Comparison of two alternate PGF_{2α} products in two estrus synchronization protocols in beef heifers

Nicola Oosthuizen[†], Alicia C. Lansford[‡], Luara B. Canal[†], Pedro L. P. Fontes[†], Carla D. Sanford[†], Carl R. Dahlen[§], Nicolas DiLorenzo[†], Rick N. Funston[‡], and G. Cliff Lamb^{||,1}

[†]North Florida Research and Education Center, Marianna, FL 32446; [‡]University of Nebraska West Central Research and Extension Center, North Platte, NE 69101; [§]Department of Animal Sciences, North Dakota State University, Fargo, ND 58108; ^{||}Department of Animal Science, Texas A&M University, College Station, TX 77843-2471

ABSTRACT: Two experiments were conducted to evaluate the effects of a high concentrate, s.c. PGF_{2α} compared with a conventionally concentrated, i.m. PGF_{2α} in estrus synchronization protocols for heifers. In Exp. 1, 869 Angus-based beef heifers were enrolled at 8 locations. All heifers were exposed to the 7-d CO-Synch + controlled internal drug release (CIDR) estrus synchronization protocol. On day 7 of the protocol heifers received 100 µg of GnRH i.m., and a CIDR insert for 7 d. On day 0, at CIDR removal, estrous detection patches were applied to heifers and, within location, heifers randomly received 1 of 2 PGF_{2α} treatments: 5 mL of Lutalyse i.m. (CONTROL; *n* = 434) or a 2 mL of Lutalyse *HighCon* s.c. (HiCON; *n* = 435). A second GnRH injection was administered at 54 ± 2 h and heifers were fixed-time AI (TAI). Heifers were evaluated for estrous activity at TAI by determining the activation of estrous detection patches. Pregnancy rates to AI (PR/AI) were diagnosed by transrectal ultrasonography between 35 and 55 d after TAI. The percentage of heifers exhibiting estrus between day 0 and TAI did not differ (*P* = 0.68) between CONTROL and HiCON treatments (47 vs. 46 ± 4%, respectively). Additionally, PR/AI were similar (*P* = 0.65) between CONTROL

and HiCON treatments (46 vs. 45 ± 3%). In Exp. 2, 190 Angus-based beef heifers were enrolled at 2 locations. Heifers were exposed to the melengestrol acetate (MGA)—PGF_{2α} protocol where they were offered 0.5 mg MGA per day from days 1 to 14. On day 33, heifers were randomly assigned to receive CONTROL (*n* = 95) or HiCON (*n* = 95) treatment, and estrous detection aids were applied. Heifers were exposed to AI 12 h after detection of estrus. Heifers not detected in estrus at location 1 received a second PGF_{2α} injection 6 d after the initial PGF_{2α} injection and were placed with fertile bulls. Heifers at location 2 that did not express estrus were administered 100 µg of GnRH i.m. and exposed to TAI 96 h after the initial PGF_{2α} injection. Transrectal ultrasonography was used to diagnose PR/AI between 51 and 57 d after the initial PGF_{2α} injection. The percentage of heifers exhibiting estrus during the estrus detection period was similar (*P* = 0.40) between CONTROL and HiCON treatments (82 vs. 87 ± 4%). Furthermore, PR/AI were similar (*P* = 0.62) between CONTROL and HiCON treatments (60 vs. 65 ± 5%). In summary, the 2 concentrations and corresponding routes of administration of PGF_{2α} were similar in efficacy at synchronizing estrus in beef heifers.

Key words: beef heifer, estrus synchronization, prostaglandin F_{2α}

© The Author(s) 2018. Published by Oxford University Press on behalf of American Society of Animal Science. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.
J. Anim. Sci. 2018.96:1388–1395
doi: 10.1093/jas/sky059

¹Corresponding author: gclamb@tamu.edu

The authors thank Zoetis Animal Health (Parsippany, NJ) for their donation of PGF_{2α} (Lutalyse and Lutalyse *HighCon*). The authors also thank ABS Global (DeForest, WI) for their semen donation, and the ABS Global

representatives, K. Porter, J. Knock, and M. Sandbulte for their assistance in conducting this experiment.

Received February 16, 2018.

Accepted February 25, 2018.

INTRODUCTION

Exogenous hormones and their analogues are used to manipulate the bovine estrous cycle to reduce the amount of labor and time expended on estrus detection. Prostaglandin F_{2α} is a fatty acid hormone commonly administered to cows and heifers as part of estrus synchronization protocols. Administration of PGF_{2α} results in regression of a functional corpus luteum between days 5 and 16 of the estrous cycle (Rowson et al., 1972), and estrus within approximately 3 d (Tervit et al., 1973).

