Evaluation of the effects of a commercially available *Salmonella* Newport siderophore receptor and porin protein vaccine on fecal shedding of *Salmonella* bacteria and health and performance of feedlot cattle

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**Objective**—To evaluate effects of a *Salmonella* Newport siderophore receptor and porin protein (SRP) vaccine on cattle health and performance and on prevalence of fecal shedding of *Salmonella* bacteria in feedlot cattle.

**Animals**—1,591 beef cattle.

**Procedures**—Cattle were randomly allocated within a replicate (n = 10 replicates [20 total pens]), administered 2 mL of a *Salmonella* Newport SRP vaccine (n = 795 cattle) or a placebo (796), and revaccinated approximately 21 days after the first administration. Health and performance data were recorded by trained feedlot personnel who were blinded to treatment. Fresh fecal samples (n = 25) were collected from pen floors on days 0, 60, and 120 and within 24 hours of cattle harvest and were subjected to selective *Salmonella* culture and serotyping by laboratory personnel who were blinded to treatment. Pen-level mixed models were used to analyze data.

**Results**—Significant differences in fecal prevalence of *Salmonella* bacteria or health and performance variables were not detected between vaccinated and control cattle. *Salmonella* bacteria were recovered from all 10 replicates, and cumulative prevalence estimates ranged from 1.5% to 22%. Overall prevalence of fecal shedding of *Salmonella* bacteria was 10.2% and 10.9% in vaccinated and control cattle, respectively. Overall morbidity risk was 34.8% for both vaccinated and control cattle. Overall mortality risks were 1.9% and 1.1% for vaccinated and control cattle, respectively.

**Conclusions and Clinical Relevance**—In this setting, administration of the *Salmonella* Newport SRP vaccine in feedlot cattle had no effect on fecal prevalence of *Salmonella* bacteria or cattle health and performance. (*Am J Vet Res* 2011;72:239–247)
prove the health and performance of cattle.15 Although production management factors may affect the prevalence of Salmonella bacteria in the feces of cattle,13,14 it is critical that new strategies are developed to effectively minimize the risks associated with this genus of bacteria.18 A novel vaccine technology that uses SRPs of Salmonella enterica serotype Newport bacteria has been described16 and has the potential to control the prevalence of Salmonella bacteria in several animal species. This novel vaccine technology makes use of an iron transport mechanism of gram-negative bacteria, which is unique to certain bacterial species but is potentially conserved among Salmonella serotypes.7,18 The method of action of the vaccine is to induce the production of antibodies against SRPs that are located on the outer membrane of certain gram-negative bacteria. Once anti-SRP antibodies bind to the corresponding outer membrane proteins, bacteria will be unable to transport iron across the cell membrane. Because iron is critically important for cell homeostasis, bacteria will die as a result of a lack of iron caused by the inhibition of iron transport mechanisms.19

A commercially available vaccine that has the SRP technology incorporated into its formulation (Salmonella Newport SRP vaccine) is approved for use in cattle for the control of fecal shedding and disease associated with Salmonella enterica subsp enterica serotype Newport. Investigators previously have provided anecdotal reports20,21 that suggest the use of this vaccine is effective for the control of clinical salmonellosis in dairy cattle. Results of 1 studya indicated that the prevalence of Salmonella bacteria in the feces of culled dairy cows that were administered the Salmonella Newport SRP vaccine (7.6%) was significantly lower than that of the prevalence in culled dairy cows that were not administered the vaccine (39.2%). However, investigators in another study21 found no significant effect of the administration of the Salmonella Newport SRP vaccine on subclinical shedding of Salmonella bacteria in the feces of dairy cattle. In yet another study20 in dairy cattle, investigators did not detect a significant effect of the administration of the Salmonella Newport SRP vaccine on fecal shedding, but they did detect a production-enhancing effect in cattle administered this vaccine (milk production was 3% higher and somatic cell counts were 30% lower during the first 30 days of lactation in cattle administered the vaccine than in cattle not administered the vaccine). In addition, SRP technology has been used to reduce the shedding of Escherichia coli O157:H7 in the feces of cattle.22

To the authors’ knowledge, studies investigating the effects of the administration of the Salmonella Newport SRP vaccine in beef cattle reared in a feedlot have not been conducted. The purpose of the study reported here was to evaluate the effects of the Salmonella Newport SRP vaccine on cattle health and performance and prevalence of shedding of Salmonella bacteria in the feces of vaccinated feedlot cattle.

