ARTICLES

A field trial to evaluate the efficacy of a commercial *Pasteurella haemolytica* bacterial extract in preventing bovine respiratory disease

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Abstract

A double blind, random, controlled field trial was conducted to ascertain the efficacy of a *Pasteurella haemolytica* bacterial extract (Presponse, Langford Inc., Guelph, Ontario) in the prevention of bovine respiratory disease and/or its effects. Calves from 13 ranches (n = 1140 calves) were assigned to one of four groups, namely: vaccinated at the ranch three weeks prior to shipping to the feedlot; vaccinated only on arrival at the feedlot; vaccinated at both locations; or not vaccinated at either location. Four replicates of auction calves (n = 731) were also assigned to either receive or not receive the vaccine on arrival at the feedlot.

The vaccine did not effect a change in morbidity rates or weight gain. Total mortality rates were increased significantly, and mortality rates from respiratory disease tended to be increased in ranch calves that were vaccinated with Presponse at the ranch. In auction calves, the relapse rates were significantly lower in vaccinated calves. There was a tendency towards a reduction of respiratory disease-related mortality, however there appeared to be no sparing against death from fibrinous pneumonia in auction calves.

Résumé

Évaluation sur le terrain de l'efficacité d'un extrait bactérien commercial de *Pasteurella haemolytica* pour la prévention de maladies respiratoires bovines

Une étude à double insu, assignée au hasard, fut effectuée sur le terrain afin d'établir l'efficacité d'un vaccin à base d'extrait bactérien de *Pasteurella haemolytica* (Presponse, Langford Inc., Guelph, Ontario), d'une part pour la prévention de maladies respiratoires bovines, et d'autre part pour ses effets. Des veaux provenant de 13 élevages (n = 1140 veaux) furent répartis en quatre groupes, à savoir ceux vaccinés à la ferme trois semaines précédant le transport au parc d'engraissement; ceux vaccinés seulement à l'arrivée au parc d'engraissement; ceux vaccinés aux deux endroits et ceux n'étant pas vaccinés. Une étude parallèle fut effectuée sur des veaux provenant de l'encan (n = 731), lesquels furent divisés en groupes de façon à recevoir ou non le vaccin à leur arrivée au parc d'engraissement. Le taux de morbidité et le gain de poids journalier ne furent pas modifiés par l'administration du vaccin. Le taux de mortalité furent augmentés de façon significative et le taux de mortalité relié à des problèmes respiratoires avait tendance à être élevé chez les veaux d'élevage vaccinés au ranch. Les données provenant du groupe de veaux vaccinés achetés à l'encan, ont démontré, de façon significative, un taux de rechute plus bas. Les résultats indiquaient une tendance vers une baisse du taux de mortalité relié aux maladies respiratoires; toutefois, le vaccin ne semblait pas procurer un effet protecteur contre la mortalité reliée aux pneumonies fibrineuses rencontrées chez les veaux achetés à l'encan. *(Traduit par Dr Thérèse Lanthier)*

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Introduction

Bovine respiratory disease (BRD) is the largest single cause of mortality in fall weaned calves in North American feedlots. Health-related costs commonly exceed $40 per calf in larger feedlots and the annual expense in Alberta alone exceeds thirty million dollars (1). Several investigators have attributed up to two-thirds of total morbidity and mortality in feedlot calves to BRD (1-3).

The etiology of this syndrome is somewhat unclear, but it is probable that *Pasteurella haemolytica* (biotype A, serotype 1) is the major bacterial pathogen involved (1,3-5). Several distinct approaches have been taken in developing vaccines to provide protection against the major etiological (bacterial and viral) component causes of BRD (6-8). Martin *et al* in a three-year field study reported that, in general, vaccinating calves on arrival at the feedlot was associated with elevated mortality (2,3). This finding, although origi-

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Table 1. Definition of treatment groups in a study of the efficacy of Presponse in feedlot calves

Calf group[a]	Source	Treatment	No. of replicates	No. of calves
1 R−F+	Ranch	Placebo on ranch on day −21 Vaccine on arrival at feedlot	13	291
2 R−F−	Ranch	Placebo on ranch on day −21 Placebo on arrival at feedlot	13	289
3 R+F−	Ranch	Vaccine on ranch on day −21 Placebo on arrival at feedlot	13	284
4 R+F+	Ranch	Vaccine on ranch on day −21 Vaccine on arrival at feedlot	13	276
5 F−	Auction market	Placebo on arrival at feedlot	4	368
6 F+	Auction market	Vaccine on arrival at feedlot	4	363
Total				1871

