Comparison of two intravaginal progesterone releasing devices in lactating dairy cows: blood progesterone profile and field fertility.
This report is summarising the results of two trials done to compare two intravaginal progesterone devices (PRID DELTA vs T-shape device 1.38g). In the first trial, circulating progesterone profiles were compared in cows treated with PRID DELTA or T-shape device (Experiment 1). In the second trial, done by Utrecht University, a large field fertility study carried out using lactating cows also compared PRID DELTA vs T-shape device. Main results of the two trials are following.

Key messages

- **PRID DELTA** significantly increased circulating progesterone in blood during progesterone device implant period, and the area under the curve of progesterone release was higher compared to T-shape device (653 vs 583 ng/mL*time, P<0.01).

- **PRID DELTA** increased the proportion of cows showing signs of natural oestrous activity in the following breeding cycle nearly 21d after 1st AI (Artificial Insemination) compared to T-shape device (28.3% vs 16%, P<0.01).

- **PRID DELTA** significantly increased the final percentage of cows that became pregnant within 21 days after initiation of AI compared to T-shape device (45.9% vs 37%, P=0.02).
Systematic reproductive protocols using exogenous compounds such as steroids and gonadotrophins to mimic physiological levels of naturally occurring hormones are routinely used in dairy herds world-wide to improve fertility and to decrease percentage of animals culled at the end of lactation due to reproductive failure.

Intravaginal progesterone (P4) devices are commonly used during these reproductive routines due to its efficacy to treat non-cycling cows. For instance, many research groups reported that lactating cows need to be exposed to P4 after calving in order to start having normal reproductive cycles. Interestingly, the physiological mechanism blocking anovular cows from having normal reproductive cycles is likely related to lower expression of estrogen receptors in the hypothalamus, and apparently P4 can successfully resolve this problem in cattle.

Progesterone may also have an important role at oocyte level to improve fertility of lactating cows. For instance, recent findings are describing positive relationship between greater circulating levels of P4 during synchronisation protocol and embryo quality. The exact mechanism by which P4 seem to improve embryo quality is not completely known but it may be related to lessen exposure of the developing oocyte to LH, avoiding its premature maturation. Therefore, intravaginal devices containing P4 and other combinations of hormones should be strategically used to target greater levels of P4 during synchronisation routines, particularly in high producing dairy cows that seem to present elevated rates of steroid hormone metabolism in liver.

Therefore, the objectives of this study were to compare circulating P4 levels after treating cows with two commercially available intravaginal devices T-shape device 1.38g or PRID DELTA 1.55g (Experiment 1), and also to assess possible differences in terms of terms of field fertility in lactating in lactating dairy cows (Experiment 2).
Experimental designs

**Experiment 1** Progesterone profile

Ovariectomised Holstein cows were used in a cross-over design (PRID DELTA, n=6 vs T-shape device, n=6). Multiple blood samples (around 10 mL) were collected into heparinized tubes throughout 7 days to measure circulating P4 according to the following schedule:

- At D0: Before treatment then T+1h, T+3h, T+6h and T+9h after treatment administration.
- D1 to D6: Twice a day at the same time of the day.
- At D7: Just before withdrawal and at 1h and 2h after withdrawal.

**Experiment 2** Field fertility comparison

Lactating dairy cows (n=774) housed in multiple herds and not detected in heat from 50 to 165 DIM were used in this trial. Cows were randomised based on ear tag numbers to receive for 7 days PRID DELTA or T-shape device, as follows:

![Figure 1. Experimental design – field fertility study (PRID DELTA vs T-shape device).](image-url)
Main results & discussion

Circulating progesterone profile

The final circulating progesterone profile comparison between PRID DELTA and T-shape device is shown in Figure 2. In both treatments blood P4 seem to increase very rapidly to nearly 4 to 5 ng/mL. Then, progesterone decreases in a fairly steady pattern until device removal 7 days later. Interestingly, PRID DELTA produced significantly greater circulating P4 levels starting on day one to the end of day 4 after device insert. In addition, area under the curve of progesterone release was also greater for PRID DELTA compared to T-shape device, respectively (653 vs 583 ng/mL*time, P<0.01).