Materials and Methods

Cattle—A commercial feedlot (approx capacity, 30,000 cattle) in south central Kansas was selected as the location of the study. A sufficient number of cattle (n = 1,591) to fill 20 pens was purchased for inclusion in the study. Feeder calves that had a mean weight of 227 to 250 kg were procured through typical industry means used by the participating feedlot and arrived in 16 truckloads to the feedlot between October 16 and 25, 2008. Cattle originated from livestock markets and ranches located in Kansas, Oklahoma, South Dakota, and Texas. All cattle were managed in accordance with the feedlot’s standard health, feeding, and management protocols that were developed and applied at the discretion of trained feedlot personnel and the consulting veterinarian and nutritionist. Cattle were fed a ration from a series of 4 step-up diets, which primarily consisted of alfalfa hay, distillers grains, and steam-flaked corn, from the time of entry (receiving) to harvest (finishing); the 4 sequential step-up diets had percentages of roughage and concentrate of 46% and 54%, 31% and 69%, 12% and 88%, and 6% and 94%, respectively. Individual animal weights were measured and recorded on days 0 and 21. Pen weights were collected on arrival at the feedlot and at preharvest sampling (within 24 hours of transport to the slaughter facility). This study was approved by the Institutional Animal Care and Use Committee at Kansas State University.

Sample size determination—Sample size estimates were based on the ability to determine a difference in prevalence of fecal shedding of Salmonella bacteria at the time of preharvest sample collection. On the basis of our preliminary data and other reports,12,23,24 we estimated that the mean apparent prevalence of Salmonella bacteria at the time of summer preharvest sample collection would be 40% (range, 0% to 80%) for cattle not vaccinated with the Salmonella Newport SRP vaccine.b We wanted to detect a reduction in apparent prevalence of Salmonella bacteria such that the mean prevalence in pens of cattle vaccinated with the Salmonella Newport SRP vaccine was 25%. Sample size estimates were generated by use of simulation and linear mixed models.7 We simulated pen prevalence data as appropriate for the study design, varied the number of pens and samples collected per pen, and analyzed these data by use of mixed models; P values for each simulation analysis were used to generate a graphical output displaying the power to detect hypothesized differences, and the sample size for which the total number of samples and the number of pens for each treatment were displayed. We estimated that 20 pens and 25 samples/pen (at the time of preharvest sampling) would be sufficient to detect a difference, as described, with a type I error rate ≤ 0.05 and a type II error rate < 0.20.

Study design—On arrival at the feedlot, cattle were allocated to pairs (replicates) of study pens. Cattle within each arrival lot were systematically allocated by groups of 3 animals into 2 holding pens until each holding pen contained the appropriate number of cattle to fill the corresponding study pens. Then, pen weights were obtained and cattle were moved to permanent study pens. The allocation process continued until 20 total pens (10 pens/treatment) were filled. Replicates of study pens were adjacent located, and the characteristics (eg, open air and dirt floor) of all pens were typical for the in-

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dustry standard. For allocation to treatment groups, 1 pen from each replicate was randomly selected by coin toss to be administered the *Salmonella* Newport SRP vaccine\(^1\) (vaccinated pen), and the other pen was selected by default to be administered a placebo\(^2\) (control pen).

Cattle were processed (on an individual-pen basis) within 48 hours after arrival at the feedlot. On the initial processing day (day 0), all cattle were administered a dose of a modified-live respiratory virus vaccine,\(^3\) *Mannheimia haemolytica* toxoid,\(^4\) ivermectin,\(^5\) tilmicosin\(^6\), and 2 mL of the *Salmonella* Newport SRP vaccine or placebo (SC in the right lateral side of the neck), which was in accordance with the manufacturers’ recommendations. On day 21, cattle in the vaccinated pens or control pens were administered a second dose of the *Salmonella* Newport SRP vaccine or the placebo, respectively; in addition, cattle were administered the first of 2 hormone implants\(^7\) and a second modified-live respiratory virus vaccine.\(^8\) To ensure feedlot processing personnel were unaware of the assignment of cattle to treatment groups, labels of the *Salmonella* Newport SRP vaccine and placebo vials were covered and coded as vaccine A and vaccine B, respectively. Furthermore, these products had the same fluid color and consistency and were both provided in 100-mL vials. In addition, personnel who administered the treatment were not the same personnel responsible for assessing cattle health and performance during the study; personnel responsible for assessing cattle health and performance also were unaware of treatment group. At approximately 80 days prior to harvest, cattle were administered a third modified-live respiratory virus vaccine,\(^9\) an external parasiticide,\(^1\) and a second hormone implant.\(^1\)