[a]R indicates ranch vaccination status, F indicates feedlot vaccination status

nally considered surprising, was consistent with published data from numerous field trials assessing vaccine efficacy (7). A subsequent field trial indicated that preimmunization, on the farm of origin, with an infectious bovine rhinotracheitis and parainfluenza type 3 vaccine did not produce a significant effect on treatment rate (9). With regard to protection against *P. haemolytica*, killed whole cell bacterins were developed initially, but they appear to have been ineffective in providing protection against pneumonic pasteurellosis (1,6,7). In some cases, the use of *P. haemolytica* bacterins was associated with increased incidence/severity of BRD (1,3,6,7). Experimental vaccines utilizing live attenuated *P. haemolytica* have exhibited a moderate degree of efficacy (6). In one recent field trial, the efficacy of one or two vaccinations with a live vaccine containing both *P. haemolytica* and *P. multocida* was investigated in 76 preconditioned and 50 nonpreconditioned calves. Vaccination did not significantly affect the morbidity or mortality rates, although the clinical scores were significantly reduced in vaccinated calves (10). However, live vaccines are impractical under field conditions due to handling, administration, and storage constraints, and have reduced efficacy because of concurrent antibiotic therapy (6). *Pasteurella haemolytica* is known to produce a potent soluble cytotoxin (leukotoxin) that acts specifically on ruminant neutrophils and alveolar macrophages (11,12). Based on this knowledge, a commercial bacterial extract vaccine which contains concentrated leukotoxin, as well as soluble cell surface antigens (12,13), was recently developed and is marketed under the trade name Presponse (Langford Inc., Guelph, Ontario).

In 1987, a field trial was conducted in a large Alberta feedlot to assess the efficacy of Presponse in reducing losses due to BRD in calves six- to eight-months old (14). The trial utilized only calves purchased from auction markets. The test calves received two doses of vaccine, most within one to five days of arrival. The calves were processed on arrival in a manner similar to the procedure used in the trial reported in this paper but, in addition, all calves with rectal temperatures >40.0°C on arrival were excluded from the trial, and all remaining calves received injections of both long and short acting tetracycline. Within one to five days, all calves with a rectal temperature >40.0°C again received an injection of tetracycline. There was no significant difference between vaccinated calves and nonvaccinated calves with regard to morbidity rate or first relapse rate. Mortality from all causes was significantly lower in vaccinated calves (4.2% versus 2.1%) as was mortality due to fibrinous pneumonia (2.2% versus 1.1%). The authors of that report also stated that "ideally calves should be vaccinated with a pasteurella vaccine as part of a preconditioning or pre-immunization program on the farm of origin" (14). Vaccination of calves at least a few weeks prior to arrival at the feedlot would also be consistent with the temporal design of the laboratory studies of the bacterial extract, in which the first injection of vaccine was given 42 to 51 days before challenge (12).

The primary objective of the field trial reported here was to evaluate the efficacy of Presponse, administered to calves at the ranch three weeks before weaning and/or upon arrival at the feedlot, at reducing the incidence and/or effects of BRD, as measured by morbidity rates and weight gains. A secondary objective was to evaluate the efficacy of a single injection of Presponse, upon arrival at the feedlot, in auction calves.

Materials and methods

Calves and processing

A total of 1871 calves was included in the study, 1140 calves from 13 participating ranches, and a further 731 calves, in four lots, purchased at auction markets. The calves were six- to eight-month-old crossbreds weighing 220-300 kg and were uniquely identified with two ear tags. Ranch calves were systematically allocated to each of the four treatment (vaccination) groups, with the starting treatment group

allocation selected at random on each ranch. Auction calves were systematically assigned to treatment group (vaccinated or not) at the time of processing. The first ranch calves arrived on October 18, 1988, the last group on November 14. The first auction calves arrived on October 26, the last on November 16, 1988.

