaccine was not effective in reducing the cumulative incidence of IBK or increasing weaning weight in beef calves. (\textit{J Am Vet Med Assoc} 2017;251:345–351)

Infectious bovine keratoconjunctivitis (pinkeye) is an important disease problem for cow-calf producers. Previous research\(^1\) has shown that that up to 17% of US beef herds are affected annually by IBK. Similar results were obtained for Missouri in a survey\(^2\) and for Colorado in a national surveillance program.\(^3\) In a survey\(^4\) of Australian beef and dairy producers, 81% of respondents reported IBK within their herds. In a New Zealand survey,\(^3\) approximately 30% of respondents reported experiencing an IBK outbreak in 1981.

Infectious bovine keratoconjunctivitis causes a spectrum of clinical signs, including lacrimation, photophobia, corneal edema, ocular pain, corneal ulceration, and loss of vision.\(^5\) Calves with IBK lesions have lower weaning weights than unaffected herd mates.\(^7\)–\(^9\) As a consequence of these adverse effects on animal health and production, prevention of IBK through vaccination is desirable.

\textit{Moraxella bovis} is considered the primary causal organism associated with IBK.\(^{10–12}\) Vaccines directed at this organism are registered for prevention and control of IBK caused by \textit{M. bovis}. All commercially available vaccines contain only \textit{M. bovis} antigens. A prior systematic review\(^13\) revealed that \textit{M. bovis} vaccines may not be highly effective in protection of cattle against IBK. It has been suggested that the failure of the vaccine may be due to commercial vaccines lacking farm-specific \textit{M. bovis} bacterins or another potential causal organism, \textit{Moraxella bovoculi}.\(^14\) However,
a randomized controlled trial involving evaluation of a farm-of-origin autogenous \textit{M. bovis} vaccine revealed no greater protection from IBK in vaccinated versus unvaccinated calves. Interestingly, no publicly available data from a randomized controlled trial appear to exist for any commercially available vaccine. Although a reported study\textsuperscript{7} involved assessment of a commercially available vaccine, the unvaccinated calves in that study failed to achieve a high enough cumulative incidence of IBK to allow proper evaluation of vaccine efficacy.

Given the lack of information about the magnitude with which the incidence of IBK could be expected to decrease through the use of \textit{M. bovis} vaccines, we decided to conduct a randomized controlled trial of a commercial \textit{M. bovis} vaccine marketed in the United States for use in cattle. The primary objective of the study reported here was to conduct an independent evaluation of the ability of a commercially available \textit{M. bovis} vaccine to control IBK in beef calves. The secondary objective was to determine whether weaning weight would be associated with vaccination against \textit{M. bovis} infection.

\section*{Materials and Methods}

\subsection*{Ethics statement}

The Animal Care and Use Committee of Iowa State University reviewed and approved the study protocol (protocol No. 5-15-8025-B). No major deviations from the approved protocol were made during the study.

\subsection*{Animals}

Calves owned by the Iowa State University McNay Research and Demonstration Farm were used in the study. This farm is located in Lucas County, Iowa, and houses approximately 260 spring-born calves each year. The herd has a long history of IBK, which we arbitrarily defined as $>15\%$ of calves affected with IBK/season.\textsuperscript{7,8} This definition of an IBK-affected herd was used in the absence of other definitions because calves can develop corneal lesions for other reasons, such as hay abrasions, but we propose that other causes of eye lesions (which would have a lower incidence) for an array of reasons in beef calves, a cumulative incidence of IBK $>15\%$ was considered to represent a herd that had IBK rather than other noninfectious causes of eye lesions (which would have a lower incidence). Fifteen percent was determined by one of the investigators (AMO) as indicative of an infectious process in the herd.

Calves at the farm are roughly separated into 3 management groups by dam parity: cows mainly $>2$ years of age, cows mainly 2 years of age, and cows mainly $<2$ years of age. Calves are raised on pasture over the summer and receive loose mineral supplement in feeders throughout the summer. All calves born in the spring of 2015 and $>2$ months of age with no visible eye lesions or scars were eligible for enrollment. Calves in the young ($\leq 2$ years of age) dam group were enrolled on July 17, 2015; those in the 2-year-old dam group were enrolled on July 16, 2015; and those in the old ($>2$ years of age) dam group were enrolled on July 15, 2015. These dates represented the point at which each group was chute processed and also received a clostridial vaccine,\textsuperscript{8} topically applied anthelmintic,\textsuperscript{b} and bovine respiratory disease vaccines.\textsuperscript{e–c}

