USING THE EAZI-BREED CIDR-G FOR OUT-OF-SEASON BREEDING IN EWES

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Introduction

Recently, both price and demand for lamb products have risen dramatically. Droughts and floods in major exporting countries and effective promotion of American lamb have changed demand for the home grown product. The regrowth of the industry requires that producers increase their production efficiency with the use of improved technologies so that they are better poised to take advantage of the improved consumer demand for lamb products. Interest in synchronization of estrus (particularly for out-of-season breeding) has increased among sheep producers as prices for off-season lambs have increased. Synchronized breeding leads to synchronized lambing, thus concentrating and reducing the labor requirements at lambing.

Background information. When estrus is synchronized, a similar percentage of ewes conceive and lamb as with natural, random mating. However, lambing occurs in shorter and more concentrated lambing periods. Ewes are bred initially in a short period of about two days, and those that do not conceive to first service remain synchronized and return to estrus within another short interval of about 5 days, an average of 16 to 17 days after the first breeding. Ewes of the same breed-type that were bred in a single day usually lamb in a 7-day period and those bred over a 3-day period lamb during a period of ten days or less. Therefore, knowing the average gestation length (about 146 days in most flocks in this region), the producer using induction and synchronization of estrus can predict the days when most lambs will be born and can schedule lambing to occur when it is most convenient, or target specific markets such as ethnic holidays.

The more uniform lamb crop facilitates both management and marketing of lambs. Marketing costs are reduced because of fewer weight/age groups to market. Lower lamb mortality can be achieved due to greater observation during the first three

days of life when the danger of mortality is highest. In a West Virginia study a decade ago, in which some flocks used progesterone and ram introduction to aid out-of-season breeding, lamb mortality to predators was reduced in the fall-born lambs to half that (3 vs 6%) observed in spring-born lambs in the same and similar flocks. Average income was increased by $4.00 per ewe. Today's lamb prices are over $2.00 per pound, so that figure can be even larger if production costs are managed well.

On Farm Studies That Led To Approval of The CIDR-G As An Aid In Out-Of-Season Breeding

Among hormonal approaches to synchronizing estrus in ewes, intravaginal delivery devices for progestogens are easiest to use and have generated the most interest in recent years. The **controlled internal drug releasing device** (CIDR-G containing 300 mg progesterone) was developed in New Zealand for use during the breeding season with a 12-day treatment. After evaluation of its effectiveness in ewes during the non-breeding season and appropriate safety studies, it was approved by FDA in 2009, for use preceding ram introduction for out-of-season breeding. The efficacy studies were done by West Virginia University in West Virginia, Pennsylvania and Ohio flocks. Release of progesterone from the CIDR declines with time and American ewes are larger than those in New Zealand, so both 12-day and short-term 5-day treatments were evaluated.

Historically, when ewes are induced to ovulate and show estrus during the nonbreeding season, ovulation rates and litter sizes (prolificacy) have been lower than those observed during the breeding season. The hormone equine chorionic gonadotropin (eCG or PMSG), which has follicle stimulating hormone (FSH) activity in ruminants is widely used in other countries, but no eCG preparation is currently approved for use in livestock in the US. The natural hormone FSH is conditionally approved for use in super-ovulation protocols in cattle, thus FSH in combination with progesterone pre-treatment and ram introduction was evaluated for possible use to increase litter size in ewes mated during the non-breeding season.

Experiment 1. **Tests of the CIDR with and without FSH**.

This study was conducted in 1998 with 298 ewes on six farms during anestrus (May to July). The ewes were assigned to one of four groups. One group received progesterone from an intravaginal releasing device for 12 days (P12) alone or with a single injection of FSH (55 mg) on day 11 (P12F). Another group of ewes was assigned to receive the progesterone-containing insert for 5 days with FSH on day 4 (P5F), while the fourth group was exposed to rams only (C). Fertile rams with painted briskets were introduced to ewes at the time of insert removal at a ewe to ram ratio of 15:1.

With either progesterone treatment, 74% of ewes showed estrus during the first 5 days after ram introduction compared to 12% in ewes introduced to rams only (Table1). The mean time from introduction of rams to estrus was 42 hours and did not differ with duration of treatment with progesterone.