**Fecal sample collection**—Freshly voided fecal samples (n = 25 local samples/pen) were collected from the pen floor on days 0, 60, and 120 and at the preharvest sampling. Each sample was collected manually by use of a clean plastic sleeve, and appropriate precautions were observed to avoid potential contamination of samples by other feces or pen floor material. After each sample was collected, the plastic sleeve was inverted and tied, labeled, and placed in a refrigerated (4°C) cooler until processing at a laboratory.\(^1\) Laboratory personnel were not aware of the treatment groups during the study period.

**Bacterial isolation and serotyping**—A previously reported\(^2\) standard isolation protocol was used to detect *Salmonella* bacteria in fecal samples. Ten grams of feces was enriched in 90 mL of tryptic soy broth\(^1\) in 532-mL stand-up sample bags.\(^1\) The stand-up sample bags then were incubated at 25°C for 2 hours, 42°C for 6 hours, and 4°C overnight. Samples were agitated and 10 mL of fecal slurry from each sample bag was added to a culture solution that contained 90 mL of tetrasionate broth\(^2\) and 1.8 mL of iodine.\(^2\) The culture solution then was incubated at 37°C for 24 hours. After incubation, 1 mL of the culture solution was subjected to immunomagnetic separation with anti-*Salmonella* magnetic beads.\(^2\) The immunomagnetic separation product was adjusted to a final volume of 100 μL with PBS solution,\(^2\) transferred into 10 mL of Rappaport-Vassiliadis broth,\(^2\) and incubated at 42°C for 16 to 18 hours. The Rappaport-Vassiliadis cultures were vortexed, and 50 μL of each culture was plated onto Hektoen enteric agar plates\(^2\) and then incubated at 37°C for 24 hours. Three colonies that had morphological characteristics consistent with *Salmonella* spp were streaked onto blood agar and incubated at 37°C for 24 hours. At least 1 isolate from each sample was tested for the *Salmonella* polyvalent O antigen as well as serogroups B, C1, C2, D1, D2, and E via slide agglutination.\(^1\) Isolates, which were presumed to be *Salmonella* spp on the basis of colony morphology observed on Hektoen enteric agar and agglutination with polyvalent O antiserum, were stored at ~80°C on cryoprotection beads.\(^1\) One isolate from each sample was sent to a reference laboratory\(^1\) for serotyping.

**Statistical analysis**—All pen-level cattle health and performance data were collected via the feedlot’s operational database. Data were recorded and descriptive analyses were performed by use of a commercially available spreadsheet program.\(^2\) Exact 95% binomial CIs were calculated for proportions by use of a function included in the spreadsheet program that outputs the inverse of the cumulative β probability density function for a specified β distribution. All multivariable analyses of fecal shedding and cattle health and performance data were performed by use of a commercial software program\(^2\) via general and generalized linear mixed models as appropriate for normal and binomial distributions.\(^2\) Logistic regression models were used to assess dichotomous outcomes (eg, morbidity, death, and fecal shedding of *Salmonella* bacteria) among vaccinated and control pens, while including pen within replicate as a random effect. A categorical variable representing sampling times (days 0, 60, and 120 and preharvest) was used when assessing repeated pen measures of fecal prevalence at all 4 sampling periods to allow the investigation of potential time-dependent effects of the vaccine. A first-order autoregressive correlation structure was used, which is a standard approach for repeated measures over equal time periods that allows for power decay of correlations.\(^1\) General linear mixed models were used to compare cumulative data for pen-level continuous outcomes (eg, ADG, F:G ratio, and treatment costs) among vaccinated and control pens, while controlling for the lack of independence within a replicate by use of a random intercept model. A value of \(P < 0.05\) was used to indicate significance for all analyses. Fit of a model was assessed by evaluating plots of residuals; for logistic models, the ratio of the inverse of the cumulative β probability density function for a specified β distribution. All multivariable analyses were performed by use of a commercial software program\(^2\) via general and generalized linear mixed models as appropriate for normal and binomial distributions.\(^2\)

**Results**

Mean weight of cattle at arrival was 256 kg (n = 1,591). Cattle were allocated to the vaccinated (n = 793) and control (796) groups with 10 pens used to house cattle for each treatment group. Data for health and performance of vaccinated and control cattle were summarized (Table 1). There was no significant (\(P = 0.80\)) difference in mean weight at arrival between treatment groups within replicates. The number of cattle per study pen ranged from 61 to 105 (mean, 79.5; median,
68) and 61 to 105 (mean, 79.6; median, 67) for the vaccinated and control pens, respectively. Mean number of days at the feedlot for the vaccinated and control pens was 228.8 (median, 229) and 228.9 (median, 229) days, respectively, and did not differ significantly.