As a result of a history of IBK occurrence, the McNay farm has served as the site for previous IBK vaccine trials\textsuperscript{7,8} and a population-based cohort study\textsuperscript{15} assessing the association between IBK and body composition traits. \textit{Moraxella bovis} has been detected in IBK-affected calves in this population via a multiplex real-time PCR assay.\textsuperscript{8,16} \textit{Moraxella bovoculi} has also been identified in this population.\textsuperscript{7} The calves at McNay farm have also been used in a cohort study\textsuperscript{7} to assess the association between \textit{Moraxella} spp and the incidence of IBK, during which \textit{M. bovoculi} and \textit{M. bovis} were recovered from IBK-positive calves. In other years, the herd has not been vaccinated against IBK. The history and recovery of \textit{M. bovis} from affected cattle in the population suggested that the McNay farm was ideal for assessing IBK vaccine efficacy. In prior years, the impact of injectable mineral supplement on IBK development was also studied at the farm, with no protective effect identified (risk ratio, 1.1; 95\% CI, 0.8 to 1.5; Fisher exact \textit{P} value $=0.68$).\textsuperscript{18}

\subsection*{Hypotheses}

The primary hypothesis was that the risk ratio (ratio of cumulative incidences) for IBK development between treatment groups (vaccinated vs unvaccinated) would not significantly differ from the null value of 1. The secondary hypothesis was that the mean difference in weaning weights between treatment groups would not significantly differ from the null value of 0. Because corneal lesions or scars develop for an array of reasons in beef calves, a cumulative incidence of IBK $>15\%$ was considered to represent a herd that had IBK rather than other noninfectious causes of eye lesions (which would have a lower incidence). Fifteen percent was determined by one of the investigators (AMO) as indicative of an infectious process in the herd.

\subsection*{Sample size}

To test the primary hypothesis, the expected sample size was calculated on the basis of a previously reported cumulative incidence of IBK at the McNay farm ($>30\%$).\textsuperscript{8} Vaccine efficacy was estimated as a risk ratio of 0.5 on the basis of the results of 3 randomized blinded trials identified in a systematic review\textsuperscript{15} of IBK vaccine efficacy. Calculation parameters included an $\alpha$ value of 0.05, power of 80\%, and 2-sided test with assumed independence of all enrolled units. These considerations resulted in a sample size of 120/treatment group. The McNay farm was expected to have at least this many calves, so all eligible calves were enrolled for pragmatic reasons. Because we did not anticipate stopping prematurely, no stopping rules were used.

\subsection*{Sequence generation and allocation concealment}

A placebo-controlled randomized parallel design was used. The unit of randomization and treatment allocation for the study was the individual calf. A
chute-processing order sheet was created with a corresponding random allocation to treatment group (vaccinated or unvaccinated) for each management group (dam parity). The randomization schedule was generated by one of the investigators (JNC) using statistical software, and this person did not assess calves for eligibility. Assessment for calf eligibility was conducted by a different investigator (AMO) prior to and without knowledge of the randomization schedule order. To conceal treatment identities during data analysis, treatment assignments were arbitrarily recoded as A or B during data input before any follow-up visits to the farm. Allocation assignment was coded in this manner to blind investigators during initial analysis performed on completion of the follow-up period. At the time of concealment, the investigator sealed the allocation codes in envelopes and did not examine the original randomization schedule until after final analysis was completed.

**Interventions**

Calf enrollment and follow-up dates were coordinated with the farm manager to coincide with routine processing. During this processing, calves were assessed by one of the investigators (AMO) for evidence of active IBK lesions or scars as they entered the chute. Eligible calves (only those with clinically normal eyes) were then randomly allocated by use of the previously created chute-processing order sheet to receive one 2-mL dose of IBK vaccine administered SC per the manufacturer’s instructions (vaccinated group) or 2 mL of sterile saline (0.9% NaCl) solution administered SC (placebo; unvaccinated group).

With each calf in a chute, a summer student or investigator (AMO) administered the assigned treatment. Calf body weight and ID were recorded, and swab specimens were collected from each eye by rolling a sterile cotton swab over the cornea and inferior cul-de-sac. Eye swab specimens were collected as part of another study involving investigation of the microbiota of the eye. Calf sex was recorded later from the farm personnel’s management data sheet.