Numerous studies have evaluated the effectiveness of various PGF_{2α} products. No differences were reported between the ability of different PGF_{2α} products to decrease progesterone concentrations (Schams and Karg, 1982; Guay et al., 1988) or induce an estrus response (Plata et al., 1990; Martineau, 2003), and have shown no differences in pregnancy rates (Salverson et al., 2002; Stevenson & Phatak, 2010). The route of PGF_{2α} administration also had no effect on the decline in progesterone concentration, nor on the proportion of cows undergoing luteal regression (Chebel et al., 2007). In addition, heifers treated with PGF_{2α} i.m. or s.c. showed similar intervals from administration to estrus (Edqvist et al., 1975; Colazo et al., 2002) and had similar rates of ovulation (Colazo et al., 2002).

A high concentrate PGF_{2α} product, Lutalyse *HighCon* (12.5 mg of dinoprost tromethamine/mL; Zoetis Animal Health), was recently been approved for use by the U.S. Food and Drug Administration. According to label directions, Lutalyse *HighCon* may be administered by i.m. or s.c. injection in bovine females. Subcutaneous administration may reduce the occurrence of blemishes on beef carcasses (Powell, 2013), improve tenderness (Griffin et al., 1998), and reduce the income lost per head at

slaughter (Hilton, 2004). To date, no research has been conducted to determine the effectiveness of this product in estrus synchronization protocols for beef heifers.

Therefore, this study was performed to evaluate the efficacy of the high concentrate PGF_{2α} product, Lutalyse *HighCon*, by determining its effectiveness in estrus response and pregnancy rates in beef heifers. We hypothesized that an s.c. injection of a high concentrate PGF_{2α} would not alter estrus response or pregnancy rates when compared with the administration of a conventional concentrate PGF_{2α} in estrus synchronization protocols for beef heifers.

MATERIALS AND METHODS

All heifers were handled in accordance with procedures approved by each collaborating university's Animal Care and Use Committee.

Experiment 1

Angus-based crossbred, yearling heifers ($n = 869$; 406 ± 2 kg BW) were enrolled at 8 locations in 2 states (South Dakota and North Dakota). Herd size ranged from 50 to 220 heifers. Within location, heifers were exposed to the 7-d CO-Synch + controlled internal drug release (CIDR) protocol. On day 7, heifers received a 2-mL i.m. injection of GnRH (Factrel; 100- μ g gonadorelin hydrochloride; Zoetis Animal Health, Parsippany, NJ) and a CIDR (EAZI-BREED CIDR; 1.38-g progesterone; Zoetis Animal Health) insert. Heifer BW was recorded at 5 of the 8 locations (SD-1, SD-3, SD-4, SD-7, and ND). On day 0, at CIDR removal, estrous detection patches (Estrotest; Rockway Inc., Spring Valley, WI) were applied, and heifers were randomly assigned to receive 1 of 2 PGF_{2α} treatments

Figure 1. Schematic of treatments. All heifers were exposed to the 7-d CO-Synch + CIDR protocol. On day 7, heifers received a 2-mL i.m. injection of GnRH (100- μ g gonadorelin hydrochloride; Zoetis Animal Health, Parsippany, NJ) and a controlled internal drug releasing (EAZI-BREED CIDR; 1.38-g progesterone; Zoetis Animal Health) insert. On day 0, at CIDR removal, estrous detection patches (Estrotest; Rockway Inc., Spring Valley, WI) were applied and heifers were randomly assigned to receive 1 of 2 PGF_{2α} treatments. Heifers assigned to the CONTROL treatment ($n = 417$) received a 5-mL i.m. injection of Lutalyse (5 mg of dinoprost tromethamine/mL; Zoetis Animal Health), whereas those assigned to the HiCON treatment ($n = 424$) received a 2-mL s.c. injection of Lutalyse *HighCon* (12.5 mg of dinoprost tromethamine/mL; Zoetis Animal Health). All heifers received a 100- μ g injection of GnRH and were exposed to TAI 54 ± 2 h after CIDR removal. Pregnancy diagnosis was performed via transrectal ultrasonography between days 35 and 55 after TAI. Final pregnancy diagnosis was performed at least 35 d after the end of the breeding season (Exp. 1).

(Figure 1). Heifers assigned to the CONTROL treatment ($n = 434$) received a 5-mL i.m. injection of Lutalyse (5 mg of dinoprost tromethamine/mL; Zoetis Animal Health), whereas those assigned to the HiCON treatment ($n = 435$) received a 2-mL s.c. injection of Lutalyse *HighCon*. All heifers received a 100- μ g injection of GnRH and were inseminated 54 ± 2 h after CIDR removal. To ensure there were sufficient experimental units to test the hypothesis, a power analyses (using various preliminary observations and published reports) indicated that 393 heifers per treatment would be sufficient to detect 3% difference in pregnancy rates ($\alpha = 0.05$; $\beta = 0.80$).