Dates of the 4 fecal sample collection periods were October 17 and 24, 2008 (day 0); December 12, 2008 (day 60); February 13 and 20, 2009 (day 120); and May 28 and June 18, 2009 (preharrow). The single sample collection date for day 60 was to accommodate closure of the participating laboratory for a holiday. The within-pen fecal prevalence of Salmonella bacteria following randomization after arrival (day 0; Figure 1) ranged from 0% (0/25) to 48% (12/25) and differed significantly (P = 0.01) among replicates but did not differ significantly (P = 0.73) between control and vaccinated pens. Overall prevalence of fecal shedding of Salmonella bacteria across all sampling times and treatment groups was 10.6% (211/2,000). Of the 211 Salmonella isolates characterized, most were from serogroups E (n = 166), C1 (21), and C2 (9; Table 2). Predominant serotypes recovered were Anatum (n = 133), Lexington var 15+, Newport (8), and Senftenberg (6).

Salmonella bacteria were recovered from all 10 replicates of pens, and cumulative prevalence estimates across all sampling times ranged from 1.3% to 22%. Unadjusted cumulative prevalence of fecal shedding was 10.2% (95% binomial CI, 8.3% to 12.1%) and 10.9% (95% binomial CI, 9.0% to 12.1%) for vaccinated and control pens, respectively. Crude prevalence estimates for each sequential sampling time across all pens were 10.0% (95% binomial CI, 7.5% to 13.0%), 2.4% (95% binomial CI, 1.3% to 4.2%), 29.4% (95% binomial CI, 25.4% to 33.6%), and 0.4% (95% binomial CI, 0.1% to 1.4%). Multivariable analysis indicated significant (P = 0.01) differences in the prevalence of Salmonella bacteria among sampling times. However, there was no significant (P = 0.89) difference between treatment groups and no significant (P = 0.12) treatment-by-sampling time interaction. These effects, or lack thereof, were evident in the display of the raw data for the fecal prevalence of Salmonella bacteria (Figure 1).

Unadjusted summary data of common feedlot cattle health and performance indices were summarized (Table 1). Furthermore, model-adjusted estimates for cumulative incidence risks of adverse health outcomes for all vaccinated and control cattle were calculated (Figure 2). On the basis of multivariable models that accounted for replicates, outcomes did not differ significantly between vaccinated and control pens. Overall morbidity risk in study cattle was 34.8% and ranged from 15.9% to 58.7% within pens; however, there was no significant difference among pens (within replicates) within each treatment group. Illness in the study population was primarily caused by respiratory tract disease and lameness; furthermore, there were no suspected or confirmed cases of salmonellosis. Overall, only 2.1% of the vaccinated cattle and 1.9% of the control cattle were treated for illness > 1 time. No significant difference was detected among pens within each treatment group for the number of cattle requiring treatment > 1

### Table 1—Unadjusted summary data of health and performance outcomes for pens of cattle vaccinated with Salmonella enterica subsp enterica serotype Newport SRP vaccine or a placebo (control pens).™

