DIB-Synch Plus

Advanced Non-Cycling Program

AgriHealth
Why Treat Non-Cycling Cows?

Treating cows that have not been detected in oestrus (“non-cycling”) prior to the planned start of mating with DIB-Synch provides a return on investment of around 3 times.

- Cows get in calf earlier
- Treated cows have more days in milk the following season
- Leads to a tighter calving spread
- More AB heifer calves

Early treatment of non-cyclers provides the best return on investment. These cows will typically receive their first insemination the first day of the AI period. Furthermore, if not pregnant to this insemination, their return (second) heat in the 4th week of mating will be more fertile. This leads to significantly more days in milk during the subsequent season.

The economic return for treating non-cycling cows diminishes later in the mating period.

Relative return on Investment for different non-cycling cow treatment times

Break Even Point

- Early treatment (10 days prior to PSM)
- Treatment 10 days after PSM
- Treatment 21 days after PSM
- Treatment 42 days after PSM

*Refer to partial budget on opposite page
What is the payback for treating early?

The following partial budget summarises the return on investment from treating non-cycling cows prior to the start of mating:

<table>
<thead>
<tr>
<th>Additional Income from DIB-Synch</th>
<th>Costs for DIB-Synch</th>
<th>Return on Investment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional days in milk 16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>kg MS / day 1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$ / kg MS $6.50</td>
<td></td>
<td></td>
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<tr>
<td>Additional Income $156.00</td>
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<td></td>
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<tr>
<td>Treatment &amp; vet cost $40.00</td>
<td></td>
<td></td>
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<tr>
<td>Costs $40.00</td>
<td></td>
<td></td>
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<tr>
<td>PROFIT $116.00</td>
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</tr>
</tbody>
</table>

This partial budget analysis excludes:

1. Additional income from extra AB calves
2. Feed required for the extra milksolids produced
3. Value of the reduced number of non-cycling cows the following season
The Proven Program

Results from a large New Zealand Study showed that under commercial farming condition the DIB-Synch program improves pregnancy outcomes.

Over 2,000 non-cycling cows from 15 commercial dairy herds from the Waikato, Central Plateau, Manawatu, Canterbury and Otago were enrolled in the Study. The Study was conducted in Spring 2010 and overseen by Veterinarians from seven New Zealand rural practices.

Study Outline:

<table>
<thead>
<tr>
<th>35 days prior</th>
<th>10 days prior</th>
<th>PSM</th>
<th>Day 35 - 90 after</th>
<th>End of mating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tail paint</td>
<td>non-cycling cows enrolled</td>
<td>PSM</td>
<td>Set time AI</td>
<td>Pregnancy test</td>
</tr>
<tr>
<td></td>
<td>Group 1 DIB-Synch</td>
<td></td>
<td></td>
<td>Pregnancy test</td>
</tr>
<tr>
<td></td>
<td>Group 2 CIDR-Synch</td>
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<tr>
<td></td>
<td>Group 3 GPG (ovsynch)</td>
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<tr>
<td></td>
<td>Group 4 DIB-Synch Plus</td>
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</tr>
</tbody>
</table>

(refer table on back cover for program details)

Results:

Cows in groups 1 and 2 had equivalent pregnancy rates, demonstrating the DIB-V progesterone insert is equally efficacious in treating non-cycling cows under New Zealand field conditions.

Cows in group 3 tended to have lower pregnancy rates to set time AI.

Key
PSM - planned start of mating
GPG - GnRH - PG - GnRH
GnRH - Gonadotropin Releasing Hormone (e.g. gonadorelin)
PG - Prostaglandin (e.g. cloprostenol)
eCG - equine Chorionic Gonadotrophin
DIB-V - Intravaginal 1 g progesterone insert
CIDR - Intravaginal 1.38 g progesterone insert
Gonasyn - gonadorelin injection
Cyclase - cloprostenol injection
Novormon eCG - eCG injection
How does the DIB-Synch ‘Plus’ program work?

Equine chorionic gonadotropin (eCG) is produced by pregnant mares from day 40 to 130 of pregnancy. The half-life of eCG is longer than other gonadotropins, and eCG possesses dual action on follicle stimulating hormone (FSH) and luteinising hormone (LH). These qualities allow a single administration of eCG to provide persistent follicle and/or luteal growth, and functional stimulation of the corpus luteum.

Administering Novormon eCG to anoestrus cows has been shown to increase follicular development, resulting in more viable follicles and culminating in ovulation of a slightly larger follicle. This occurs via the effect of eCG on the LH and FSH receptors of the forming follicle.

In addition, eCG tends to cause an increase in luteal volume and function which results in improved production of progesterone. The progesterone produced by the corpus luteum after ovulation is responsible for maintaining the pregnancy.