The trial was conducted doubly blind by using a placebo that was indistinguishable, grossly, from the vaccine. The vials contained either a 2 mL dose of the double adjuvant used in the commercial vaccine, or 2 mL of the commercial vaccine Presponse. The identity of these products was not revealed until after the trial was completed. Table 1 outlines the treatment protocol for each of the groups. The pre-immunization program began at the ranches three weeks prior to weaning and shipment. After approximately three weeks the ranch calves were assembled and transported to a 15,000 head capacity commercial feedlot in southern Alberta. The distances from the ranches to the feedlot varied between 10 and 500 km, and involved transit times of from 1 to 12 hours, respectively. The calves were housed in 1 of 15 open dirt pens surrounded on three sides by a 2.5 m windbreak-type fence with a fence line feed bunk on the fourth side. Water was provided from electrically heated water bowls. Ranch calves of all four treatment groups were commingled in pens, as were the vaccinated and unvaccinated auction calves. Ranch and auction calves were maintained in separate pens. The ranch calves were housed in 11 adjoining pens with a mean of 104 calves per pen. The auction market calves were housed in four pens with a mean of 183 calves per pen. All calves were fed a barley silage-based growing ration with protein and energy levels to sustain growth at 1 kg gain/day.

Within 24 hours of arrival the ranch cattle were processed as follows: branding and ear tagging; implantation of Ralgro (Pitman Moore Inc., Mundelein, Illinois, USA); an intramuscular injection of a *Haemophilus somnus* bacterin (Boehringer Ingelheim Ltd., Burlington, Ontario); a subcutaneous injection of an 8-way combined clostridial bacterial-toxoid (Tasvax, Coopers Agropharm Inc., Ajax, Ontario); an intramuscular injection of 6 mL of Ivermectin (MSD Agvet, Pointe Claire-Dorval, Quebec), and an intramuscular injection with a live bovine respiratory syncytial virus and parainfluenza type 3 virus, and killed bovine virus diarrhea virus and infectious bovine rhinotracheitis virus vaccine (Horizon IV, Diamond Scientific, Etobicoke, Ontario). On three farms, all physically close to the feedlot, the owners vaccinated all their calves with the same viral vaccine. This involved a total of 256 ranch calves. The allocation of Presponse to calves on these farms was systematic as mentioned previously.

A sample of calves, a minimum of six per treatment group, was bled at the ranch, on arrival at the feedlot, and regularly thereafter for serological studies. These data will be reported subsequently.

Ranch calves were weighed individually within 48 hours of arrival. Auction market calves were processed on arrival, but not weighed until the purchasing lot was completed and the calves allocated to pen (generally within 48-72 hours of arrival). Care was taken to ensure that weighing conditions were similar for all calves regardless of origin.

Clinical assessment

The calves were viewed daily by trained feedlot personnel. All calves exhibiting symptoms of illness, such as depression, dull appearance, anorexia, labored breathing, excessive nasal discharge, or coughing, were removed from the pens for examination and treatment. A diagnosis of undifferentiated BRD was made on these "pulled" calves if, on the first examination by animal health staff, the animal had no clinical signs which indicated that organ systems other than the respiratory system were involved. Most, but not all, cases of BRD were febrile (>39.5°C) on examination. Hence, for purposes of analysis, BRD morbidity rates also were classified according to the rectal temperature at the time of first examination into all cases, cases >40.0°C, and cases >40.5°C.

A relapse was defined as a calf that was treated for BRD, subsequently recovered and returned to its home pen, but thereafter was pulled and treated again as a BRD case.

Postmortem examinations were performed on dead animals by a veterinarian and the cause of death was based on grossly detectable pathological changes. Samples of lung tissue were taken by the attendant veterinarian from selected animals (approximately 75%) for bacteriological and histological studies to confirm the diagnosis.

The following outcomes up to 28 days postarrival were identified: morbidity; mortality from all causes; mortality associated with BRD; mortality associated with fibrinous pneumonia (FP); relapse; and weight gain (between day 0 and day 90 postarrival).

Statistical methods

Data were analyzed by the Statistical Analysis System computer programs (SAS Institute, Box 8000, Cary, North Carolina, USA). The unit of analysis for all outcomes was the individual. Statistical evaluation of outcomes was performed separately in ranch and auction calves.

The 2 × 2 factorial design of the study (15), allowed contrasts of the effects of ranch vaccination versus feedlot vaccination — providing the joint effects of vaccination at both locations were additive (i.e. no interaction was present). In each analysis, the presence of interaction was assessed by an appropriate test (Breslow-Day or F test) (SAS Stat Guide, 15). For both categorical and continuous outcomes, the data were analyzed by initially ignoring, and later accounting for, individual ranch and auction lot effects. Categorical outcomes were analyzed using chi-square and Mantel-Haenszel techniques, continuous outcomes by analysis of variance methods. The number experiencing mortality was relatively small (statistically speaking), hence Fischer's exact test, or extensions thereof, was used to assess differences in mortality rates. Data from ranch calves were analyzed separately from data for auction calves.

