Use and Reuse of CIDRs to Synchronize Estrus

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EAZI-BREED™ CIDR® Cattle Inserts (pronounced "SEE-der") have been available in Canada for several years, but were approved for use in the United States in June of 2002. CIDRs sold in Canada contain 1.90 grams of progesterone in elastic rubber molded over a nylon spine (Figure 1). The CIDRs sold in the U.S. have been reengineered to contain only 1.38 grams of progesterone in elastic rubber molded over the nylon spine. Reengineering was done to reduce the initial progesterone load (1.9 to 1.38 g) and to reduce the residual progesterone remaining in the insert after use, while at the same time maintaining biological performance (Rathbone et al., 2002).

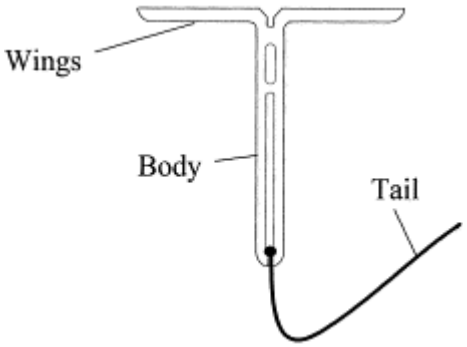

Figure 1. EAZI-BREED™ CIDR® containing progesterone in elastic rubber molded over a nylon spine

In vivo studies indicated that the surface area of a CIDR affected plasma progesterone levels of the treated animal more than the concentration of progesterone "loaded" into the CIDR. Furthermore, slicing of CIDRs that had been used for 7 d revealed that progesterone was only released from the outermost 1 mm of silicone elastomer. Characterization of the insert sold in Canada showed that the skin thickness varied from 1 to 5 mm. Consequently, it was determined that a reengineered insert could be designed with an even 1-mm-thick skin over its entire surface (except for the wing tips for animal comfort and safety reasons), thereby reducing the amount of progesterone loaded in the insert, without reducing the release rate of progesterone. The reengineered CIDR has the same surface area and is coated with the same elastic coating containing 10% w/w of progesterone as the original model. Hence, it is not surprising that the release rates of progesterone from the CIDRs containing 1.9 or 1.38 g of progesterone are similar.

Statistical analysis of the progesterone profiles of cows receiving an insert containing 1.9 or 1.38 g of progesterone were bioequivalent over an insertion period of 7 d. Data presented in Figure 2A and 2B depict the plasma concentrations of progesterone following insertion of a CIDR containing 1.9 or 1.38 g of progesterone in non-lactating, bilaterally ovariectomized Holstein–Friesian cows weighing between 500 and 600 kg. Ovariectomy was performed to remove the

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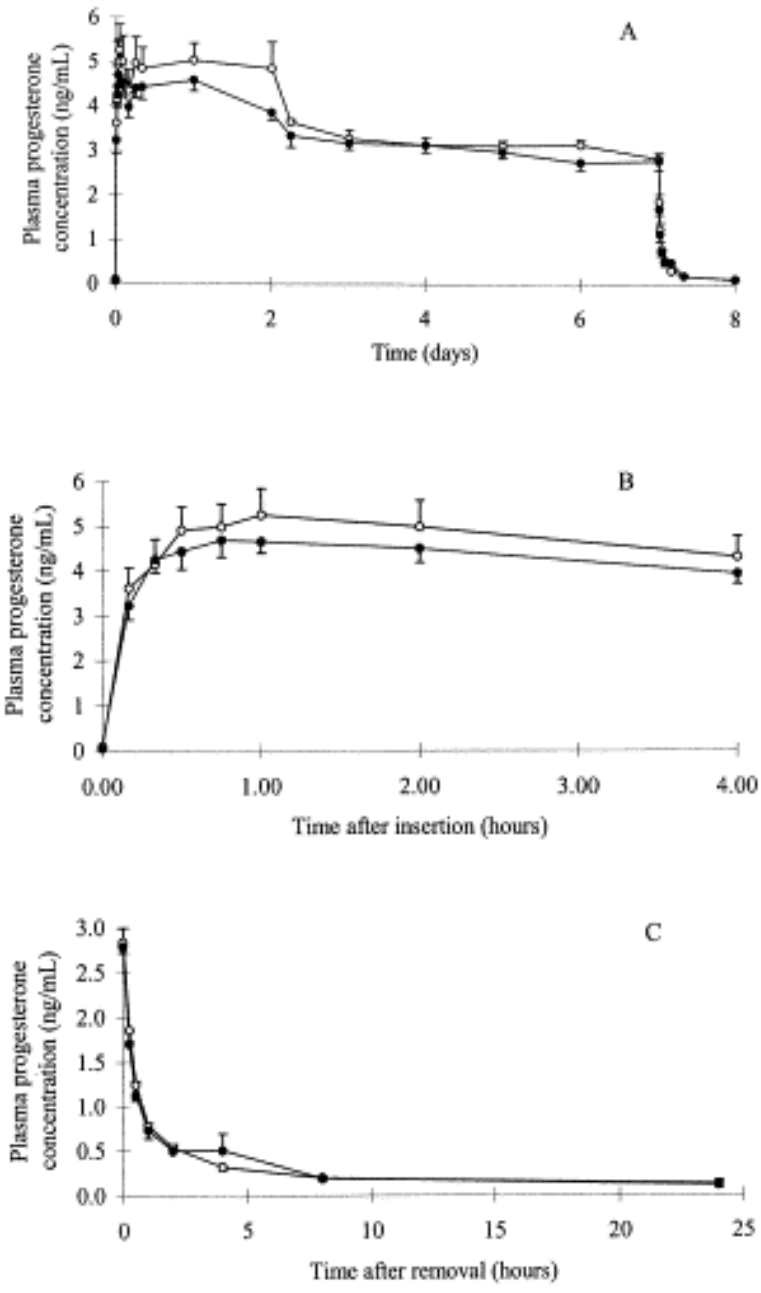