Finally, a more effective endocrine feedback mechanism is understood to be partially responsible for the significant lift in 28 day pregnancy rates. It is believed the stronger luteal function produced by the eCG effect results in fewer ‘phantom’ pregnancies. This is because cows are more likely to ‘return’ and ovulate at 18 - 24 days for those cow where conception does not occur at the initial ovulation.
DIB-V Progesterone Insert

DIB-V is a 1 gram progesterone intravaginal insert, registered for controlled breeding in cows and heifers.

Indications
- treatment of post-partum anoestrus (non-cycling cows)
- synchronisation and control of the oestrus cycle

The advantages of DIB-V
- Proven - under New Zealand commercial farming conditions²
- Provides optimised dose of progesterone for modern seven day breeding programs
- Superior V-shape design with more pliable silicon elastomer form
- Significantly less pus at removal³
- Excellent retention rates⁴
- Improved cow comfort reported by New Zealand dairy farmers⁵

Progesterone Dose
- The amount of progesterone in intravaginal inserts varies and has decreased over time (range 1.9g to 1g)
- Over this period most progesterone based programs have reduced the length of time the device is inserted, from 14 to 7 days
- The progesterone is not fully absorbed following standard use, leaving significant levels of progesterone in used inserts

Many studies have demonstrated bioequivalence of the various inserts
- no difference between treatments in peak plasma progesterone levels
- no difference in total progesterone concentration over the seven day treatment period between 1.38g and 1g inserts
- no clinical difference in pregnancy rates between inserts in large scale commercial trials

DIB-V provides sufficient progesterone for modern seven day programs
- why give more hormone than is needed?
Injectable solution containing gonadorelin acetate (50 µg/mL)

Gonadorelin is a synthetic analogue of GnRH (gonadorelin releasing hormone).

GnRH stimulates the release of FSH (follicle stimulating hormone) and LH (luteinising hormone) from the pituitary gland

**Indications**

- Oestrus synchronisation in anoestrous cows
- Ovulation synchronisation
- Fertility improvement
- Treatment of ovarian follicular cysts

Gonasyn complements use of the DIB-V progesterone insert and Cyclase in DIB-Synch oestrus synchrony programs, and also Novormon eCG in DIB-Synch Plus programs

Gonasyn has been proven in the DIB-Synch and DIB-Synch Plus programs under New Zealand commercial farming conditions

DIB-Synch and DIB-Synch Plus programs are designed for simplicity - all injections are a 2mL dose, including Gonasyn

**TIP: Dose Surety**

It is important to deliver the correct dose of GnRH.

Insufficient GnRH runs the risk of the follicle failing to mature and ovulate. Conversely, higher than optimal levels of GnRH results in overstimulation of the pituitary and subsequent release of stores of FSH and LH. This is why certain GnRH analogues were developed as sterility treatments for cattle. If no reserve of LH, the end result can be suppression of LH secretion for an extended period of time. However, pulsatile release of LH is required for follicular growth and development so too much GnRH can be counterproductive.
Novormon eCG is equine Chorionic Gonadotrophin (eCG, PMSG); freeze dried with diluent for reconstitution. Reconstituted solution contains 200 IU/mL eCG.

Novormon eCG is highly purified and has an optimal FSH / LH ratio. Dual action on FSH and LH stimulates follicular growth and ovulation.

Novormon eCG increases ovulation rates and stimulates oestrus in anoestrus animals. Ovulation rates increase with increasing dose levels. In fact it causes superovulation at higher doses.

The administration of Novormon eCG together with removal of the progesterone insert optimises the fertility of the subsequent ovulation².

Indications

- Induction of ovulation and superovulation
- As a complement to anoestrus treatments

The dose of Novormon eCG for oestrous synchronisation in cattle is 2mL (400 IU eCG)

Novormon eCG complements use of the DIB-V progesterone insert, Gonasyn and Cyclose in DIB-Synch Plus oestrus synchrony programs

Novormon eCG has been proven in the DIB-Synch Plus program under New Zealand commercial farming conditions²

DIB-Synch and DIB-Synch Plus programs are designed for simplicity - all injections are a 2mL dose
Advanced treatment for non-cyclers

Large scale NZ dairy cow trialwork in Spring 2010 showed adding eCG to the treatment program adds an average 2.8 days in milk, compared with traditional 7 day progesterone based synchrony programs such as DIB-Synch.