Table 2. A summary of outcomes in a field trial of Presponse

	Treatment group					
	Ranch source calves				Auction calves	
Outcome	1 R−F+[a]	2 R−F−	3 R+F−	4 R+F+	5 F−	6 F+
Total mortality	0	2	6	4	12	12
Total mortality rate	0.0[b]	0.7[bc]	2.1[cd]	1.5[cd]	3.3[e]	3.3[e]
BRD mortality	0	1	5	2	12	8
BRD mortality rate	0.0[b]	0.4[bc]	1.8[c]	0.7[bc]	3.3[d]	2.2[d]
FP mortality	0	0	1	1	5	7
FP mortality rate	0.0[b]	0.0[b]	<0.1[b]	<0.1[b]	1.4c[c]	1.9[c]
Morbidity (>39.5°C)	134	122	122	107	274	259
Morbidity rate (>39.5°C)	46.1[b]	42.2[b]	43.0[b]	38.8[b]	74.5[c]	71.4[c]
Morbidity (>40.0°C)	82	80	83	71	225	201
Morbidity rate (>40.0°C)	28.2[b]	27.7[b]	29.2[b]	25.7[b]	61.1[c]	55.4[c]
Morbidity (>40.5°C)	47	57	52	45	174	154
Morbidity rate (>40.5°C)	16.2[b]	19.7[b]	18.3[b]	16.3[b]	47.3[c]	42.4[c]
Number relapsed	36	34	32	27	134	100
Relapse rate	26.9[b]	27.9[b]	27.1[b]	25.7[b]	48.9[c]	38.9[d]
90 day weight gain (kg)	104.5[b]	104.2[b]	104.6[b]	103.6[b]	95.7c[b]	95.2[c]

[a]R indicates ranch vaccination status, F indicates feedlot vaccination status
Within an outcome, and calf source, means superscripted by different letters were significantly different at $p < 0.05$

In ranch calves, subsequent to examining for ranch vaccination and feedlot vaccination effects, the trial design was treated as completely randomized with four treatments in ranch calves. When the overall tests revealed significant differences ($p < 0.05$), the treatments producing the significance were identified by partitioning the chi-square test or by using Duncan's multiple range test (15).

The number of ranch calves used in the study was deemed a priori to be sufficient for 80% power given morbidity rates in vaccinated and unvaccinated calves of 40% and 25%, and differences in weight gain of 10% between vaccinated and unvaccinated calves, with a mean weight gain of 95 kg and a variance of 950 kg^2. The design provided a power of only about 55% to detect a 50% decrease in mortality rates from 4% to 2%. Hence, the major outcomes for the trial were morbidity rates, relapse rates, and weight gain.

Results

The first calves were processed at the feedlot on October 18, and the last calves on November 16, 1988. There were 234 bulls, 417 heifers, and 1220 steers. The average weight of calves on arrival was 235 kg, and at day 90 it was 336 kg.

On arrival, 585 calves had temperatures in excess of 40.0°C, 195 calves in excess of 40.5°C. The calves with rectal temperatures on arrival of >40.0°C did not have an increased risk of subsequent BRD. The calves with rectal temperatures on arrival of >40.5°C were more likely to be subsequently pulled and treated as cases of BRD than other calves (odds ratio = 1.8, $p < 0.01$). As calves with these elevated temperatures (>40.5°C) were essentially equally distributed across vaccination groups, within source of calves (7.7%, 9.7%, 9.2%, 8.2%, 29.7%, and 35.4%, in groups 1 through 6 respectively), no adjustment for rectal temperature on arrival was made in analyses.

A total of 1018 (54.4%) calves was treated for BRD within 123 days of arrival, 990 (52.9%) within 90 days of arrival. Of the 1018 calves treated, 716 (38.2% of 1871) had rectal temperatures in excess of 40°C, and 513 (27.4% of 1871) in excess of 40.5°C, at first treatment (Table 2). Approximately 26% of the cases >40.0°C were treated within one week of arrival, over 68% by two weeks postarrival. There was no visual difference in the epidemic curves among the vaccine groups within ranch or auction calves. The auction calves had a much larger peak of treatments in the first week after arrival than the ranch calves (Table 3).