The monitoring period for IBK development began after treatment administration and continued until the calves were weaned. During this period, calves observed with active IBK were treated with 1 SC injection of injectable long-acting oxytetracycline product at the manufacturer’s recommended dose (20 mg/kg [9 mg/lb]) or 1 SC injection of florfenicol at the manufacturer’s recommended dose (40 mg/kg [18 mg/lb]). Florfenicol was used when injectable long-acting oxytetracycline product was not available chute-side.

**Outcome assessment**

Body weights of calves at enrollment and weaning were measured by farm personnel or by 1 investigator (JNC) using the chute scale. All calves were otherwise examined on pasture throughout the summer of 2015. Development of IBK lesions in ≥1 eye of a calf (ie, cumulative incidence of IBK) was the primary outcome of interest. To increase the sensitivity of IBK detection, calves were monitored until weaning and this outcome was detected 2 ways. First, farm personnel monitored calves for the development of IBK while calves were on pasture during routine management. Monitoring occurred daily or every other day, consistent with standard animal husbandry practices approved by Iowa State University. Farm personnel had been previously trained in identifying the clinical signs of IBK, which include blepharospasm, tearing, or corneal lesions. Because it was considered possible that the personnel might miss active lesions while calves were on pasture, calves with scars suggestive of IBK were also considered as incident cases to increase the sensitivity of detection. Therefore, the second approach to detection of IBK involved examination when calves were handled for routine management procedures over the summer or at weaning. When the entire group was handled, farm personnel or coinvestigators (AMO and TJE) assessed the calves for active IBK lesions or evidence of scars from IBK.

The investigators recognized that some calves may have had active lesions that were missed and completely resolved with no scars by weaning; therefore, we did not expect the sensitivity of our detection methods to be 100%. However, because such cases of IBK would likely be evenly distributed between treatment groups, no systematic bias should have existed. The investigators also recognized that it was possible that a proportion of calves could have developed lesions or scars for reasons other than IBK, and this would lower the specificity of IBK detection. Because assessors were blinded to treatment, any bias introduced by misclassification could be expected to have been nondifferential in nature. Given that the unit of treatment was individual calves (and not individual eyes), no differentiation was made between calves with unilateral or bilateral lesions. Body weights were recorded for each calf at weaning and used to assess the secondary outcome.

**Blinding**

Farm personnel served as caregivers during the monitoring period and were blinded to the calves’ vaccination status (ie, they were not aware of the vaccination status of any calf). The people assessing outcomes were also blinded to treatment group assignment (ie, they had no knowledge of the treatment allocation schedule at enrollment or treatment group assignment during the monitoring period).

**Statistical analysis**

Data management was performed with commercially available software. Data analysis was conducted in a blinded manner by one of the investigators (JNC) by use of the arbitrarily assigned treatment group labels A and B. Treatment group identities were ascertained by examining the contents of the sealed
envelopes containing the allocation codes only after the models for the primary outcome were completed, and then the analyst decided how to model the secondary outcome, weaning weight. Only calves with complete records for all variables were included in the analysis. Accuracy of data transcription from paper records was validated after follow-up by selecting a subset of calf IDs and ensuring the information was transferred correctly.

Descriptive statistics were computed regarding calf sex, cumulative incidence of IBK, enrollment body weight, and weaning weight for the vaccine and placebo groups. Descriptive data are reported as frequencies or mean (SD). We did not test the distribution of the outcome, relying instead on visual inspection. For hypothesis testing of the mean difference, we relied on the central limit theorem that the mean difference was normally distributed. To compare both outcomes between treatment groups, both unadjusted and adjusted analyses were used (2-tailed tests; \( \alpha = 0.05 \)). The unadjusted analysis was considered the primary one, with the adjusted estimates reported for comprehensiveness. This was because the sample size had been estimated on the basis of an unadjusted analysis and, in the study protocol submitted for approval before the study began, an unadjusted analysis was proposed. No adjustments were made for multiple hypothesis tests because inferences were drawn from unadjusted models only.