Figure 2. Plasma progesterone concentrations in ovariectomized cows following insertion (A and B) or removal (C) of a CIDR containing 1.9 (o) or 1.38 g (•) of progesterone (from Rathbone et al., 2002)

endogenous source of progesterone so that any plasma progesterone measured could only have come from the CIDR insert. Note the rapid increase in mean progesterone concentrations following CIDR insertion depicted in Figure 2B. Mean plasma progesterone concentrations increased from less than 0.1 ng/ml to greater than 3 ng/ml within 12 minutes after insertion of either a 1.9- or 1.38-g CIDR. Plasma concentrations of progesterone decreased slowly during the 7-d insertion period (Figure 2A), but remained greater than 2.5 ng/ml just prior to insert removal. Upon removal of the CIDRs (Figure 2C) the mean plasma progesterone concentrations decreased from less than 3 ng/ml to less than 0.5 ng/ml within 1 h. Progesterone reached pre-insertion levels by 8 h after CIDR removal.

Estrus synchronization programs using the CIDR insert have varied. The approved and manufacturer-recommended protocol indicates that the CIDR should be administered intravaginally, one per animal, in cows or heifers and left in place for 7 d (Figure 3). Prostaglandin $F_2\alpha$ ($PGF_2\alpha$) is administered 1 d before insert removal to synchronize estrus in more cattle. Breeding is recommended to occur after estrus detection.

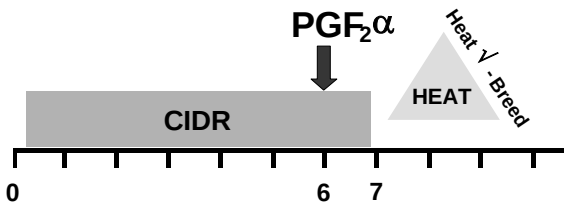

Figure 3. Manufacturer's recommendation for use of EAZI-BREED™ CIDR®

The timing of estrus following recommended administration of the CIDR and $PGF_2\alpha$ has been very synchronous (Figure 4). More than 60% of the animals consistently exhibit estrus within a 24-h period. Pregnancy rates of cattle bred 12 h after estrus detection have been satisfactory.

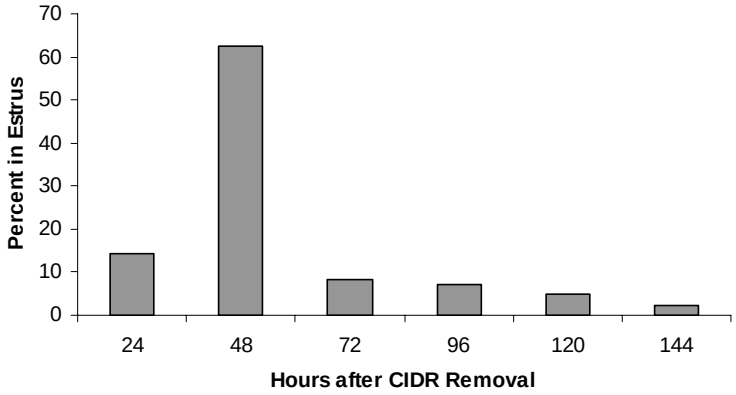

Figure 4. Distribution of estrus following use of EAZI-BREED™ CIDR® and $PGF_2\alpha$ treatment (from Lucy et al., 2001)