The number treated for BRD in ranch calves was 485 (42%), 305 (26.7%), and 194 (17%) for all cases, cases >40.0°C, and cases >40.5°C, respectively. The calves from the three ranches which were processed on the farm of origin tended to have a lower rate of morbidity (33% vs 45%) than calves processed at the feedlot. However, the difference was not significant and the apparent sparing effect was only seen on one of the three ranches. Overall, controlling for potential farm differences, the Mantel-Haenszel test for differences in morbidity by vaccine group was nonsignificant for both ranch and feedlot locations. Although the vaccine effect on morbidity was nonsignificant, overall, one purchase group (lot) had a significant reduction in BRD morbidity in Presponse vaccinated calves. The number treated for BRD in auction calves was 533 (72.9%), 411 (56.2%), and 319 (43.6%) for all cases, cases >40.0°C, and cases >40.5°C respectively. Vaccination was not related to morbidity in auction calves.

Ignoring the factorial design when examining the percentage of cattle treated and the percentage of cattle

Table 3. Time of BRD occurrence, postarrival, by vaccination and source

Group[a]	Source	BRD cases[b]	Time of treatment postarrival (days) >7	7–14	14–21	>20
1	Ranch	All	15	42	26	51
R−F+		>40.0°C	8	31	18	22
		>40.5°C	5	19	10	11
2	Ranch	All	10	45	28	39
R−F−		>40.0°C	5	32	22	21
		>40.5°C	3	22	15	16
3	Ranch	All	13	28	33	48
R+F−		>40.0°C	6	23	24	25
		>40.5°C	4	12	17	17
4	Ranch	All	11	34	22	40
R+F+		>40.0°C	8	26	16	18
		>40.5°C	4	19	11	9
5	Auction	All	105	116	31	22
F−	market	>40.0°C	88	93	25	8
		>40.5°C	66	82	15	4
6	Auction	All	94	113	27	25
F+	market	>40.0°C	74	94	20	9
		>40.5°C	50	81	15	6

[a]R indicates ranch vaccination status, F indicates feedlot vaccination status
[b]BRD cases classified as all animals, only those with rectal temperature >40.0°C, or only those with rectal temperature >40.5°C that were treated for BRD
Within source, the distribution of BRD with time did not differ by vaccine group (chi-square not significant at p = 0.05)

which relapsed (Table 2), no significant differences were observed among the vaccination groups in ranch calves (groups 1, 2, 3 and 4). Ranch calves vaccinated only at the feedlot had a significant reduction in total and BRD-related mortality relative to other ranch calf treatment groups.

Auction market calves receiving a single Presponse vaccination on arrival at the feedlot (group 6) had a lower relapse rate compared to nonvaccinated auction calves (group 5) ($p < 0.05$). No other statistically significant effects were observed in auction calves.

Differences in weight gain among ranch calves (groups 1 through 4) were not statistically significant, and there was no interaction between source and treatment on weight gain. There was no significant difference in weight gain between the vaccinates and nonvaccinates in auction calves.

There were 36 deaths; 34 of these occurred by 90 days after arrival (Table 2). Twenty-six of the 34 dead calves had pneumonia, and 14 of these had fibrinous pneumonia. About 40% of deaths occurred by two weeks postarrival. Two of the test animals died from anaphylactic shock at the time of induction processing at the feedlot. One of these had received Presponse at the feedlot (group 6) during the induction process, whereas the other animal had not (group 3). Two calves died of bloat (one in each of groups 2 and 6), and one of a broken neck (group 4). The total mortality rate in ranch calves was 1.3% overall, 0.8% for BRD-related mortality, and 0.2% for FP-related mortality. The total mortality rate in auction calves was 3.3%, the BRD-related mortality was 2.7%, and the FP-related mortality was 1.6%. The Mantel-Haenszel test indicated no effect of feedlot vaccination on total or BRD mortality. There was a significant increase in total mortality (chi-square = 4.34) in ranch-vaccinated calves, and a similar tendency for BRD-related mortality (chi-square = 3.28) at the 5% level of significance. No analyses were performed on FP-related mortalities in ranch calves, but both deaths occurred in calves vaccinated with Presponse at the ranch of origin.

Although not evaluated statistically, calves from auctions had a higher percentage of calves that were febrile on arrival, had higher morbidity and mortality rates, higher relapse rates, and lower weight gains than ranch calves.

Discussion

For purposes of discussion and comparison with previous trials, cases of BRD will be restricted to those with rectal temperatures in excess of 40°C. However, it should be noted that, out of 28 of the 34 calves which died during the study period and had a recorded rectal temperature at first treatment (six calves died before temperatures could be taken), three were below 40°C; two of these died of pneumonia, and one of fibrinous pneumonia.