Estrous detection patches were utilized for estrus detection between CIDR removal and fixed-time AI (TAI). Heifers were considered to be in estrus when at least 50% of the rub-off coating was removed from the patch, or when the patch was absent at TAI. No less than 10 d after TAI, heifers were exposed to bulls for the remainder of the breeding season at 6 locations (SD-1, SD-2, SD-3, SD-4, SD-7, and ND).

Transrectal ultrasonography (Aloka 500V, Vancouver, BC, Canada or Ibex Pro, E.I. Medical Imaging, Loveland, CO) was performed by 2 experienced veterinarians between days 35 and 55 after TAI to determine the presence of a conceptus heartbeat, thereby assessing pregnancy rates to AI (PR/AI). Final pregnancy rates were determined by transrectal ultrasonography at least 35 d after the end of the breeding season.

Experiment 2

Yearling, Angus-based crossbred heifers ($n = 190$) were managed at 2 locations. Heifers at location 1 ($n = 100$; 340 ± 3 kg BW; L1) were managed at the West Central Research and Extension Center near North Platte, NE. Each heifer was offered a ration consisting of 6.4-kg grass hay, 3.6-kg wet corn gluten feed, and 0.45 kg of 1 of 2 mineral supplements.

Heifers were synchronized using a melengestrol acetate (MGA)—PGF_{2 α} protocol (Figure 2). Heifers were offered 0.5 mg of MGA (Zoetis Animal Health, Parsippany, NJ) pellets in their diet per day from days 1 to 14. On day 33, heifers were blocked by previous developmental treatments (Springman et al., 2017) and assigned to either CONTROL ($n = 50$) or HiCON ($n = 50$) treatment. An estrous detection patch was applied concurrently with the PGF_{2 α} injection.

All heifers were managed together and continuously observed for estrus from days 33 to 39. Heifers were considered to be expressing estrus when at least 50% of the rub-off coating was removed from the patch or when the patch was absent. Heifers were AI 12 h after estrus was detected. Heifers not detected in estrus between days 33 and 39 ($n = 16$) were given an injection of Lutalyse *HighCon* and placed with 2 bulls for natural service exposure. Heifers exposed to AI were placed in a separate pasture for 10 d before being placed with those not detected in estrus. Heifers remained with bulls for a 60-d breeding season at a ratio of 1:50. Pregnancy rates to AI and final pregnancy rates were diagnosed via transrectal

Figure 2. MGA-PGF_{2 α} protocol. MGA (Zoetis Animal Health, Parsippany, NJ) was offered to heifers at a rate of 0.5 mg/d for 14 d. On day 33, heifers were administered either 5 mL of Lutalyse (CONTROL; $n = 95$; Zoetis Animal Health) i.m. or 2 mL of Lutalyse *HighCon* (HiCON; $n = 95$; Zoetis Animal Health) s.c. Estrus detection (ED) was conducted for 6 d following PGF_{2 α} treatment at location 1. Heifers not detected in estrus were given a second PGF_{2 α} injection and were placed with bulls. Heifers at location 2 that did not express estrus by 96 h after PGF_{2 α} treatment were administered 2 mL of GnRH (Factrel; Zoetis Animal Health), and exposed to TAI. Pregnancy was diagnosed via transrectal ultrasonography between 51 and 57 d after initial PGF_{2 α} injection. Final pregnancy diagnosis was conducted via transrectal ultrasonography 129 and 107 d after PGF_{2 α} treatment, for locations 1 and 2, respectively (Exp. 2).

ultrasonography (Aloka, Hitachi Aloka Medical America Inc., Wallingford, CT) 51 and 127 d after the initial PGF_{2α} injection, respectively.

A second group of yearling, Angus-based cross-bred heifers was managed at the Kelly Ranch near Sutherland, NE ($n = 90$; 326 ± 4 kg BW; location 2, L2) and was offered a ration containing 0.6-kg wet distiller grains, 2.4-kg grass hay, 3.2-kg corn silage, and 0.2-kg balancer pellets. Heifers were synchronized with the MGA-PGF_{2α} protocol as previously described for L1 and assigned randomly to receive CONTROL ($n = 45$) or HiCON ($n = 45$) treatment.