Other researchers have attempted to combine the use of a CIDR with estradiol or gonadotropin-releasing hormone (GnRH) administration at the time of insertion to more effectively control follicular growth during CIDR insertion and to administer either GnRH or estradiol to induce a timed ovulation following CIDR removal (Martinez et al., 2002a, 2002b; Stevenson et al., 2003b). In many cases single, timed AI following these ovulation control programs has resulted in pregnancy rates equal to those of synchronized animals bred after estrus detection. The timed ovulation programs may also be useful to eliminate heat detection of embryo transfer recipients. Transfer of embryos to cows with a palpable corpus luteum (CL) 7 days after administration of GnRH or 8 days after administration after estradiol to induce estrus has been successful.

REUSE OF CIDRs CONTAINING 1.9 or 1.38 g PROGESTERONE

After insertion for 7 d, a CIDR containing either 1.9 or 1.38 g of progesterone will contain residual progesterone (Table 1). The residual progesterone is available if the CIDR is cleaned and reinserted into the vagina of another cow. Hence, the reutilization of CIDRs has been reported in the scientific literature (Rhodes et al., 2002; Stevenson et al., 2003a) and is a practice that is becoming common in the field.

Table 1. Mean (± S.E.M.) progesterone (P_4) load in 1.9-g and 1.38-g CIDR insert before and after insertion of the insert for 7-d period

Type of CIDR	Intial P_4 load (g)	Residual P_4 load (g)	Estimated P_4 released (g)
Conventional	1.92 ± .04	1.31 ± .01	.61 ± .01
Reengineered	1.34 ± .06	.72 ± .02	.62 ± .02

(adapted from Rathbone et al., 2002)

The manufacturer recommends **NOT** to reuse a CIDR device. Information available on the package and on the manufacturers website (http://www.cidr.com/) clearly advises against reuse with the following warning:

> *"EAZI-BREED™ CIDR® Cattle Insert is designed for one-time use. Used inserts may contain bacteria that cannot be removed. Potency and sterility cannot be assured with multiple use. After removing each EAZI-BREED CIDR Insert, dispose of it immediately in a sealed, plastic container in accordance with applicable local, state and federal regulations."*

Because reuse of CIDRs has become a common practice and because producers constantly inquire about the efficacy of reusing CIDRs, we have conducted two studies to investigate the reuse of CIDRs. The first study was designed to characterize the ability of new and used CIDRs, originally containing 1.9 g of progesterone, to inhibit estrus when inserted into nonlactating, cycling beef cows whose CLs were regressed.

Study #1 Seventeen cows with a CL (>13 mm diameter) detected by ultrasonography were administered $PGF_2\alpha$ (25 mg and 12.5 mg at 12-h interval, im) and assigned to one of five treatments (Figure 5). Cows received either a new, 1.9-g CIDR (n=5) or a CIDR that had been placed intravaginally for 7 d on one (2^{nd} use; n=4), two (3^{rd} use; n=4) or three (4^{th} use; n=4) previous occasions. Estrus was detected twice daily via visual observation and ovulation was confirmed 7 d after detection of estrus by ultrasonography.

Blood samples were collected on a daily (Day 1-7; 28-33) or alternate-day schedule (Day 8-28). Samples were allowed to clot for 2 h and serum was collected, frozen and assayed to determine progesterone concentrations. CIDRs were removed on Day 28 of the experiment or at the time an animal was detected in estrus.