The percentages of ewes lambing to the first (42%) and to both first and second service periods (64%) in progesterone-treated ewes were not affected by duration of progesterone treatment. In ewes introduced to rams only, the values were 0 and 41%, respectively (Table 1). Therefore, treatment with progesterone increased the overall proportion of ewes lambing by 23 percentage points. Ewes lambing to the first service period that were treated with progesterone and given an injection of FSH had a larger litter size (0.2 to 0.3 more lambs born per ewe lambing) than ewes exposed to rams only (Table 1). Ewes treated with progesterone lambed earlier and in a more synchronized pattern (Figure 1). The majority (60 to 70%) of progesterone-treated ewes that lambed did so during the first 8 days of the lambing period. There was no lambing between days 9 and 15, but another period of lambing occurred between day 16 to 25. Ewes introduced to rams lambed continuously between days 14 and 29 of the lambing period.

Table 1. Summary of reproductive performance of anestrous ewes in response to ram introduction (C), or ram introduction + 12-d progesterone pre-treatment (P12), 12-d progesterone pre-treatment + FSH (P12F) or 5-d progesterone pre-treatment +FSH (P5F).

Variable \ Treatment	C	P12	P12F	P5F
N	73	73	71	77
Ewes marked by rams,%	12[a]	77	66[b]	79
Ram introduction to raddle markings, h	56[a]	42	40	43
Pregnancy rate[1],%	3[a]	50	44	48
Conception rate[2],%	10[a]	63	61	56
Pregnancy rate[3] 2nd service period:	50	63	60	61
Ovulation rate[4]	-	1.9 ± 0.1	2.2 ± 0.2	2.2 ± 0.2
Percent ewes lambing:				
(a) From 1st service period,%	0[a]	45	38	42
(b) Both service periods, %	41[a]	66	64	63
Lambing rate[5]:, mean ± SE				
(a) Lambing to 1st service period	-	0.74 ± 0.1	.72 ±.1	0.75 ± .1
(b) Both service periods	0.6 ± 0.1[a]	1.0 ± 0.1	1.1 ± 0.1	1.1 ± 0.1
Prolificacy[6], Mean ± SE:				
(a) Lambing to 1st service period	-	1.6 ± 0.1	1.9 ± 0.1	1.8 ±0.1
(b) Lambing to both service periods	1.5 ± 0.1	1.5 ± 0.1	1.6 ± 0.1	1.8 ± 0.1
Ram Introduction to lambing, days	165 ± 2[a]	152 ± 1	153 ± 1	153 ± 1

[a] (progesterone vs control, P < 0.01), [b] (P12F vs P5F, P < .05) values in same row without common superscript differ.

[1] Number of ewes diagnosed pregnant on d 26 - 31 as a percentage of all ewes in a treatment group.

[2] Number of ewes diagnosed pregnant on d 26 - 31 as a percentage of ewes marked by rams.

[3] Number of ewes pregnant on d 46 – 51 expressed as a percentage of ewes not pregnant on d 26 – 31.

[4] Number of CL observed in ewes diagnosed pregnant on d 26-31.

[5] Lambs born per ewe exposed.

[6] Lambs born per ewe lambing.