Heifers were observed for estrus continuously from days 33 to 36. Heifers detected in estrus were AI approximately 12 h later. Heifers not expressing estrus by 96 h ($n = 14$) were administered 2 mL of GnRH and TAI. Ten days following AI, 2 bulls were placed with heifers at a ratio of 1:45 during a 40-d breeding season. Pregnancy rates to AI were diagnosed via transrectal ultrasonography 57 d after the initial PGF_{2α} injection, and BW was concurrently recorded. A final pregnancy diagnosis was performed 50 d after the initial pregnancy diagnosis on heifers not diagnosed pregnant to AI, and BW was simultaneously recorded.

Statistical Analysis

The GLIMMIX procedure of SAS (SAS Institute, Inc., Cary, NC) was used for all statistical

analyses. For Exp. 1, the model included the fixed effects of treatment, location, and the treatment $\times$ location interaction. The response variables analyzed were estrus expression, PR/AI, and final pregnancy rates. For Exp. 2, the model included the fixed effects of treatment, location, and the treatment $\times$ location interaction. The response variables analyzed were estrus detection time points, ADG, PR/AI, and final pregnancy rates. Artificial insemination sire and AI technician were distributed evenly among treatments; therefore, these variables were not included in the model. Individual heifer was considered the experimental unit. Means were declared significant for both experiments at $P \leq 0.05$, with $0.05 < P < 0.10$ considered a tendency.

RESULTS AND DISCUSSION

Experiment 1

Initial BW differed ($P < 0.01$) among locations, but did not differ ($P = 0.49$) between treatments (406 ± 2 kg). Body weight among locations ranged from 380.6 ± 4.0 kg at location SD-4 to 432.4 ± 2.2 kg at location SD-7. Estrus response rates for all heifers at all locations are summarized in Table 1. Estrus expression between day 0 and TAI did not differ between CONTROL and HiCON treatments ($P = 0.68$); however, estrus expression differed among locations ($P < 0.01$),

Table 1. Estrus response at the time of fixed-time AI in heifers after receiving conventional or high concentrate PGF_{2α} (Exp. 1)

Item	Treatment ^a		Overall	SEM	P-value
	CONTROL	HiCON			
	n/n (%)				
Location					
SD-1	11/25 (44.0)	16/25 (64.0)	27/50 (54.0) ^{wxy}	13.9	0.15
SD-2	15/29 (51.7)	17/27 (63.0)	32/56 (57.1) ^{wx}	13.1	0.39
SD-3	33/70 (47.1)	30/70 (42.9)	63/140 (45.0) ^{xyz}	8.3	0.61
SD-4	13/31 (41.9)	10/29 (34.5)	23/60 (38.3) ^{yz}	12.7	0.56
SD-5	27/63 (42.9)	18/64 (28.1)	45/127 (35.4) ^z	8.7	0.09
SD-6	25/40 (62.5)	29/43 (67.4)	54/83 (65.1) ^w	10.8	0.65
SD-7	43/110 (39.1)	38/110 (34.6)	81/220 (36.8) ^z	6.6	0.49
ND	35/65 (53.9)	41/67 (61.2)	76/132 (57.6) ^w	8.5	0.39
Overall	202/433 (46.7)	199/435 (45.7)		3.8	0.68

^aAll heifers were estrus synchronized using the 7-d CO-Synch + CIDR protocol. On day 7, heifers received a 100-μg injection of GnRH (Factrel; Zoetis Animal Health, Parsippany, NJ) and a CIDR (EAZI-BREED CIDR; Zoetis Animal Health) insert. On day 0, at CIDR removal, estrous detection patches (Estroject; Rockway Inc., Spring Valley, WI) were applied and heifers were randomly assigned to receive 1 of 2 PGF_{2α} treatments. Heifers assigned to the CONTROL treatment ($n = 417$) received a 5-mL i.m. injection of Lutalyse (5 mg of dinoprost tromethamine/mL; Zoetis Animal Health), whereas those assigned to the HiCON treatment ($n = 424$) received a 2-mL s.c. injection of Lutalyse *HighCon* (12.5 mg of dinoprost tromethamine/mL; Zoetis Animal Health). All heifers received a 100-μg injection of GnRH and were exposed to TAI 54 ± 2 h after CIDR removal. Estrous detection patches were concurrently observed for activation. Heifers were considered to be in estrus when at least 50% of the rub-off coating was removed from the patch, or when the patch was absent.

^{w,x,y,z}—Percentages within column for location differ ($P \leq 0.05$).

with the greatest estrus response at location SD-6 ($65 \pm 5\%$) and poorest at location SD-5 ($36 \pm 4\%$). No treatment $\times$ location interaction was detected ($P = 0.37$). Lactating dairy cows receiving dinoprost tromethamine either i.m. or s.c. had a similar decline in concentrations of progesterone, and the proportion of cows that underwent luteal regression by 12, 24, 36, and 48 h after PGF_{2 α} treatment was similar between treatments (Chebel et al., 2007). In addition, beef heifers receiving an i.m. or s.c. injection of dinoprost tromethamine had no difference in estrus response (Colazo et al., 2002). In the current study, the lack of difference between estrus response of CONTROL and HiCON treatment groups indicates that both treatments were equally effective at inducing regression of the corpus luteum when administered in the 7-d CO-Synch + CIDR protocol.