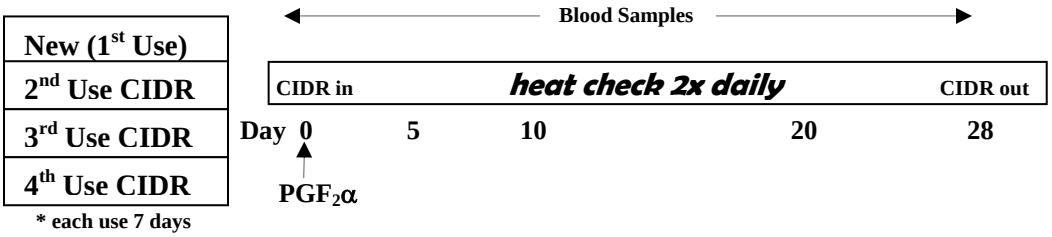

Figure 5. Design of experiment to compare ability of new or reused CIDRs (1.9 g P_4) to suppress estrus for 28 days (Study #1)

Cows receiving a new, 2nd-use or 3rd-use CIDR did not exhibit estrus during the 28 d in which a CIDR was in place. However, each of these cows exhibited estrus within 0.5 to 3 d after removal of the CIDRs on Day 28 of the experiment. The 4th –use CIDRs failed to inhibit estrus and ovulation for 28 d in three of four cows. Estrus was detected after 9.5, 28 and 28 d, respectively, in three animals that received a CIDR used for the 4th time.

Mean progesterone concentrations from Day 1 (24 h after CIDR insertion) through Day 33 of the experiment for cows that received a new, 2nd-use, 3rd-use or 4th-use CIDR were 1.96, 1.38, 1.05 and .72 ng/ml, respectively. Progesterone profiles are depicted in Figure 6.

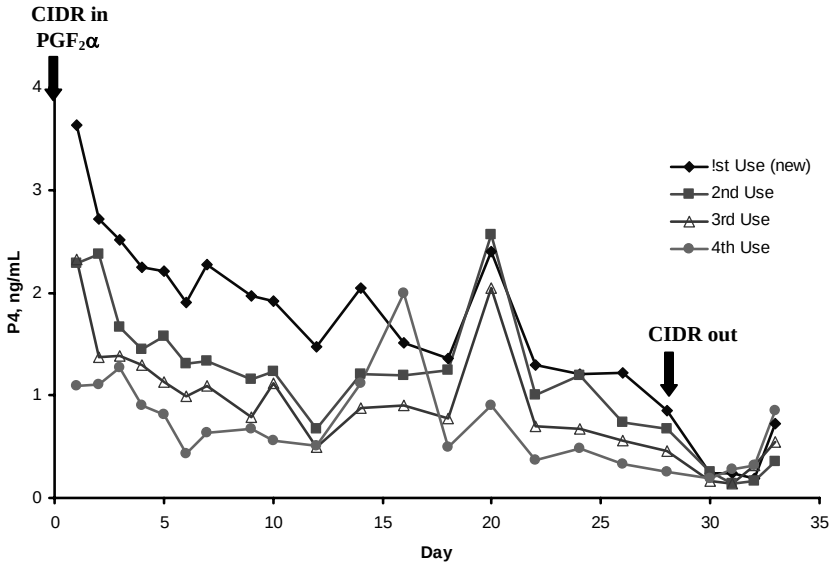

Figure 6. Serum progesterone concentrations in cows fitted with a new or reused CIDR (1.9 g P4) for 28 d following injection of $PGF_2\alpha$ to regress the CL.

These data indicate that a new CIDR containing 1.9 g of progesterone is effective in suppressing estrus for 28 d when placed intravaginally. Furthermore, 1.9-g CIDRs used for the 2nd or 3rd time (7-d uses previously) were also able to suppress estrus and block ovulation for 4 weeks.

However, the progesterone released from a CIDR used for the 4th time was unable to suppress estrus for 28 consecutive days. This information made it clear that the CIDRs could be reused as an estrus synchronization tool, but that with each use the initial spike and sustained release of progesterone was lower. This data was limited to the use of a CIDR with an initial loading of 1.9 g of progesterone. Hence, a second study was performed to compare performance of new and reused CIDRs containing 1.9 or 1.38 g of progesterone.

Study #2 The purpose of this experiment was to determine if new or reused CIDR inserts containing 1.9 or 1.38 g of progesterone could effectively inhibit estrus and ovulation when administered to cows following a luteolytic dose of prostaglandin $F_2\alpha$ (Figure 7). Sixty eight cows on Day 11 of the estrous cycle with a corpus luteum (>13 mm diameter) detected by transrectal ultrasonography were administered $PGF_2\alpha$ (25 mg and 12.5 mg at 12-h interval, im) and assigned the following day to one of 12 treatment groups. Thirty-three cows received a new CIDR containing 1.38 g of progesterone (n=5) or a 1.38-g CIDR that had been placed intravaginally for 7 d on one (2nd use; n=6), two (3rd use; n=6), three (4th use; n=5), four (5th use; n=6) or five (6th use; n=5) previous occasions. In addition, 35 cows (5 or 6 per group) were fitted with a new CIDR containing 1.9 g of progesterone or a 1.9 g-CIDR that had been used for 7 d from one to five times previously. CIDRs remained in place for 7 d. Cows were fitted with an electronic estrus detection monitor (HeatWatch®) at the time of CIDR insertion. Estrus was detected continuously from the time the CIDR was inserted until each animal exhibited estrus following CIDR removal. If estrus was detected while the new or reused CIDR was in place, ovulation was confirmed by examining the ovaries of each cow 7 d after detection of estrus to confirm the presence of a CL.