The null hypothesis for the primary outcome of interest (cumulative incidence of IBK) was evaluated by means of Mantel-Haenszel analysis, which allowed for control of a covariate (management group [dam parity]) and calculation of the risk ratio. An open-source web-based epidemiological data analysis package was used for this purpose. The hypothesis that the risk ratio was not different from 1 was tested by use of the Mantel-Haenszel \( \chi^2 \) test. The effect of the vaccine was estimated by calculation of the Mantel-Haenszel risk ratio and 95% CI. Given that vaccination was considered the exposure, a point estimate \(< 1\) would suggest the vaccine was effective against IBK development. The Breslow-Day test for interaction was used to test the hypothesis that management group affected the estimated risk ratio.

The null hypothesis for the secondary outcome of interest (weaning weight) was evaluated by means of unadjusted and adjusted generalized linear models and a linear mixed-effects model. In these analyses, treatment group was considered the explanatory variable of interest. For the adjusted analysis, enrollment body weight and calf sex were included as fixed effects and management group as a random effect in the linear mixed-effects model. Calves in the placebo (unvaccinated) group were used as the referent group. The hypothesis was tested by use of a likelihood ratio test for the variable treatment group. The effect of the vaccine on body weight was estimated by calculation of the mean difference between groups. With the placebo group as the reference, a positive mean difference estimate from the model would suggest an association between vaccination and weight gain in the calves.

An ancillary analysis was conducted to evaluate the association between cumulative incidence of IBK and weaning weight. Investigation of the association between the cumulative incidence of IBK and weight loss was not a primary objective of the study but was planned prior to the study. A linear mixed-effects model was used for this purpose, with weaning weight as the outcome and IBK status (ie, active lesion or scar at follow-up) as the explanatory variable of interest. Enrollment body weight and calf sex were included in the model as fixed effects, and management group was included as a random effect. Calves with IBK were used as the referent group. A negative estimate (mean difference) suggests a lower weaning weight for calves with IBK versus calves without clinical signs of IBK.

All regression models were generated by use of open-access statistical software and a generalized linear model or linear mixed-effects model approach. Fit of the model with body weight as the outcome variable was assessed by examination of residual plots.

## Results

### Animals

At enrollment, corneal lesions were detected in 23 (38.3%) calves in the 2-year-old dam management group, and these calves were therefore excluded. In total, 112 calves were initially enrolled in the vaccinated group and 111 in the unvaccinated group. One vaccinated calf and 2 unvaccinated calves were lost to follow-up, leaving 111 and 109 calves, respectively, in the study. One vaccinated calf and 5 unvaccinated calves had incomplete records, leaving 110 and 104 calves, respectively, for inclusion in the analyses (Table 1). Reasons for incomplete records included lack of an accurate body weight measurement (at enrollment or weaning), incorrect recording of calf ID, and passing

### Table 1—Characteristics of beef calves prior to SC administration of one 2-mL dose of a commercial vaccine against *Moraxella bovis* (vaccinated group) or one 2-mL dose of sterile saline (0.9% NaCl) solution (unvaccinated group).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vaccinated (n = 110)</th>
<th>Unvaccinated (n = 104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Old (&gt; 2 y) dam</td>
<td>48 (43.6)</td>
<td>44 (42.3)</td>
</tr>
<tr>
<td>2-y-old dam</td>
<td>18 (16.4)</td>
<td>18 (17.3)</td>
</tr>
<tr>
<td>Young (&lt; 2 y) dam</td>
<td>44 (40.0)</td>
<td>42 (40.4)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>128.30 (24.54)</td>
<td>126.10 (25.97)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>63 (57.3)</td>
<td>55 (52.9)</td>
</tr>
<tr>
<td>Female</td>
<td>47 (42.7)</td>
<td>49 (47.1)</td>
</tr>
</tbody>
</table>

Data represent number (%) for management group and sex and mean (SD) for body weight.
through the chute without recorded data (1 calf). One calf was not excluded for an unverified calf ID because it was matched up correctly after the entire ID list was examined.

For calves in the 2-year-old dam management group only, additional processing was performed on August 20, 2015. The additional processing was due to an IBK outbreak observed by McNay farm personnel. As a result, for IBK incidence, data for the 2-year-old dam management group were collected during the outbreak and not at weaning. Calves in the young dam group were weaned on October 2, 2015; those in the 2-year-old dam group were weaned on September 28, 2015; and those in the old dam group were weaned on September 30, 2015. The McNay farm personnel provided weaning weights for the 2-year-old dam group.