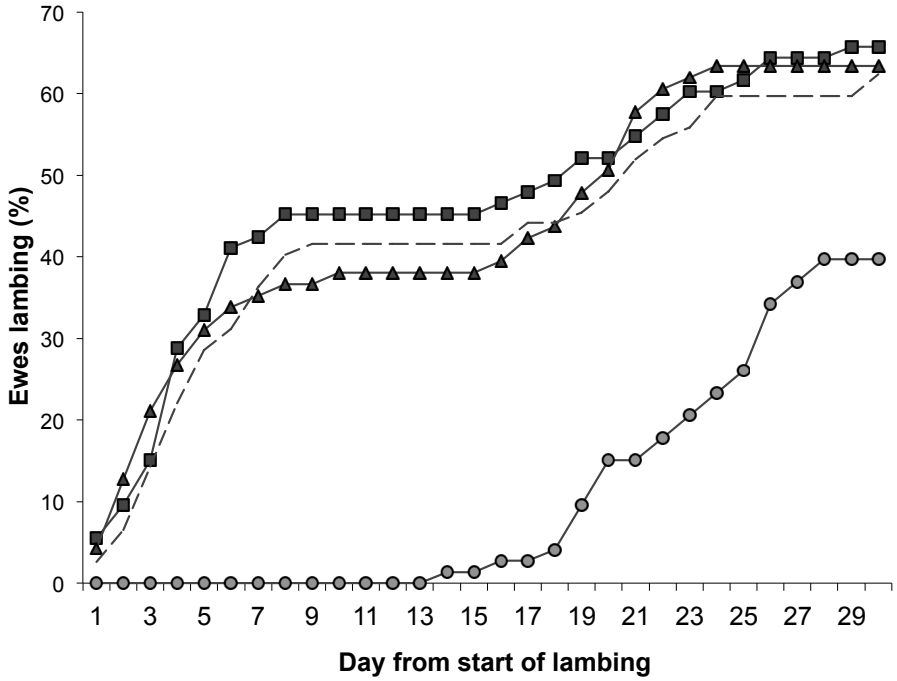

Figure 1. Lambing patterns as indicated by the cumulative percentages of ewes lambing in control ewes (C, --•--), ewes pre-treated with PCL inserts for 12 d without (P12, --■--), or with FSH 24 h before insert removal (P12F, --▲--) and ewes treated with PCL inserts for 5 d with FSH 24 h before insert removal (P5F, -------).

Experiment 2. **Examination of short-term treatment with the CIDR**.

In experiment 1, treatment for 5 days seemed to be equally effective as treatment for 12 days, but the 5-day treatment was done only with FSH. Experiment 2 was aimed at testing the efficacy of a 5-day treatment with the CIDR-G device with or without FSH given one day before removal of inserts, and compared to introduction of rams only. In this study, conducted in 1999, a total of 653 ewes on 7 farms were assigned to be controls (C; introduced to rams only), or to receive the CIDR-G device for 5 days, alone (P5) or in combination with an injection of FSH 1 day before insert removal (P5F).

Results were similar to those in experiment 1 (Table 2). More ewes treated with progesterone (P5 and P5F) were marked by rams during the first 3 days after ram introduction (77 vs 20%), and lambed to the first (46 vs 0%) or both services (63 to 67

vs 45%). Thus an additional 18 to 22% of the ewes treated lambed due to progesterone pre-treatment. Ewes that were treated with FSH and lambed to the first service tended to have a larger litter size than ewes not treated with FSH and control ewes.

In both studies, response varied among farms (24 to 87%) and to a limited extent with the face color of the ewe. The greatest overall responses in terms of ewes lambing were observed in white-faced ewes (69%) other than North Country Cheviots. Only a few North Country Cheviot ewes were studied, but none lambed.

Experiment 3. **Effects of dosage and injection time on the response to FSH.** In a third experiment, conducted during 2000, different dosages of FSH and times that FSH was injected relative to removal of the intravaginal insert were examined. Dosages of FSH of 42 or 68 mg increased ovulation rate slightly when given 12 hours before insert removal, but injection of FSH 36 hours before insert removal was ineffective. Despite the greater ovulation rate, numbers of lambs born were not increased in most flocks. Treatment with FSH increased the proportion of potential offspring (number of ovulations not represented by lambs born) lost from .25 to .71 as dosage of FSH increased. It is important to realize that ovulation rate is not the only factor limiting litter size in sheep.

Overall, progesterone treatment before ram introduction can be used to induce a synchronized fall lambing in the majority of ewes, which can allow producers to take advantage of seasonally higher lamb prices. Increases in litter size were not sufficient to justify the addition of FSH to the treatment regimen of progesterone and ram introduction.

It must be emphasized that results will vary from farm to farm, and that rams vary (both with breed and individually) in fertility and should be subjected to breeding soundness exams, especially before use in out-of-season breeding. Ewe: ram ratio should not exceed 18:1 for mature rams or 15:1 for ram lambs in single sire lots, although groups of 3 sound rams of either age can handle up to 18 ewes per ram in a multiple sire lot.