<table>
<thead>
<tr>
<th>Variable</th>
<th>Vaccinated pens (n = 10)</th>
<th>Control pens (n = 10)</th>
<th>P value††</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cattle</td>
<td>795†</td>
<td>796†</td>
<td>—</td>
</tr>
<tr>
<td>Entry weight (kg)</td>
<td>255.6 ± 11.08</td>
<td>256.5 ± 11.90</td>
<td>0.80</td>
</tr>
<tr>
<td>No. of cattle with morbidity¶</td>
<td>277 (84.8)</td>
<td>277 (84.8)</td>
<td>0.99</td>
</tr>
<tr>
<td>No. of cattle retreated¶</td>
<td>17 (2.1)</td>
<td>15 (1.9)</td>
<td>0.72</td>
</tr>
<tr>
<td>No. of cattle culled for health reasons¶</td>
<td>9 (1.1)</td>
<td>4 (0.5)</td>
<td>0.23</td>
</tr>
<tr>
<td>No. of cattle that died¶</td>
<td>15 (1.9)</td>
<td>9 (1.1)</td>
<td>0.22</td>
</tr>
<tr>
<td>Case fatality risk (%)§</td>
<td>5.4</td>
<td>3.3</td>
<td>0.16</td>
</tr>
<tr>
<td>Treatment cost/animal ($)§</td>
<td>5.91 ± 3.78</td>
<td>5.85 ± 2.46</td>
<td>0.93</td>
</tr>
<tr>
<td>ADG (kg)§</td>
<td>1.38 ± 0.12</td>
<td>1.40 ± 0.12</td>
<td>0.13</td>
</tr>
<tr>
<td>F:G ratio§</td>
<td>5.58 ± 0.16</td>
<td>5.57 ± 0.18</td>
<td>0.74</td>
</tr>
<tr>
<td>Cost of gain (§)</td>
<td>1.56 ± 0.03</td>
<td>1.58 ± 0.05</td>
<td>0.56</td>
</tr>
<tr>
<td>Adjusted ADG (kg)***</td>
<td>1.41 ± 0.12</td>
<td>1.42 ± 0.15</td>
<td>0.88</td>
</tr>
<tr>
<td>Adjusted F:G ratio***</td>
<td>5.46 ± 0.19</td>
<td>5.47 ± 0.27</td>
<td>0.71</td>
</tr>
<tr>
<td>Adjusted cost of gain ($)§**</td>
<td>1.54 ± 0.04</td>
<td>1.54 ± 0.07</td>
<td>0.89</td>
</tr>
<tr>
<td>Hot carcass weight (kg)§</td>
<td>376.5 ± 12.42</td>
<td>378.3 ± 14.78</td>
<td>0.38</td>
</tr>
<tr>
<td>Carcass yield (%)§</td>
<td>64.7 ± 0.53</td>
<td>64.9 ± 0.39</td>
<td>0.12</td>
</tr>
<tr>
<td>Carcass price adjustment ($/45.5 kg of carcass weight)††</td>
<td>0.95 ± 0.62</td>
<td>1.05 ± 1.07</td>
<td>0.70</td>
</tr>
</tbody>
</table>

*©Cattle in the vaccinated and control pens were injected with the Salmonella Newport SRP vaccine or a placebo, respectively; vaccine was administered in accordance with the manufacturer’s recommendations. †Within a row, there was a lack of significant (P = 0.05) vaccine effects on each outcome; P values were determined by use of multivariable logistic and linear models, which accounted for the paired-pen (replicate) study design. ‡Cattle were systematically allocated by groups of 3 animals into 2 pens until 20 pens (10 pens/treatment) were filled. §Values are reported as mean ± SD. †Value is reported as the number (%). **Represents a cause for inclusion in an overall culling rate, and these reasons were primarily associated with respiratory tract disease and lameness; furthermore, there were no suspected or confirmed cases of salmonellosis. #Value is based on all causes of morbidity and subsequent death. **Value is adjusted for dead and culled cattle. T†Carcass price is an economic index representing carcass premiums and discounts associated with USDA quality grade, yield grade, and several other carcass variables assessed after harvest.

Values of premiums and discounts are based on carcass characteristics at the time of harvest.

— = Not determined.
time. Overall mean treatment (ie, medication) costs in vaccinated and control cattle were $5.91 and $5.85/animal, respectively, and no significant difference in mean treatment costs was detected between pens within each treatment group. During the study, 13 cattle were culled because of illness, and no significant difference in culling was detected among pens within each treatment group. Overall mortality risk in the study population was 1.5% and ranged from 0% to 4.9% within pens. Overall mortality risk in pens of vaccinated and control cattle did not differ significantly.

Significant differences for any of the standard measures of feedlot performance were not detected among pens of vaccinated and control cattle (Table 1). On the basis of analysis of pens within replicate, ADG for pens of vaccinated and control cattle did not differ signifi-

Figure 1—Fecal prevalence of Salmonella bacteria in each vaccinated (n = 10; gray bars) and control (10; black bars) pen within a replicate in samples collected on days 0, 60, and 120 and at preharvest sampling. Cattle in the vaccinated and control pens were injected with 2 mL of the Salmonella Newport SRP vaccine or a placebo, respectively; vaccine was administered in accordance with the manufacturer’s recommendations. Error bars represent the exact 95% CIs for proportions. Multivariable logistic regression analysis of these data, which was used to account for the paired-pen (replicate) study design, indicated significant differences in prevalence of Salmonella bacteria among sampling times, but no significant difference between treatment groups or a treatment-by-sampling time interaction.