Outcomes

The criterion for a herd at risk for IBK (incidence > 15% in the unvaccinated group) was met, with 62 of the 104 (59.6%) calves developing IBK (Table 2). The cumulative incidence of IBK in the young dam management group was 41% (18/44) for vaccinated calves and 38% (16/42) for unvaccinated calves; in the 2-year-old dam group was 72% (13/18) and 50% (9/18), respectively; and in the old dam group was 71% (34/48) and 84% (37/44), respectively.

The unadjusted risk ratio for IBK was 0.99 (95% CI, 0.79 to 1.24). This point estimate and interval indicated no evidence that the cumulative incidence of IBK (between processing and weaning) differed between vaccinated and unvaccinated calves (P = 0.94). The Breslow-Day test for interaction failed to result in rejection of the null hypothesis that the risk estimates would be homogeneous across management groups (P = 0.17), and therefore the unadjusted and adjusted estimates were quite similar (Table 2). Weaning weight did not differ significantly between treatment groups, thereby providing no evidence to reject the secondary null hypothesis that weaning weight would differ between vaccinated and unvaccinated calves.

Calves in which IBK was identified had a mean weaning weight of 175.37 kg (385.8 lb; SD, 28.38 kg [62.4 lb]). Calves that did not develop IBK during the monitoring period had a mean weaning weight of 189.10 kg (416.0 lb; SD, 28.93 kg [63.6 lb]). After adjustment for covariates (enrollment body weight, sex, and a random effect for management group), the difference between calves that did and did not develop IBK was significant (mean difference, –5.19 kg [11.4 lb]; 95% CI, –9.37 to –1.00 kg [–20.6 to –2.2 lb]).

Discussion

As supported by a review of the published literature index in CAB Abstracts, the present study represents the first reported assessment of a commercially available IBK vaccine in beef calves. We found no evidence to reject the primary null hypothesis that vaccination with the commercially available vaccine against M. bovis was not associated with a reduction of the cumulative incidence of IBK in our study population. The McNay farm met our definition of a herd at risk for IBK given that nearly 60% of unvaccinated calves developed IBK lesions or scars between processing and weaning. The estimate of the risk ratio suggested almost no difference in cumulative incidence of IBK between treatment groups (adjusted risk ratio, 0.99; 95% CI, 0.80 to 1.22). This lack of an apparent vaccine effect was further supported by the results of secondary hypothesis testing. The difference in weaning weight between treatment groups was quite small, and the 95% CI included 0 (Table 2).

Ancillary data analysis supported previous reports3,8,15 that IBK is associated with a significant decrease in weaning weights.

The manufacturer’s label10 for the vaccine used in the present study describes the product as “a single dose pinkeye bacterin,” and 1 dose is purported to be sufficient for prevention of an outbreak. The label further states, “Administer a 2ml dose subcutaneously to cattle 2 months of age or older. You should receive protection for an entire season. You should booster 1 dose the next year.” Additional instruction for outbreaks includes, “Since pinkeye tends to move through a cattle herd during a period of 2-3 months, vaccinating in the face of an outbreak can stop the procession of the disease and bring the outbreak to a conclusion.” The manufacturer’s website (not the label) also suggests that repeating the vaccine might be helpful.20 However, our intent was to assess the vaccine as marketed and labeled, and other approaches to vaccine administration have not been evaluated.

Although the purpose of the present study was to determine whether the IBK vaccine was effective

Table 2—Cumulative incidence of IBK (processing to weaning; No. [%]) and mean (SD) weaning weight for the calves in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Vaccinated (n = 110)</th>
<th>Unvaccinated (n = 104)</th>
<th>Total (n = 214)</th>
<th>Unadjusted estimate* (95% CI)</th>
<th>Adjusted estimate† (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of IBK</td>
<td>65 (59.1)</td>
<td>62 (59.6)</td>
<td>127 (59.3)</td>
<td>0.99 (0.79 to 1.24)</td>
<td>0.99 (0.80 to 1.22)</td>
</tr>
<tr>
<td>Weaning weight (kg)</td>
<td>183.08 (30.12)</td>
<td>178.69 (28.44)</td>
<td>180.95 (29.33)</td>
<td>4.40 (–3.46 to 12.25)</td>
<td>2.12 (–1.73 to 5.96)</td>
</tr>
</tbody>
</table>