Table 2. Summary of reproductive performance of anestrous ewes in response to ram introduction (C), or ram introduction + 5-d CIDR pre-treatment without (P5) or with FSH (P5F).

Variable/Treatment	Control	P5	P5F
N	125	257	271
Ewes in estrus[1], %	20	75 [a]	79 [a]
Ovulation rate	-	1.95 ± .1	1.96 ± .1
Conception rate[2], %	0	70 [a]	66[a]
Pregnancy rate**, %**			
First service period[3]	0	53 [a]	52 [a]
Second service period[4]	57	45	54
Percent ewes lambing**, %**			
From first service period	0	46[a]	46[a]
To both service periods	45	63[a]	67[a]
Lambing rate[5] (mean ± SE)			
First service period	-	.68 ± .1	.77 ± .1
Both periods	.7 ± .1	.96 ± .1[a]	1.07 ± .1[a]
Prolificacy[6] (mean ± SE)			
First service period	-	1.50 ± .1	1.67 ± .1
Second service period	1.52 ± .1	1.47± .1	1.47 ± .1
Overall	1.52 ± .1	1.49 ± .1	1.6 ± .1

[a] ($P < .001$), [b] ($P < .05$) values in same row without common superscript differ

[1] Number of ewes marked by raddled rams as a percentage of all ewes treated

[2]Number of ewes diagnosed pregnant on d 26 - 31 as a percentage of ewes exhibiting estrus.

[3]Number of ewes diagnosed pregnant on d 26 - 31 as a percentage of all ewes treated.

[4]Number of ewes pregnant on d 46 – 51 expressed as a percentage of ewes not pregnant on d 26 – 31.

[5]Lambs born per ewe exposed.

[6]Lambs born per ewe lambing.

Not only ovulation rate, but also embryonic and fetal losses contribute to number of lambs born. In experiments 1and 2, 91 and 88% of pregnancies to first service were retained to lambing and 73 and 80% of pregnancies resulting from the second service period were retained. In further studies of 957 pregnant, non-lactating ewes of mixed breeding on 9 cooperating farms, individual embryos or fetuses were lost from multiple pregnancies, as well as complete losses of either single or multiple pregnancies. More ewes lost some, not all, embryos/fetuses from day 25 to term than had complete loss of a pregnancy. Losses of potential offspring occurred throughout gestation, with 4.3% of ewes experiencing loss of one or more embryos from day 25 to 45, 5.1% losing one or more fetuses from day 45 to 65, and 10.2% from day 65 to term. Mean losses of embryos or fetuses averaged 3.3% from day 25 to 45, 2.7% from day 45 to 65, 2.3% from day 65 to 85, and 8.5% from day 85 to term.

Lactating Ewes: A Limiting Factor during Anestrus

Lactation has little or no inhibitory effect on the ability of ewes to exhibit reproductive cycles during the breeding season. Estrus accompanied by ovulation occurs about 35 days after parturition in fall-lambing ewes, regardless of whether they are suckling lambs or non-lactating. However during anestrus, lactating ewes usually respond poorly to attempts to induce breeding activity by ram introduction or treatment with progestogens. Effects of lactation on response to treatment with progesterone were examined in ewes that were treated in early July. The lambs had been weaned from ewes in one group and ewes in the other group were in the second and third month of lactation. All ewes received CIDR devices for 5 days before introduction of rams.

In experiment 1, 105 weaned ewes and 53 lactating ewes were studied. Half of each group received an additional treatment of 30 micrograms of estradiol benzoate in 1 mL corn oil 24 hours after insert removal and ram introduction. The other half received 1 mL corn oil. Weaned ewes had higher pregnancy rates by ultrasonography at 26 to 30 days after first (59%) or second service (74%)