Pregnancy rates to TAI for all heifers at all locations are summarized in Table 2. Pregnancy rate to TAI did not differ between CONTROL and HiCON treatments ($P = 0.65$); however, there was an effect of location ($P < 0.01$) on PR/AI, which was greatest at location SD-4 ($61 \pm 6\%$), and poorest at location SD-5 ($38 \pm 4\%$). No treatment $\times$ location interaction was detected ($P = 0.18$). At the conclusion of the breeding season, final pregnancy rates did not differ between CONTROL and HiCON treatments ($P = 0.95$). Final pregnancy rates differed ($P < 0.01$) among location and ranged from 78% to 98% (Table 3).

Each location was unique in its management practices, and thus, location affected the estrus synchrony and fertility in this study. Each location was producer-owned and differed in nutrition, facilities, animal handling practices, and individual production goals. Varying management practices among locations may have contributed to the reported differences in estrus response, PR/AI, and final pregnancy rates observed.

Experiment 2

Initial BW was similar ($P = 0.36$) between treatments (333 ± 4 kg); however, BW differed ($P = 0.01$) between locations (340 vs. 326 ± 3 kg, L1 vs. L2). Additionally, BW at first pregnancy diagnosis was similar ($P = 0.26$) between treatments (392 ± 4 kg) but also differed ($P = 0.04$) by location (386 vs. 397 ± 4 kg, L1 vs. L2). Heifers at L2 had a greater ADG ($P < 0.01$) between day 33 and AI pregnancy diagnosis compared with heifers at L1 (0.90 vs. 1.3 ± 0.03 kg/d). At final pregnancy diagnosis, heifer BW was similar ($P = 0.71$) between locations (424 ± 14 kg), and treatment groups ($P = 0.85$; 425 ± 11 kg). The discrepancy in BW and ADG between locations could be a result of different nutritional management strategies. Heifers at L2 initiated the study at a lower BW, yet due to a higher energy ration fed through the treatment period, may have compensated to reach a similar final BW.

Table 2. Pregnancy rates to fixed-time AI in heifers after receiving conventional or high concentrate PGF_{2 α} (Exp. 1)

Item	Treatment ^a		Overall	SEM	P-value
	CONTROL	HiCON n/n (%)			
Location					
SD-1	12/25 (48.0)	9/25 (36.0)	21/50 (42.0) ^{yz}	13.9	0.39
SD-2	9/29 (31.0)	16/27 (59.3)	25/56 (44.6) ^{xyz}	13.2	0.03
SD-3	34/70 (48.6)	29/70 (41.4)	63/140 (45.0) ^{yz}	8.3	0.39
SD-4	22/31 (71.0)	15/29 (51.7)	37/60 (61.7) ^x	12.7	0.13
SD-5	27/63 (42.9)	21/64 (32.8)	48/127 (37.8) ^z	8.7	0.25
SD-6	19/40 (47.5)	25/43 (58.1)	44/83 (53.0) ^{xy}	10.8	0.33
SD-7	44/110 (40.0)	40/110 (36.4)	84/220 (38.2) ^z	6.6	0.58
ND	28/66 (42.4)	28/67 (41.8)	56/133 (42.1) ^{yz}	8.7	0.94
Overall	195/434 (44.9)	183/435 (42.1)		3.8	0.65

^aAll heifers were estrus synchronized using the 7-d CO-Synch + CIDR protocol. On day 7, heifers received a 100- μ g injection of GnRH (Factrel; Zoetis Animal Health, Parsippany, NJ) and a CIDR (EAZI-BREED CIDR; Zoetis Animal Health) insert. On day 0, at CIDR removal, estrous detection patches (Estroject; Rockway Inc., Spring Valley, WI) were applied and heifers were randomly assigned to receive 1 of 2 PGF_{2 α} treatments. Heifers assigned to the CONTROL treatment ($n = 417$) received a 5-mL i.m. injection of Lutalyse (5 mg of dinoprost tromethamine/mL; Zoetis Animal Health), whereas those assigned to the HiCON treatment ($n = 424$) received a 2-mL s.c. injection of Lutalyse *HighCon* (12.5 mg of dinoprost tromethamine/mL; Zoetis Animal Health). All heifers received a 100- μ g injection of GnRH and were exposed to TAI 54 ± 2 h after CIDR removal. Pregnancy rate to TAI was recorded between days 35 and 55 after TAI.