Table 2—Summary of Salmonella serotypes isolated from fecal samples of cattle vaccinated with a Salmonella Newport SRP vaccine or a placebo.*

<table>
<thead>
<tr>
<th>Serotype†</th>
<th>Serogroup</th>
<th>Vaccinated pens</th>
<th>Control pens</th>
<th>Total‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatum§</td>
<td>E</td>
<td>67</td>
<td>66</td>
<td>133 (63.0)</td>
</tr>
<tr>
<td>Lexington var 15+</td>
<td>E</td>
<td>11</td>
<td>11</td>
<td>22 (10.4)</td>
</tr>
<tr>
<td>Lille</td>
<td>C1</td>
<td>3</td>
<td>8</td>
<td>11 (5.2)</td>
</tr>
<tr>
<td>Newport</td>
<td>C2</td>
<td>4</td>
<td>4</td>
<td>8 (3.8)</td>
</tr>
<tr>
<td>Senftenberg</td>
<td>E</td>
<td>1</td>
<td>5</td>
<td>6 (2.8)</td>
</tr>
<tr>
<td>3,15;10–</td>
<td>—</td>
<td>5</td>
<td>0</td>
<td>5 (2.4)</td>
</tr>
<tr>
<td>6,7–1,5</td>
<td>E</td>
<td>1</td>
<td>3</td>
<td>4 (1.9)</td>
</tr>
<tr>
<td>Tennessee</td>
<td>C1</td>
<td>4</td>
<td>0</td>
<td>4 (1.9)</td>
</tr>
<tr>
<td>Enteritidis</td>
<td>D1</td>
<td>0</td>
<td>3</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Others and nontypeable</td>
<td>—</td>
<td>6</td>
<td>9</td>
<td>15 (7.1)</td>
</tr>
<tr>
<td>Total</td>
<td>—</td>
<td>102</td>
<td>109</td>
<td>211 (100)</td>
</tr>
</tbody>
</table>

*Only 1 isolate from each sample was sent to a laboratory for serotyping of the Salmonella isolates.†Within a row, values are reported as total number (%).§Serotype designation includes all variants (n = 2) of Salmonella Anatum 15+.

See Table 1 for remainder of key.
the portion of the feedlot where the pens included in this study were located; thus, all cattle in these study pens were not exposed to a sufficient number of *Salmonella* bacteria to determine vaccine efficacy.

The last explanation, which also may be formally characterized as herd immunity, was suggested by investigators of another study20 as a plausible explanation for the low prevalence of *Salmonella* bacteria in vaccinated and control cattle in a dairy production system. A significant herd immunity effect on the fecal shedding of *E.coli O157* in feedlot cattle also has been described.28 In that study,28 unvaccinated feedlot cattle were 59% less likely to have detectable amounts of *E.coli O157* in their feces when housed with cattle that were vaccinated for *E.coli O157*; although that study28 of *E.coli O157* was not a pen-level investigation of the shedding of *Salmonella* bacteria, it suggests that herd immunity may be an important factor when evaluating the effect of a vaccine on fecal bacteria in feedlot production systems. Therefore, it is evident that an evaluation of vaccinated and control cattle located in adjacent pens within a single segment of a feedlot may not be an ideal study design for assessing the efficacy of vaccines against *E.coli O157* or *Salmonella* bacteria.

The results of a recent observational study37 indicated that the administration of the *Salmonella Newport* SRP vaccine may reduce the shedding of *Salmonella* bacteria in the feces of cull dairy cows. However, results of the study reported here revealed similar amounts of shedding of *Salmonella* bacteria in vaccinated and control cattle and were consistent with the results of 2 randomized controlled trials20,31 conducted in dairy cattle. Investigators in one of these trials20 administered the *Salmonella Newport* SRP vaccine to 75 cows in a 1,200-cow dairy herd and did not detect significant differences in fecal shedding of *Salmonella* bacteria between treatment groups; however, they detected significantly higher milk production and lower cumulative somatic cell counts in vaccinated cows. Investigators of the other trial20 administered the *Salmonella Newport* SRP vaccine to 25% of the mature dairy cows within 2 herds that had a history of salmonellosis and did not detect significant differences in fecal shedding of *Salmonella* bacteria between vaccinated and control cattle; in addition, measurements of health and performance variables were not made.21 In both trials,20,21 an inability to detect a difference in fecal shedding may have been affected by herd immunity or the relatively small proportion of cattle vaccinated within herds and variability of shedding of *Salmonella* bacteria in the feces that contributed to a small effective sample size for the potential to detect differences. However, results of these trials20,21 also may indicate a lack of efficacy of the *Salmonella Newport* SRP vaccine for the reduction of fecal shedding of the diverse *Salmonella* serotypes found in bovine production systems. In the study reported here, *Salmonella Anatum* was predominantly detected, whereas other serotypes, which included *Salmonella Newport* for which the *Salmonella Newport* SRP vaccine has labeled indications, were detected infrequently or rarely. The distribution and diversity of serotypes that were detected in the present study are similar to the findings of other studies12,15,23,29 on the shedding of