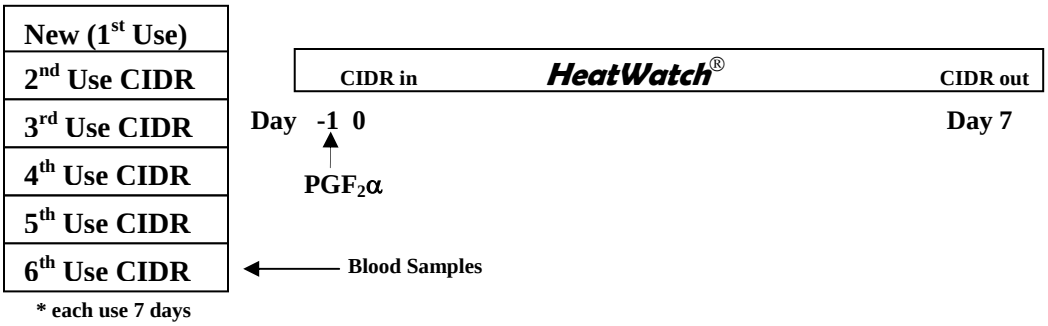

Figure 7. Design of experiment to compare ability of new or reused CIDRs (1.9 g or 1.38 g P_4) to suppress estrus for 7 days (Study #2)

Blood samples were collected frequently from cows receiving a 6th-use CIDR for 48 h after CIDR insertion and then daily until the cows exhibited estrus or the CIDR was removed. Samples were allowed to clot for 2 h and serum was collected, frozen and assayed to determine progesterone concentrations.

Estrus was suppressed during the 7-d insertion period in all cows receiving a new, 2nd use, 3rd use and 4th use CIDR, regardless of whether the CIDR originally contained 1.9 or 1.38 g of progesterone. During the 7-d insertion period of cows receiving a 5th-use CIDR 50% (3/6) of the cows fitted with 1.38 g CIDR exhibited estrus, but none of the six cows receiving a 1.9-g CIDR used for the 5th time exhibited estrus. Among cows receiving a 6th-use CIDR, all of the cows fitted with a 1.38-g CIDR exhibited estrus during the 7-d insertion period and 20% (1/5) of the cows fitted with a 1.9-g CIDR were detected in estrus before the CIDR was removed.

Mean serum progesterone concentration during the 7-d period when the 6th-use CIDR was in place was greater in cows that received the 1.9-g CIDR (1.1 ng/ml) than in cows that received a 1.38-g CIDR (0.8 ng/ml). The progesterone profiles are depicted in Figure 8.

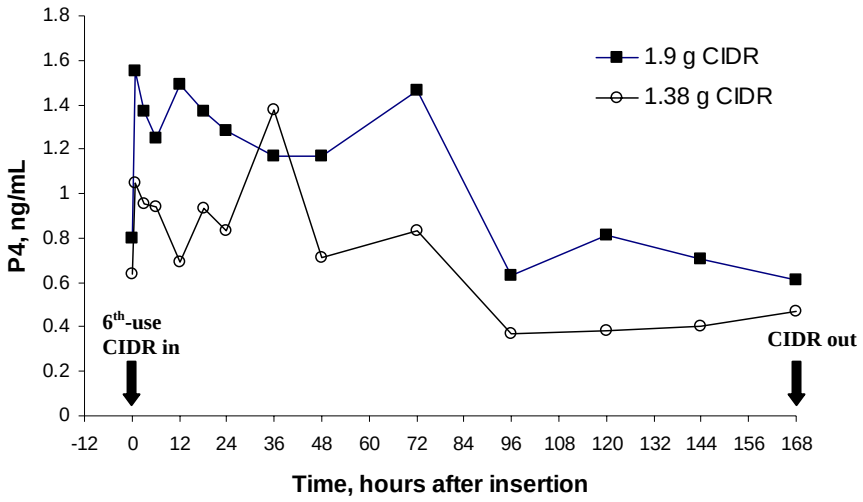

Figure 8. Serum progesterone concentrations in cows fitted with a 6th use CIDR (1.9 or 1.38 g P_4) for 7 d following injection of $PGF_2\alpha$ to regress the CL.