periods than the lactating ewes (38 and 44%, respectively). Thus 81% of weaned ewes, but only 44% of the lactating ewes lambed. Lambs born per ewe exposed (lambing rate) averaged 1.26 and 0.61, respectively. Lambing rate was higher in ewes treated with estrogen, (1.1) than in ewes receiving corn oil (0.8). In experiment 2, 106 weaned ewes and 44 lactating ewes received 0, 15 or 30 micrograms of estradiol benzoate 24 hours after insert removal and ram introduction. More weaned (76%) than lactating (27%) ewes were pregnant to first service. More of the weaned (82%) than lactating (27%) ewes lambed, and lambs born per ewe exposed averaged 1.25 and 0.31, respectively. Treatment with estrogen increased pregnancy rate to first service and ewes lambing in weaned, but not in lactating ewes. In conclusion, currently available methods are not suitable for induction of breeding out-of-season in lactating ewes. During March or April through July, it is recommended that lambs be weaned for at least 10 days before initiation of treatments to induce a fertile estrus.

Conclusions from efficacy studies and recommended use.

Treatment of ewes during the anestrous period with progesterone for as little as 5 days before ram introduction can result in synchronized fall lambing in greater than 65% of ewes treated, an improvement of 20 percentage points over ram introduction alone. Treatment with FSH one (1) day before progesterone removal, will sometimes yield a small increase in litter size in ewes bred out-of-season, but only in flocks with naturally low ovulation rates, and FSH increased embryonic and fetal mortality. Therefore, general use of FSH cannot be recommended.

CIDR-G devices are now approved for use in the US sheep industry and marketed in this country; treatment with a CIDR device for 5 days before ram introduction can be used to induce out-of-season breeding. This regimen can allow producers to target lamb markets when prices are highest. Its utilization in the industry could help to ensure a consistent supply of lamb. Caution: Rams should be kept on a higher protein ration, given a breeding soundness exam, shorn 6 to 8 weeks before

breeding and limited to 18 ewes per mature ram in multiple sire lots or, if in single sire lots, limited to about 12 ewes per ram lamb at the synchronized estrus.

Treatment with a CIDR device for 5 days, with $PGF_2\alpha$ at device removal, can allow producers to plan lambing dates and concentrate labor at lambing time for ewes bred in season. **However, this use has not been approved for marketing in the US.**

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Sample Schedule for Breeding 100 Ewes on May 21 to 23, 2013

March 28-April 2 – Select and shear 8 to 10 rams to be considered for breeding. **Keep rams separate from ewes until end of treatment.**
May 1-4 – Conduct breeding soundness exams on rams; select 6 or 7 for use and replace failed rams if necessary.
May 15 – Insert CIDRs in 100 ewes according to the package insert directions.

Directions: (Taken directly from Pfizer Literature)
For induction of estrus in ewes (sheep) during seasonal anestrus:
● Administer one EAZI-BREED CIDR Sheep Insert per ewe for 5 days.
Insertion:

1. Avoid contact with skin by wearing latex gloves when handling inserts.
2. Only use the specially designed EAZI-BREED CIDR Sheep Insert Applicator for administration.
3. Restrain ewes appropriately (head catch, squeeze chute, gate, etc.) prior to administration.
4. Wash the EAZI-BREED CIDR Sheep Insert Applicator in a non-irritating antiseptic solution, and then lubricate the front portion of the EAZI-BREED CIDR Sheep Insert Applicator with a veterinary obstetrical lubricant.
5. Push the flexible tail end of the EAZI-BREED CIDR Sheep Insert into the EAZI-BREED CIDR Sheep Insert Applicator taking care to assure the tail is extending upward through the slot of the EAZI-BREED CIDR Sheep Insert Applicator and is pointed toward the handle.