Field fertility study

The effect of type of intravaginal P4 device on pregnancies per AI (P/AI) following 1st postpartum AI is shown in Figure 3. Overall, PRID DELTA tended (P=0.10) to produce greater P/AI at 1st AI when compared to T-shape device (Figure 3).
After 1st AI, cows were visually monitored for oestrous activity during the expected returning cycle around 21d later. An ultrasound examination was also performed in all cows detected in heat to confirm the absence of an active CL. Thus, out of cows not conceiving after 1st synchronized AI, more cows were detected in returning oestrous when previously treated with PRID DELTA compared to cows receiving T-shape device (PRID DELTA= 28.3% vs T-shape device= 16.0%, P<0.01 – Figure 4, below). Perhaps because PRID DELTA induced more cows to start cycling normally after 1st AI. This could be the case particularly in anovular cows before 1st AI, but this observation needs to be confirmed with further studies.

In addition, out those cows detected in heat around 21d previous AI, there was no effect of type of P4 device used in the previous AI on P/Al in returning breedings (PRID-DELTA = 55.9% vs. T-shape device = 54.7%; P = 0.91). It is though remarkable that conception results were very high for this 2nd AI ~21 days following synchronisation.

Interestingly, because more cows that received PRID DELTA were detected in heat 21d after 1st synchronised breeding, as a result PRID DELTA significantly (P=0.02) produced more pregnant cows within 21 days, as shown in Figure 5.

Figure 4. Percentage of cows detected in oestrous in the following cycle for cows treated with PRID DELTA (orange bar) and T-shape device (grey bar).

Figure 5. Final percentage of pregnant cows after 1st AI (treated with PRID DELTA or T-shape device) and 2nd AI (bred after natural oestrous ~21d after 1st AI) in lactating Holstein cows.
Conclusions

PRID DELTA significantly increased circulating progesterone in blood during progesterone device implant period, and tended to increase fertility results in the first postpartum AI when compared to cows treated with T-shape device. In addition, PRID DELTA also increased the proportion of cows showing signs of natural oestrous activity in the following breeding cycle nearly 21d after 1st AI compared to T-shape device. Most importantly, PRID DELTA significantly increased the final percentage of cows that became pregnant after two breeding cycles.

References


PRID®DELTA 1.55g. Vaginal delivery system for cattle

**COMPOSITION:** progesterone 1.55 g per device.

**INDICATIONS:** For the control of the oestrus cycle in cows and heifers including: Synchronisation of oestrus in cycling cattle. To be used in combination with a prostaglandin (pGF2). Induction and synchronisation of oestrus in non-cycling cattle. To be used in combination with a prostaglandin and equine Chorionic Gonadotropin (eCG, in the past called pMSG).

**CONTRA-INDICATIONS:** Do not use in sexually immature heifers. Do not use before 35 days have passed since previous calving. Do not use in animals suffering from infectious or non-infectious disease of the genital tract. Do not use in pregnant animals. See section Use during pregnancy and lactation.

**ADVERSE REACTIONS:** During the course of the seven day treatment, the device may induce a mild local reaction (i.e. inflammation of the vaginal wall). A clinical study carried out with 319 cows and heifers has demonstrated that 25% of animals presentedropy or cloudy vulvar secretions at the device removal. This local reaction disappears rapidly without any treatment between removal and insemination and does not affect fertility at inseminations nor pregnancy rates. If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary.

**DOSAGE, ROUTE AND METHOD OF ADMINISTRATION:** Vaginal use. 1.55 g of progesterone / animal for 7 days. Using an applicator, insert one device into the vagina of the animal. The intravaginal device should stay in place for 7 days. In cycling cattle, the device has to be used in combination with a prostaglandin, injected 24 hours prior to removal of the device. In non-cycling cattle, an injection of a prostaglandin must be done 24 hours prior to removal of the device and an injection of eCG at the time of removal. The device is intended for single use only.

**WITHDRAWAL PERIOD:** Meat and offal: zero days. Milk zero days. During the treatment meat, offal and milk can be delivered for human consumption CATEGORY: List II. pOMV.

**PRESENTATIONS:** cardboard box containing 10 sachets of 1 device. polyethylene box containing 50 sachets of 1 device. Sachet containing 10 devices.

**NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER:** CEVA SANTE ANIMALE - 10 av. de la Ballastière - 33500 LIBOURNE.

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