These data indicate that regardless of initial loading of progesterone (1.9 or 1.38 g), new CIDRs and CIDRs reused for up to and including the 4th use were able to suppress estrus during the 7-d insertion period. CIDRs containing 1.38 g of progesterone failed to suppress estrus after fewer uses (5th use) than CIDRs that originally contained 1.9 g of progesterone (6th use). Furthermore, the average serum progesterone concentrations in cows receiving a 6th-use CIDR were lower in cows receiving the 1.38-g CIDR than in cows receiving the 1.9-g CIDR.

The data in the studies reported above support the concept that CIDRs can be used up to four times to suppress estrus during a 7-d insertion period. Conversely, it is apparent from the progesterone profiles of cows receiving new and reused CIDRs that the progesterone released from the CIDR diminishes with each reuse. While the progesterone released from a reused CIDR may be adequate to suppress estrus, there has been no research to evaluate the other

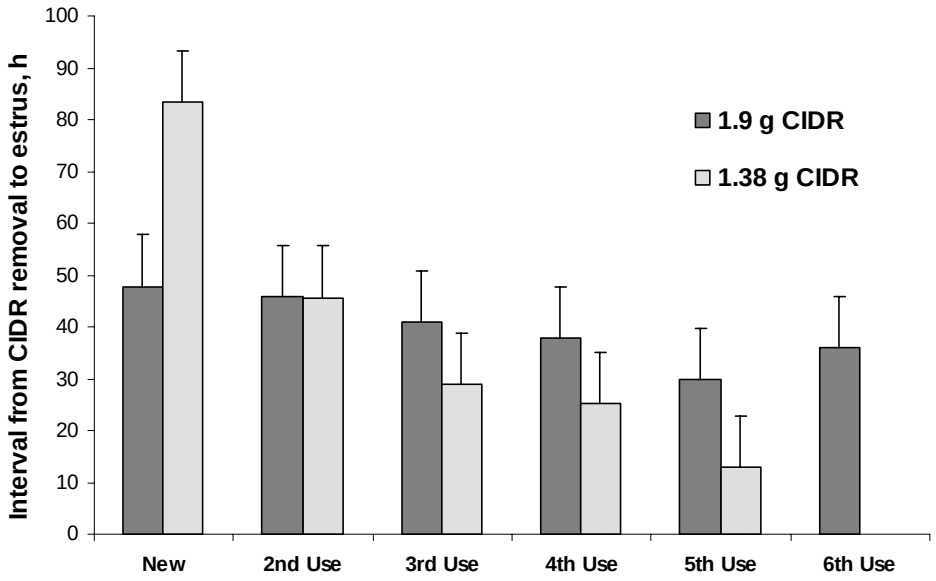

Figure 9. Interval from CIDR removal to estrus in cows fitted with a new or reused CIDR (1.9 or 1.38 g P_4) for 7 d following injection of $PGF_2\alpha$ to regress the CL.

possible effects of lower levels of progesterone released from reused CIDRs (e.g., effects on gonadotropin secretion, follicular turnover, uterine proliferation, etc). The fact that CIDRs releasing different levels of progesterone may evoke different biological responses is illustrated by the timing of estrus following removal of new and reused CIDRs from cows in Study #2 (Figure 9). Although the numbers of animals in that study were small, the timing of the onset of estrus appeared to occur earlier following removal of a 3^{rd} , 4^{th} or 5^{th}-use CIDR than following use of a new CIDR. This may indicate that when reused CIDRs are employed, the expected timing of estrus and ovulation or the prescribed timing for injection of estradiol or GnRH to induce estrus may need to be altered.

CONCLUDING STATEMENT

The use of CIDRs in estrus synchronization and ovulation control programs is increasing. With the expected approval for use in lactating dairy cattle in the U.S., popularity of the CIDR will increase further. Reuse of CIDRs by producers is inevitable. The manufacturer's warnings about contamination and potential disease transmission that may accompany reuse are justifiable, as are concerns regarding differences in the effects of lower levels of progesterone released from reused CIDRs. Producers who reuse CIDRs should be made aware of the potential dangers and further effort should be made to characterize differences in the response to new and reused CIDR inserts.

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