^{x,y,z}Percentages within column for location differ ($P \leq 0.05$).

Table 3. Final pregnancy rates in heifers after receiving conventional or high concentrate PGF_{2α} (Exp. 1)

Item	Treatment ^a		Overall	SEM	P-value
	CONTROL	HiCON			
	n/n (%)				
Location					
SD-1	14/16 (87.5)	13/17 (76.5)	27/33 (81.8) ^{yz}	8.8	0.21
SD-2	28/29 (96.6)	26/27 (96.3)	54/56 (96.4) ^x	6.8	0.97
SD-3	69/70 (98.6)	68/70 (97.1)	137/140 (97.9) ^x	4.3	0.74
SD-4	26/31 (83.9)	21/29 (72.4)	47/60 (78.3) ^z	6.5	0.08
SD-5 ^b	—	—	—	—	—
SD-6 ^b	—	—	—	—	—
SD-7	105/110 (95.5)	103/110 (93.6)	208/220 (94.6) ^x	3.4	0.59
ND	18/21 (85.7)	34/36 (94.4)	52/57 (91.2) ^{xy}	6.9	0.21
Overall	260/277 (93.9)	265/289 (91.7)		2.6	0.95

^aAll heifers were estrus synchronized using the 7-d CO-Synch + CIDR protocol. On day 7, heifers received a 100-μg injection of GnRH (Factrel; Zoetis Animal Health, Parsippany, NJ) and a CIDR (Eazi-Breed CIDR; Zoetis Animal Health) insert. On day 0, at CIDR removal, estrous detection patches (Estroject; Rockway Inc., Spring Valley, WI) were applied and heifers were randomly assigned to receive 1 of 2 PGF_{2α} treatments. Heifers assigned to the CONTROL treatment (*n* = 417) received a 5-mL i.m. injection of Lutalyse (5 mg of dinoprost tromethamine/mL; Zoetis Animal Health), whereas those assigned to the HiCON treatment (*n* = 424) received a 2-mL s.c. injection of Lutalyse *HighCon* (12.5 mg of dinoprost tromethamine/mL; Zoetis Animal Health). All heifers received a 100-μg injection of GnRH and were exposed to TAI 54 ± 2 h after CIDR removal. Final pregnancy diagnosis was performed at least day 35 after the end of the breeding season.

^bHeifers at SD-5 and SD-6 were not exposed to clean-up bulls after TAI; therefore, they were not included in overall pregnancy diagnosis analyses.

^{x,y,z}Percentages within column for location differ (*P* ≤ 0.05).

The percentage of heifers detected in estrus is summarized in Table 4 and was similar between CONTROL and HiCON treatments at ≤60 h (*P* = 0.15), ≤72 h (*P* = 0.51), and at 72 h (*P* = 0.27). These data indicate that the percentage of heifers that expressed estrus in the CONTROL and HiCON treatment groups was similar at each interval. There was a tendency (*P* < 0.08) for a location effect at ≤60 and ≤72 h. The tendency for a location effect on estrus response times was likely a result of differing management practices. The total percentage of heifers observed in estrus throughout the detection period was also similar between treatment groups (*P* = 0.40) and is comparable to results of a 5-mL i.m. injection of dinoprost tromethamine previously reported (Salverson et al., 2002). Beef heifers administered with dinoprost tromethamine s.c. had similar mean intervals to estrus and rates of ovulation to heifers administered i.m. (Colazo

et al., 2002). Heifers in the current study received the same total quantity of dinoprost tromethamine (25 mg/dose), regardless of treatment, therefore, similar estrus response and timing were expected.

Heifer pregnancy rates are summarized in Table 5. A treatment × location interaction (*P* = 0.03) was detected for PR/AI between L1 (44 vs. 64 ± 7%, CONTROL vs. HiCON) and L2 (73 vs. 62 ± 7%, CONTROL vs. HiCON). The PR/AI achieved were similar to those reported in previous studies (Springman et al., 2017; Tibbitts et al., 2017). Final pregnancy rates were similar between treatments (*P* = 0.11) and did not differ (*P* = 0.96) by location.