![Figure 2—Cumulative incidence risks of adverse health outcomes (morbidity, retreatment, culling, and death) for all vaccinated (n = 10; gray bars) and control (10; black bars) pens of cattle. Risks and corresponding 95% CIs are model-adjusted estimates calculated via logistic regression models that accounted for the paired-pen study design; outcomes did not differ significantly between treatment groups.](image-url)

**Discussion**

The study of feeder cattle in a commercial feedlot production system reported here revealed no significant differences between cohorts of vaccinated and control cattle in the prevalence of fecal shedding of *Salmonella* bacteria or cattle health and performance variables. These findings may have been caused by several factors. First, there may have been a lack of efficacy of the *Salmonella Newport* SRP vaccine in cattle located in this type of a production setting. Second, there may have been an insufficient number of *Salmonella* bacteria in this environment, which may have reduced the ability to detect differences between the treatment groups.

Last, the use of the *Salmonella Newport* SRP vaccine in a subset of the population (10 pens) may have reduced the overall exposure of cattle to *Salmonella* bacteria in

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Figure 2—Cumulative incidence risks of adverse health outcomes (morbidity, retreatment, culling, and death) for all vaccinated (n = 10; gray bars) and control (10; black bars) pens of cattle. Risks and corresponding 95% CIs are model-adjusted estimates calculated via logistic regression models that accounted for the paired-pen study design; outcomes did not differ significantly between treatment groups.
Salmonella bacteria in the feces of cattle; however, this diversity in Salmonella bacteria may have affected our ability to detect significant vaccine effects.

Fecal prevalence of Salmonella bacteria in the present study was much lower than we expected for feedlot cattle in this region, particularly at the time of the pre-harvest sampling (< 1%). In another study, a much higher fecal prevalence of Salmonella bacteria in feedlot cattle has been reported; thus, the sample size calculations for the present study were based on an expected prevalence of 40% in nonvaccinated cattle. The lower observed prevalence of Salmonella bacteria in the present study combined with the extreme variability in prevalence among replicates and within replicates over time would have adversely affected our ability to detect significant vaccine effects. However, the prevalence at 120 days (29.4%) in the study reported here was not low, and all but 1 replicate had Salmonella-positive fecal samples, which indicated that cattle were broadly exposed to Salmonella bacteria at some level during the study period. Within-pen prevalence of Salmonella bacteria at the time of that sample collection (day 120) ranged between 0% (0/25) and 80% (20/25), but prevalence estimates among pens within replicates were similar. Given the paired-pen allocation of cattle at arrival, data suggested that shedding of Salmonella bacteria was largely affected by cattle source or factors associated with arrival at the feedlot, even after the cattle had been in the feedlot for several months (Figure 1).

Similar to the objective for many other field studies of Salmonella spp, including studies in which investigators evaluated the efficacy of the Salmonella Newport SRP vaccine, evaluation of the prevalence of fecal shedding of Salmonella bacteria was a primary objective of the study reported here. Although concentrations of Salmonella organisms within positive fecal samples and prevalence (and concentration) of Salmonella bacteria on the hides of cattle may be important indicators of preharvest food safety, we did not measure these indicators in the study reported here. There may have been a significant difference in the concentration of Salmonella bacteria in positive fecal samples even though there were no significant differences in prevalence between vaccinated and control pens. Determination of the presence or concentration of Salmonella bacteria on cattle hides after transport to the slaughter facility also may have revealed differences between cohorts of cattle because evidence suggests prevalence increases during transport. Surprisingly, only 0.4% (2/500) of samples were positive among all pens immediately prior to harvest; this is arguably the most important potential food safety indicator that was measured. Given those prevalence results, it is extremely unlikely that determining the concentration of Salmonella bacteria within these positive fecal samples (n = 2) would have provided additional useful information for the evaluation of vaccine efficacy. This extremely low prevalence, following the much higher prevalence at 120 days, again may be perceived as the potential effect of herd immunity and reduced overall exposure in the study environment or simply may be because of time-dependent effects that were not measured. Preharvest samples were collected in the present study during the summer months, which is presumably the time of year when the shedding of Salmonella bacteria is most common in feedlots.