Despite using Presponse in what seemed to be a biologically sensible manner, in that it should have provided sufficient time for a protective immune response, no major benefits to vaccination were seen in this trial. In fact, there was a significant increase in overall mortality and a tendency for an increase in BRD-related mortality, in ranch-vaccinated calves. These untoward effects were not due to calves from just a few source ranches, as only one ranch had more than one death in any of the treatment groups, and

even in that instance only two animals died from that ranch treatment group. The trend towards a reduction in morbidity in the calves vaccinated with viral vaccines on the farm of origin may be explained, in large part, by these farms being located close to the feedlot. Hence, these calves were transported for only an hour or so. Morbidity rates and weight gains did not seem to be influenced by Presponse in ranch calves. The lack of reduction of morbidity rates in calves from auctions, by vaccination with Presponse, has also been noted previously in preliminary results from a field trial in Ontario (16).

In auction calves, one positive effect was seen in that the vaccinated calves had a significantly lower relapse rate than nonvaccinated calves. There was virtually no difference in relapse rates in the corresponding vaccination groups (group 1 versus 2) of ranch calves. The tendency towards lower relapse rates is in agreement with the trends seen in previous field trial results (14,16). Because it was very difficult to access the computerized rectal temperature data on the relapses, no temperature criteria were applied to relapses. The level of mortality in the auction calves in the trial reported herein was somewhat lower than in the previous trial of Presponse (14). The absolute decrease of 1.1% (a relative decrease of about 33%) in mortality in feedlot-vaccinated calves was not declared significant, possibly due to the small (in a statistical sense) number of calves under study that died. As mentioned earlier, in the current study the power of our trial to detect a 50% reduction in mortality was low (55%; about twice as many calves were needed to detect a reduction from 4% to 2% with 80% power, and a greater number of ranch-source calves would be needed given the lower mortality rates experienced by calves from ranches). Counteracting this potential decrease, however, was the observation that the FP-related mortality was highest in the group of auction calves vaccinated with Presponse on arrival. This observation tends to negate inferences about a possible benefit of Presponse on BRD-related mortality.

Reasons why the vaccine did not show an overall beneficial effect are not readily apparent. In the previous field trial, the vaccine was shown to reduce mortality rates in auction calves, but did not alter, significantly, either the morbidity or relapse rates (14). In the current trial we did not exclude calves with elevated rectal temperatures on arrival, nor did we prophylactically treat calves with antimicrobials. The effects of these differences in trial design on the outcomes are unknown. Early experience with Presponse in Ontario feedlots, with western auction calves, has also failed to demonstrate a significant effect of vaccination on morbidity, relapse, or mortality (although mortality in these calves is traditionally low and the Ontario trials have a limited power to detect significant effects on mortality) (16). Previous serological studies have demonstrated that BRD cases have a higher rate of seroconversion to the cytotoxin of *P. haemolytica* than untreated controls. However, the differences, although statistically significant, were not large (17).

In discussing the results of this trial, there has been speculation about the effect of the placebo, the carrier for the vaccine. Some suggest that the carrier, an "immunomodulator", in Presponse is itself quite immunogenic and protective, thus decreasing our ability to demonstrate the effectiveness of the vaccine. This may be true, but no valid field data are availabe to evaluate the hypothesis. In our opinion, this purported "adjuvant effect" would not seem to be a logical explanation for the similarity of outcomes. Nor does the purported adjuvant effect explain the increase in death losses in ranch-vaccinated calves, and the tendency toward a higher number of FP-related deaths in feedlot-vaccinated auction calves. It is not clear what, if any, placebo was used in the previous trial of Presponse (14).

Although not an objective of this trial, our data indicated that source of cattle was a major factor affecting the incidence and/or effects of BRD. Calves moved directly from ranches to feedlots, regardless of vaccination status, had lower morbidity and mortality, and better weight gains, than calves purchased from auction markets. The extent to which number of calves per pen may have affected this outcome is unknown. Larger group sizes tend to have more health problems (2,3), however, in this trial the density of calves per pen was lowest for the auction calves. The two day maximum difference in weighing times notwithstanding, the ranch calves also gained more weight than calves purchased from auction markets. These observations may reinforce the role of stress and exposure to pathogenic organisms on the occurrence of BRD. Subsequent serological studies on these calves' sera may reveal the extent to which the ranch and auction calves differed with regard to antibody response on and after arrival at the feedlot, and may also be of value in explaining the apparent untoward effects noted in ranch-vaccinated and feedlot-vaccinated calves.

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