The following year, in 2017, additional yearling Angus-based heifers located at WCREC (*n* = 98) were exposed to an MGA-PGF_{2α} protocol. Heifers were managed the same as L1, with the exception that all heifers received a 2-mL s.c. injection of

Table 4. Time of estrus for yearling beef heifers given 2 alternate PGF_{2α} injections (Exp. 2)

	Treatment ^a		SEM	P-value ^b		
	CONTROL	HiCON		TRT	Location	T × L
Estrus response, %						
≤60 h	48	59	5.2	0.15	0.07	0.81
72 h	22	16	4.3	0.27	0.69	0.72
≤72 h	71	75	4.7	0.51	0.08	0.96
Total response	82	87	3.9	0.40	0.85	0.40

^aHeifers were administered 1 of 2 alternate PGF_{2α} products on day 33 as part of a MGA-PGF_{2α} protocol. CONTROL: 5 mL of Lutalyse (Zoetis Animal Health, Parsippany, NJ; *n* = 95) i.m. or HiCON: 2 mL of Lutalyse *HiCon* (Zoetis Animal Health; *n* = 95) s.c.

^bTRT: PGF_{2α} injection treatment main effect; Location: location main effect; T × L: PGF_{2α} injection treatment × location interaction.

Table 5. Pregnancy rates of yearling beef heifers given 1 of 2 alternate PGF_{2α} injections (Exp. 2)

	Treatment ^a		SEM	P-value ^b		
	CONTROL	HiCON		TRT	Location	T × L
AI pregnancy ^c , %	63	60	5.3	0.62	0.06	0.03
Overall pregnancy ^d , %	98	93	2.7	0.11	0.96	0.85

^aHeifers were administered 1 of 2 alternate PGF_{2α} products on day 33 as part of a MGA-PGF_{2α} protocol. CONTROL: 5 mL of Lutalyse (Zoetis Animal Health, Parsippany, NJ; n = 95) i.m. or HiCON: 2 mL of Lutalyse *HighCon* (Zoetis Animal Health; n = 95) s.c.

^bTRT: P-value represents the main effects of treatment; Location: P-value represents main effects of location; T × L: P-value represents the treatment × location interaction.

^cPregnancy was diagnosed via transrectal ultrasonography a minimum of 51 d after PGF_{2α} treatment.

^dFinal pregnancy diagnosis was conducted via transrectal ultrasonography a minimum of 107 d after PGF_{2α} treatment.

Lutalyse *HighCon* on day 33. Heifers were observed for estrous activity for 4 d after PGF_{2α} injection and were AI 12 h after estrus detection. Heifers that were not detected in estrus (n = 13) received a second injection of Lutalyse *HighCon* and were placed with fertile bulls for a 45-d breeding season. Heifers that were exposed to AI were placed in a separate pasture for 10 d and then placed with the heifers that did not express estrus. The percentage of heifers exhibiting estrus was 52 ± 5% at ≤60 h, 77 ± 4% at ≤72 h, and 24 ± 4% at 72 h, with a total estrus response of 87 ± 3%. The percentage of heifers confirmed pregnant to AI was 70 ± 5%, and final pregnancy rate was 93 ± 3%. This additional data further support the results from Exp. 1 and 2 that Lutalyse *HighCon* is effective at synchronizing estrus in beef heifers. However, we realize the limitations of the Exp. 2 based on the power of the experiment to determine differences among treatments, but the collective data and nonsignificance of the statistical analyses support our conclusions.

In both experiments, heifers in the HiCON treatment had similar rates of estrus expression when compared with the CONTROL heifers. Furthermore, AI and final pregnancy rates were similar between treatments.

IMPLICATIONS

The beef industry regularly incurs economic losses due to carcass lesions resulting from improper injection technique (Pratt, 2004). Intramuscular injections cause muscle trauma which results in an increase in connective tissue around the site during wound healing; therefore, this tissue damage negatively affects beef tenderness (Boleman et al., 1998) and consumer acceptability of beef (Fajt et al., 2011). Additionally, needle movement which can occur during administration of an i.m. injection may result in a portion of the exogenous product being administered subcutaneously (Powell, 2013). The Beef Quality Assurance program advises producers

to use an s.c. route of administration when possible to improve tenderness. Subcutaneous injections may result in a reduced amount of carcass damage and less trimming at slaughter and are thus more favored in the beef industry. Lutalyse *HighCon* is a high concentrate PGF_{2α} product that may be administered either i.m. or s.c. Lutalyse *HighCon* is a novel, high concentrate PGF_{2α} product on the pharmaceutical market that is a suitable alternative to conventionally concentrated PGF_{2α} products, such as Lutalyse, in estrus synchronization protocols for beef heifers.