Partial Budget - DIB-Synch Plus vs traditional 7 day progesterone programs

<table>
<thead>
<tr>
<th></th>
<th>DIB-Synch Plus</th>
<th>Cost of eCG</th>
<th>Return on Investment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional days in milk</td>
<td>2.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>kg MS / day</td>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$ / kg MS</td>
<td>$6.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional Income</td>
<td>$27.30</td>
<td>$6.50</td>
<td>$20.80</td>
</tr>
<tr>
<td>Costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROFIT</td>
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</tbody>
</table>

Cumulative Pregnancy Rates - eCG effect

Graph 4. Cumulative pregnancy curve - effect of eCG treatment  P<0.05
Injectable solution containing cloprostenol (as sodium) 250 µg/mL
Cyclase is a synthetic analogue of prostaglandin F2a
Cyclase is indicated for the luteolysis of functional corpora lutea in cows, pigs and horses

**Indications**

- Controlled breeding programs
- Treatment of anoestrus
- Improvement of reproductive efficiency
- Oestrus synchronisation and ovulation
- Termination of early pregnancy
- Removal of mummified foetus
- Parturition induction
- Retained foetal membranes and chronic purulent endometritis (pyometra)
- Luteal cysts

The dose of Cyclase in cattle is single or repeat doses of 2mL (500µg cloprostenol)
Cyclase complements use of the DIB-V progesterone insert and Gonasy in DIB-Synch oestrus synchrony programs, and also Novormon eCG in DIB-Synch Plus programs
Cyclase has been proven in the DIB-Synch and DIB-Synch Plus programs under New Zealand commercial farming conditions

The DIB-Synch and DIB-Synch Plus programs are designed for simplicity - all injections are a 2mL dose
Treating heifers

The advantages of synchronising heifers are

- Compact calving, over a short period - consolidated mob simpler to manage
- More days in milk
- More time to begin cycling prior to mating
- Faster genetic gain and additional AB heifer calves

There are two commonly used programs for heifer synchrony.

The DIB-CoSynch program (see outline below) allows the use of set time AI.

**DIB-CoSynch** *(Heifer synchrony)*

<table>
<thead>
<tr>
<th>Day 0 am/pm</th>
<th>Insert DIB-V</th>
<th>Day 7 am/pm</th>
<th>Remove DIB-V</th>
<th>Day 9 pm</th>
<th>Day 10 am</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Insert DIB-V</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inject 2mL Gonazyn</td>
<td></td>
<td>Inject 2mL Cyclase</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Double PG Program involves two injections of PG (with heat detection for four days).

**Double PG Program**

<table>
<thead>
<tr>
<th>Day 0</th>
<th>Day 11</th>
<th>Day 12</th>
<th>Day 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inject 2mL Cyclase</td>
<td>Inject 2mL Cyclase</td>
<td>Inseminate to detected heat</td>
<td>Most heifers will cycle on days 13-14</td>
</tr>
</tbody>
</table>

The corpus luteum is responsive to Cyclase between day 5 and 16 of the oestrus cycle. The first injection brings all heifers into this window at the time of the second injection, 11 days later.

**Planned Start of Mating for Heifers**

It is recommended to begin calving heifers one to two weeks prior to the mixed age cow herd. This gives first calvers additional days between calving and mating. This is important because first calvers take longer than mature cows to recommence cycling following calving.

Key: DIB CoSynch - Program with DIB progesterone insert and timed injections of Gonazyn and Cyclase  
PG - prostaglandin (eg cloprostenol)  
AI - artificial insemination  
AB - artificial breeding
Advanced Non-Cycling Cow Programs

### DIB-Synch

<table>
<thead>
<tr>
<th>Day 0</th>
<th>Day 7</th>
<th>Day 9</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>am/pm</td>
<td>am/pm</td>
<td>pm</td>
<td>am</td>
</tr>
</tbody>
</table>

- **Insert DIB-V**
  - Inject 2mL Gonasy

- **Remove DIB-V**
  - Inject 2mL Cyclase

- **Inseminate to detected heat. N.B. Day 9 Gonasy injection is optional for inseminated cows.**

- **Set time AI 16 - 20 hours after 2nd Gonasy injection**

### DIB-Synch Plus

<table>
<thead>
<tr>
<th>Day 0</th>
<th>Day 7</th>
<th>Day 9</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>am/pm</td>
<td>am/pm</td>
<td>pm</td>
<td>am</td>
</tr>
</tbody>
</table>

- **Insert DIB-V**
  - Inject 2mL Gonasy

- **Remove DIB-V**
  - Inject 2mL Cyclase and 2mL Novormon eCG

- **Inseminate to detected heat. N.B. Day 9 Gonasy injection is optional for inseminated cows.**

- **Set time AI 16 - 20 hours after 2nd Gonasy injection**

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Gonasy (A10642), Cyclase (A10490) and Novormon eCG (A10641) are Restricted Veterinary Medicines, available only under veterinary authorisation. DIB-V (A10319) is a registered Veterinary Medicine. Registered pursuant to the ACVM Act, 1997.

References:
1. The In-Calf Book, Dairy NZ 2007