*Value is reported as relative risk for incidence and mean difference (effect size) for weaning weight. †For incidence, an adjustment to the relative risk was made for management group. For weaning weight, an adjustment to mean difference was made for enrollment body weight, sex, and management group (random effect).
rather than to determine its mechanism of action, several possible explanations exist for the lack of an association with cumulative incidence of IBK or weaning weight. Moraxella bovis (the vaccine target) may not be the causative agent, and the reported consistent recovery of M bovis from IBK lesions is instead incidental. This possibility appears unlikely given that the body of evidence strongly suggests a causal role of M bovis in IBK. Although there is some discussion of the causal role of M bovoculi, no hypothesis-testing study has yet provided evidence of this. Historically, M bovis or other Moraxella spp have been recovered or identified via culture or PCR methods from active IBK lesions to suggest a causal association. However, our group has strongly argued against the idea that recovery of M bovoculi from active lesions is proof of causation. Because eye swab specimens could not be acquired immediately following initiation of infection and, owing to the potential for opportunistic secondary invaders following infection, it is not possible to make causal inference about organisms isolated from active lesions. As a result, we decided the best way to diagnose IBK in the calf herd was not on the basis of organisms recovered from old lesions but rather the clinical signs consistent with IBK, coupled with the long history of IBK in the herd and high infectivity rate.

Another explanation for the lack of treatment effect in the study reported here could be antigen presentation failure. If a vaccine does contain the appropriate (infecting) M bovis antigen, it may be ineffective or provoke a nonprotective immune response. Certainly, evidence from prior reviews and randomized controlled trials of vaccines intended to protect against IBK has consistently failed to identify a protective effect.

Another explanation for the lack of treatment effects in the present study could be that the study design introduced bias attributable to herd immunity. Vaccination of only a portion of the at-risk population is done with the presumption that protection against IBK is solely at the individual level (ie, the individual calf’s immune response). This perspective overlooks the role herd immunity may have in the prevention of disease spread. As a result, the lack of any observable treatment effect may be due to an insufficient proportion of vaccinated and thus protected calves in the population. This possibility was also unlikely in the present study given that herd immunity should be associated with the protection of all calves in the herd, whereas we observed a high incidence of IBK (approx 60%) suggesting that if protection occurred at all, it was not very effective. Finally, it may be proposed that any vaccine effect was overwhelmed by disease effects; however, we are unaware of any evidence for such efficacy thresholds in veterinary science.

The efforts taken when designing the present randomized blinded controlled trial should increase confidence in the results. By randomization to treatment group and blinding at all levels (enrollment, outcome assessment, and analysis), we aimed to ensure that major sources of internal bias were unlikely to explain or influence the study results. The potential impact of confounding, misinformation bias, and selection bias on the outcome would have been minimized through the randomization and blinding. Any misinformation bias related to identification of IBK active lesions or scars could be expected to be nondifferential. Loss to follow-up and incomplete or missing calf data was minimal for both the vaccinated (n = 2) and unvaccinated (7) groups. Further, we followed the manufacturer’s directions and administered the vaccine to calves > 2 months of age.

Overall, the study reported here provided an assessment of a commercially available vaccine marketed for the prevention of IBK, and results suggested that this product was ineffective in protecting beef calves against the disease in our herd. Additionally, we found no evidence to suggest that vaccinated calves had a greater weaning weight than unvaccinated calves. Consistent with prior studies, we found that IBK was associated with weight loss in calves, and our prior experience suggests the disease is painful. Therefore, a need remains to develop effective vaccines for prevention of this painful, production-limiting disease.

Acknowledgments
The authors thank Kevin Maher of Iowa State University’s McNay Research and Demonstration Farm for his generous help and cooperation during the study and Chase Prouty for assistance with supply organization, sample collection, and calf vaccination.

Footnotes
a. Ultrabac7/Somubac, Pfizer, New York, NY.
b. Dectomax, Pfizer, New York, NY.
c. Bovishield Gold 5, Pfizer, New York, NY.
d. TSV 2 Naselgen, Pfizer, New York, NY.
e. One Shot, Pfizer, New York, NY.
h. MAXI/GUARD Pinkeye bacterin (catalog No. 01000-2; serial no. 545; expiration date, Apr 23, 2016), Addison Biological Laboratory, Fayette, Mo.
i. Liquamycin LA-200, Zoetis, Parsippany, NJ.
j. Nuflor, Merck Animal Health, Madison, NJ.
k. Microsoft Excel for Mac 2011, Microsoft Corp, Redmond, Wash.

References