LITERATURE CITED

- Boleman, S. L., S. J. Boleman, W. W. Morgan, D. S. Hale, D. B. Griffin, J. W. Savell, R. P. Ames, M. T. Smith, J. D. Tatum, T. G. Field, et al. 1998. National beef quality audit-1995: survey of producer-related defects and carcass quality and quantity attributes. *J. Anim. Sci.* 76:96–103.
- Chebel, R. C., J. E. Santos, H. M. Rutigliano, and R. L. Cerri. 2007. Efficacy of an injection of dinoprost tromethamine when given subcutaneously on luteal regression in lactating holstein cows. *Theriogenology* 67:590–597. doi:10.1016/j.theriogenology.2006.09.007.
- Colazo, M. G., M. F. Martínez, J. P. Kastelic, R. J. Mapletoft, and T. D. Carruthers. 2002. The ischiorectal fossa: an alternative route for the administration of prostaglandin in cattle. *Can. Vet. j.* 43:535–541.
- Edqvist, L. E., I. Settergren, and G. Aström. 1975. Peripheral plasma levels of progesterone and fertility after prostaglandin-2α induced oestrus in heifers. *Cornell Vet.* 65:120–131.
- Fajt, V. R., S. A. Wagner, L. L. Pederson, and B. Norby. 2011. The effect of intramuscular injection of dinoprost or gonadotropin-releasing hormone in dairy cows on beef quality. *J. Anim. Sci.* 89:1939–1943. doi:10.2527/jas.2010-2923.
- Griffin, D. D., D. R. Smith, and D. M. Grotelueschen. 1998. Proper injection procedures for cattle. In: 1998 Nebraska Extension Publication. Pub. No. G98-1351-A. University of Nebraska, Lincoln, NE. p 1–4.
- Guay, P., D. Rieger, and S. Roberge. 1988. Superovulatory and endocrine responses in holstein heifers treated with either prostaglandin f(2α), cloprostenol or fenprostalene. *Theriogenology* 29:1193–1199. doi:10.1016/S0093-691X(88)80044-X

- Hilton, W. M. 2004. Beef quality assurance injection sites and techniques. In: 2004 Purdue Extension Publication. Pub. No. VY-60-W. Purdue University, West Lafayette, IN. p. 1–3.
- Martineau, R. 2003. Dinoprost versus cloprostenol : does route of injection modulate their efficacy in dairy cattle? *Bov. Pract.* 37:10–19.
- Plata, N. I., J. C. Spitzer, C. E. Thompson, D. M. Henricks, M. P. Reid, and T. J. Newby. 1990. Synchronization of estrus after treatment with luprostitol in beef cows and in beef and dairy heifers. *Theriogenology* 33:943–952. doi:10.1016/0093-691X(90)90057-Z
- Powell, J. 2013. Injection site management. In: 2013 Univ. of Arkansas Division of Agriculture Research and Extension Publication. Pub. No. FSA3109. University of Arkansas, Fayetteville, AR. p. 1–4.
- Pratt, J. H. 2004. Injection damage. In: Andrews, A. H., editor. *Bovine medicine: diseases and husbandry of cattle*. Blackwell Publishing, Ames, IA; p. 1078–1080.
- Rowson, L. E., R. Tervit, and A. Brand. 1972. The use of prostaglandins for synchronization of oestrus in cattle. *J. Reprod. Fertil.* 29:145.
- Salverson, R. R., J. M. DeJarnette, C. E. Marshall, and R. A. Wallace. 2002. Synchronization of estrus in virgin beef heifers using melengestrol acetate and pgf_{2α}: an efficacy comparison of cloprostenol and dinoprost tromethamine. *Theriogenology* 57:853–858. doi:10.1016/S0093-691X(01)00692-6
- Schams, D., and H. Karg. 1982. Hormonal responses following treatment with different prostaglandin analogues for estrous cycle regulation in cattle. *Theriogenology* 17:499–513. doi:10.1016/0093-691X(82)90176-5
- Springman, S. A., H. R. Nielson, T. L. Meyer, M. Kirby, J. Teichert, and R. N. Funston. 2017. Effect of heifer development system on reproduction and subsequent gain as a pregnant heifer. In: 2017 Nebraska Beef Cattle Report. Pub. No. MP104. Univ. of Nebraska–Lincoln. p. 5–7.
- Stevenson, J. S., and A. P. Phatak. 2010. Rates of luteolysis and pregnancy in dairy cows after treatment with cloprostenol or dinoprost. *Theriogenology* 73:1127–1138. doi:10.1016/j.theriogenology.2010.01.014.
- Tervit, H. R., L. E. Rowson, and A. Brand. 1973. Synchronization of oestrus in cattle using a prostaglandin f_{2α} analogue (ici 79939). *J. Reprod. Fertil.* 34:179–181. doi:10.1530/jrf.0.0340179
- Tibbitts, B. T., T. L. Kelly, D. J. Meyer, and R. N. Funston. 2017. Comparison of timed insemination vs. modified estrus detection protocol in beef heifers. *Prof. Anim. Sci.* 33:97–100. doi:10.15232/pas.2016-01535