Health and performance indicators for cattle included in the present study were typical for this type of cattle and production system. All performance measures were extremely similar among pens in both treatment groups, which suggested that there were no significant vaccine effects. We failed to find evidence that the Salmonella Newport SRP vaccine affected health and performance variables despite the fact that multiple outcome variables were analyzed. To prevent further multiplicity in the analysis, potential carcass effects were assessed by use of a pen-level mean carcass price adjustment, which is an economic index representing carcass premiums and discounts associated with USDA quality grade, yield grade, and several other carcass variables assessed after harvest. If the Salmonella Newport SRP vaccine was considered to be an effective preharvest food safety intervention, it would be important to demonstrate no adverse effects on cattle health and performance. In addition, preharvest interventions that would enhance the safety of beef by reducing the prevalence of Salmonella bacteria in the feedlot environment could theoretically improve cattle health and performance.

In general, adverse health outcomes were not rare in this study population; thus, potential health effects of the vaccine could have been detected had they existed. However, there were no reported clinical effects consistent with salmonellosis in the cattle of the present study. As described in another study, the lack of health and performance effects could have been attributable to an insufficient challenge dose of Salmonella bacteria or to diversity among Salmonella serotypes. Subclinical shedding of Salmonella bacteria has been associated with some adverse health outcomes in feedlot cattle, such as lot-level measures of hospital pen mortality rate and retreatment risks as well as individual-animal case fatality risk for cattle with respiratory tract disease. However, the effect on case fatality risk was only detected for cattle shedding serogroup B Salmonella spp and was not associated with overall shedding of Salmonella bacteria. In addition, investigators in that study failed to find associations between shedding of Salmonella bacteria and several other common health variables measured in feedlots; the authors suggested that some Salmonella serotypes might be considered commensal bacteria in feedlot cattle.

To our knowledge, the study reported here was the first study conducted to evaluate the effects of the Salmonella Newport SRP vaccine in cattle maintained in a commercial feedlot production setting. Although we did not detect any effects of vaccination with the Salmonella Newport SRP vaccine on the fecal prevalence of Salmonella bacteria or cattle health and performance, we recognize that further investigation of the use of this vaccine in other cattle production settings could provide evidence of vaccine efficacy. We also recognize that long-term herd vaccination strategies may need to be considered to affect subclinical fecal shedding in cattle. This may be the reason that a recent observational
study revealed a lower fecal prevalence of Salmonella bacteria in culled dairy cows that had been administered the Salmonella Newport SRP vaccine, compared with that for culled dairy cows that had not been administered the vaccine. However, in 2 other experimental trials, in which investigators allocated dairy cows to receive this same vaccine, no effect of vaccine administration on fecal shedding of Salmonella bacteria was detected. We also recognize that the lower than expected prevalence of Salmonella bacteria in feces combined with the extreme variability in prevalence among replicates and within replicates over time may have adversely affected the ability to detect significant vaccine effects in the study reported here. Furthermore, the present study was conducted in only 1 commercial feedlot, and prevalence and serotypes of Salmonella bacteria vary among feedlots and regions. Because the control of Salmonella bacteria in commercial feedlot production systems may enhance food safety and potentially cattle health and performance, further studies are necessary to validate control methods.

References


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Correction: Evaluation of 12- and 24-month survival rates after treatment with masitinib in dogs with nonresectable mast cell tumors

In the report “Evaluation of 12- and 24-month survival rates after treatment with masitinib in dogs with nonresectable mast cell tumors” (*Am J Vet Res* 2010;71:1354–1361), the legend for Figure 1 on page 1357 is incorrect. The correct legend is as follows: Figure 1—Kaplan-Meier curves for TTP in 132 dogs with nonresectable MCTs (A), 38 dogs with nonresectable tumors that had mutated c-Kit (B), and 86 dogs with nonresectable tumors that had WT c-Kit (C). In each graph, curves represent placebo-treated dogs (black diamonds; determined at the time treatments were unblinded in the pivotal study), masitinib-treated dogs (black circles; determined at the time treatments were unblinded in the pivotal study), and dogs in the follow-up study reported here (white circles).