6. Fold the wings of the EAZI-BREED CIDR Sheep Insert to make it longer and continue to advance the EAZI-BREED CIDR Sheep Insert into the applicator until it is fully seated. When fully seated only the tips of the wings should protrude (one half inch) from the end of the EAZI-BREED CIDR Sheep Insert Applicator.
7. Lubricate the protruding tips of the wings of the EAZI-BREED CIDR Sheep Insert with veterinary obstetrical lubricant.
8. Clean the exterior of the vulva.
9. Open the lips of the vulva and gently place the loaded EAZI-BREED CIDR Sheep Insert Applicator through the vulva. The slot in the EAZI-BREED CIDR Sheep Insert Applicator should face upwards.
10. Once the loaded EAZI-BREED CIDR Sheep Insert Applicator is past the vulva slope the EAZI-BREED CIDR Sheep Insert Applicator slightly upwards (35 - 45° angle) by lowering the handle, and then forward, without forcing, until the EAZI-BREED CIDR Sheep Insert Applicator is fully inserted or resistance is felt.
11. Squeeze the finger grips within the handle of the EAZI-BREED CIDR Sheep Insert Applicator to deposit the EAZI-BREED CIDR Sheep Insert in the anterior vagina and then pull the EAZI-BREED CIDR Sheep Insert Applicator backwards to remove it from the vagina.
12. With the EAZI-BREED CIDR Sheep Insert correctly placed, with the wings open in the anterior portion of the vagina, the tail of the EAZI-BREED CIDR sheep Insert should be visible, pointing downward from the vulva of the ewe. Tails of EAZI-BREED CIDR Sheep Inserts that protrude more than 2.5 inches from the vulva may be clipped to minimize removal by other sheep.

May 20 – Remove CIDRs from ewes according to package directions and **introduce rams immediately and leave for ~26 days.** Dispose of used CIDRs properly.

Removal:

- Used (removed) EAZI-BREED CIDR Sheep Inserts still contain some progesterone. Used EAZI-BREED CIDR Sheep Inserts must be stored in a sealable container until disposed. Sealed bag/container with used EAZI-BREED CIDR Sheep Inserts must be properly disposed in accordance with applicable local, state and Federal regulations.

After insert removal, use standard flock breeding procedures to breed ewes on induced estrus. Make sure to have a sufficient number of rams to adequately breed all ewes in estrus. Breeds of rams may vary in libido in the non-breeding season. Therefore a ewe to ram ratio up to 18:1 is recommended for multi-sire situations. For single sire lots, 12:1 for ram lambs and up to 18:1 for yearling rams are recommended limits.

1. Remove EAZI-BREED CIDR Sheep Inserts by pulling, gently but firmly, on the protruding polyester tail.
2. EAZI-BREED CIDR Sheep Inserts may reverse direction within the vagina; therefore, if the polyester tail of the insert is not visible on the day of removal, check the vagina to determine if an insert is present.

FIELD EXPERIENCE WITH USE OF CIDR-G IN 2010 and 2011

Examples of results with CIDR-G inserts this past year and preliminary data from a demonstration and study in progress (2011) are shown in Appendix Tables 1 and 2, respectively.

Appendix Table 1. Summary of pregnancy data for a flock of purebred Dorset ewes (Flock 1) and a hair sheep flock (Flock 2) synchronized out-of-season with a 5-day CIDR-G followed by ram introduction – May and June, 2010

Variable	Flock 1	Flock 2
Total number of ewes	98 (2 lost)	77
Percent ewes lambing		
First service period	54	47
Second service period	19	31
Third	4	13
Total	77	88
Prolificacy		
First service period	1.73	1.61
Second service period	1.82	1.38
Third service period	1.30	1.20
Overall	1.67	1.47

Appendix Table 2. Summary of diagnosed pregnancies in a flock of crossbred ewes (mostly Dorset and Texel) exposed in July, 2011.

Variable	CIDR-Treated Ewes	Control Ewes
Number of ewes	101	22
Number lost CIDRs	2	
Number scanned for pregnancy	98	21
Number pregnant (%)		
First service period	**57 (58.2)**	**1 (4.8)**
Second service period	18 (44.0)	15 (75.0)
Total	75 (76.5)	16 (76.2)
Prolificacy at pregnancy diagnosis		
First service period	1.58	2.0
Second service period	1.50	1.53
Overall	1.56	1.56

	CIDR Only	Plus PG-600 (240 eCG, 120 hCG)
	48	50
Number pregnant (%)		
First service period	28 (58.3)	29 (58.0)
Second service period	11 (55.6)	7 (33.3)
Total	39 (81.2)	36 (73.4)
Prolificacy at pregnancy diagnosis		
First service period	1.57	1.59
Second service period	1.45	1.57
Overall	1.54	1.58

Inskeep, D'Souza and Knights unpublished