



TEATSEAL & DRY COW SOLUTIONS
PROVIDING TECHNICAL SUPPORT
FOR VETERINARIANS

TEATSEAL & DRY COW SOLUTIONS GUIDE MENU

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SECTION 1

**PRESCRIBING
DRY COW
THERAPY**



MILK QUALITY OVERVIEW

Dry cow therapy can have a large influence on milk quality because the dry and peripartum periods are critical points for mastitis management. When prescribing dry cow therapy, veterinarians aim for cows to enter the herd next season without intramammary infections (IMI) and with low somatic cell counts and low risks of clinical mastitis. Choosing evidence-based dry cow therapies, administered using best practice technique, will help ensure that farmers and veterinarians achieve the best results.

The purpose of dry cow therapy is to cure existing IMI and prevent new infections from forming over the dry period. The ideal approach on a dairy farm depends on the prevalence of IMI at drying off and the risk of new infections being established over the dry period, particularly at each end of the dry period.

Over the last few decades, the prevalence of IMI with major pathogens at drying off has reduced substantially on most farms in New Zealand, as seen by decreasing bulk tank somatic cell counts and lower numbers of cows with high somatic cell counts at herd tests. This reduction is in part thanks to the use of antibiotic dry cow therapy (ABDCT), culling and other farm management interventions. On farms with a low prevalence of major pathogen IMI at drying off, the main purpose of dry cow therapy has shifted from cure to prevention. The blanket use of ABDCT, in which all cows in a herd are treated with ABDCT regardless of their IMI status, is becoming increasingly difficult to justify. While ABDCT still plays an important role in milk quality, the role of non-antibiotic internal teat sealants is growing. Research has demonstrated that internal teat sealants are at least as effective as antibiotic dry cow therapy at preventing new IMI due to their long duration of action.

A new strategy, called targeted antibiotic dry cow therapy, has emerged whereby ABDCT is used only in cows with evidence of subclinical infection. Changing to a more targeted use of ABDCT across the New Zealand dairy industry requires a change in how dry cow therapy decisions are made and how dry cow therapy is administered. A large opportunity exists for veterinarians to play an essential role in helping farmers through this change by providing evidence-based advice and product stewardship, particularly in relation to administration technique.

APPLYING TARGETED ANTIBIOTIC DRY COW THERAPY

Veterinarians are challenged to reduce unnecessary antimicrobial dry cow therapy use while still optimising milk quality. The goal of targeted antibiotic dry cow therapy is to identify as many infected cows as possible and treat them with antibiotic dry cow therapy (with or without an internal teat sealant) and minimise the number of misclassified infected cows that lose an opportunity to be cured. At the same time, the number of uninfected cows that are unnecessarily treated with an antibiotic dry cow therapy should also be minimised.

To do this, the infection status of cows must be identified. The most accurate method of determining IMI status is to perform microbiology on every quarter of every cow, which is of course rarely feasible. We therefore rely on indirect tests, in particular somatic cell count (SCC) data from herd testing, which has become the industry standard. However, many farmers do not complete three or four herd tests for the season, and many do not herd test at all.

Zoetis has funded research to help veterinarians implement targeted antibiotic dry cow therapy in the face of incomplete milk quality data. This study, conducted by Cognosco and published in the *New Zealand Veterinary Journal*¹, evaluated various tests used alone or in combination for determining IMI status and compared them against the gold standard of microbiology. The information generated by this study has been incorporated into Zoetis' dry cow therapy decision tree (Figure 1), which is based on DairyNZ's Technote 14² (Figure 2).

To decide if a dairy farmer should use Teatseal® alone at drying off, veterinarians should first consider the herd overall and then, if the herd meets the criteria, consider individual cows.

HERD LEVEL DECISIONS:

Herds with a high risk of cow-associated mastitis may require blanket ABDCT due to a higher rate of new IMI in late lactation. Consider the herd's bulk milk somatic cell count (BMSCC) and the incidence and aetiology of clinical mastitis. High or volatile BMSCCs and signs of a *Staph aureus* mastitis problem (such as bacteriological culture, poor response to treatment and high recurrence rates) may indicate a high risk of mastitis due to cow-associated bacteria. In contrast, a low BMSCC herd with a high incidence of *Strep uberis* clinical mastitis in the spring suggests that blanket ABDCT is unlikely to improve milk quality if internal teat sealants are prescribed and correctly administered.

COW LEVEL DECISIONS:

Veterinarians should aim to ask two separate questions:

1. Does this cow require an ABDCT?

2. Would this cow benefit from an internal teat sealant?

Question 1 can be answered by looking at herd test somatic cell count data or by performing a rapid mastitis test (RMT) at drying off. SCC data are preferred because they provide a numeric value and do not rely on an operator scoring the RMT, but RMT has been shown to be as accurate as SCC when applied correctly¹. The standard approach is to apply a cut point of 150,000 cells/ml and treat all cows that have not exceeded that cut point at one or more herd tests with an internal teat sealant alone. However, veterinarians may choose to use a different cut point according to the farm situation and the farmer's goals. A range of cut points has been used in studies found in the literature, which are summarised in Table 1.

Using SCC information from only the last herd test has been shown to be as accurate as using the highest SCC from any herd test of the lactation¹, indicating that a single herd test may be sufficient for making dry cow therapy decisions. However, veterinarians should consider how stable the herd's infection prevalence is and how close to drying off the herd test is performed. Previous research showed that herd test data collected more than 80 days prior to drying off performed poorly for predicting infection status at drying off.³

Again, herds with high risks of cow-associated mastitis are not good candidates for targeted antibiotic dry cow therapy.

Question 2 can be answered by considering risk factors for environmental mastitis on the farm in question. DairyNZ recommends all cows receive an internal teat sealant if the herd as a high risk of environmental mastitis, which could be argued to apply to most of New Zealand's spring-calving herds.

In summary, when prescribing dry cow therapy, consider the herd overall and then individual cows. Determine if the herd has a high risk of cow-associated mastitis and environmental mastitis separately. When making cow-level decisions, ask whether the cow requires and ABDCT and then whether she would benefit from an internal teat sealant separately.



FIGURE 1. DECISION TREE FOR PRESCRIBING TEATSEAL ALONE TO COWS AT DRYING OFF.

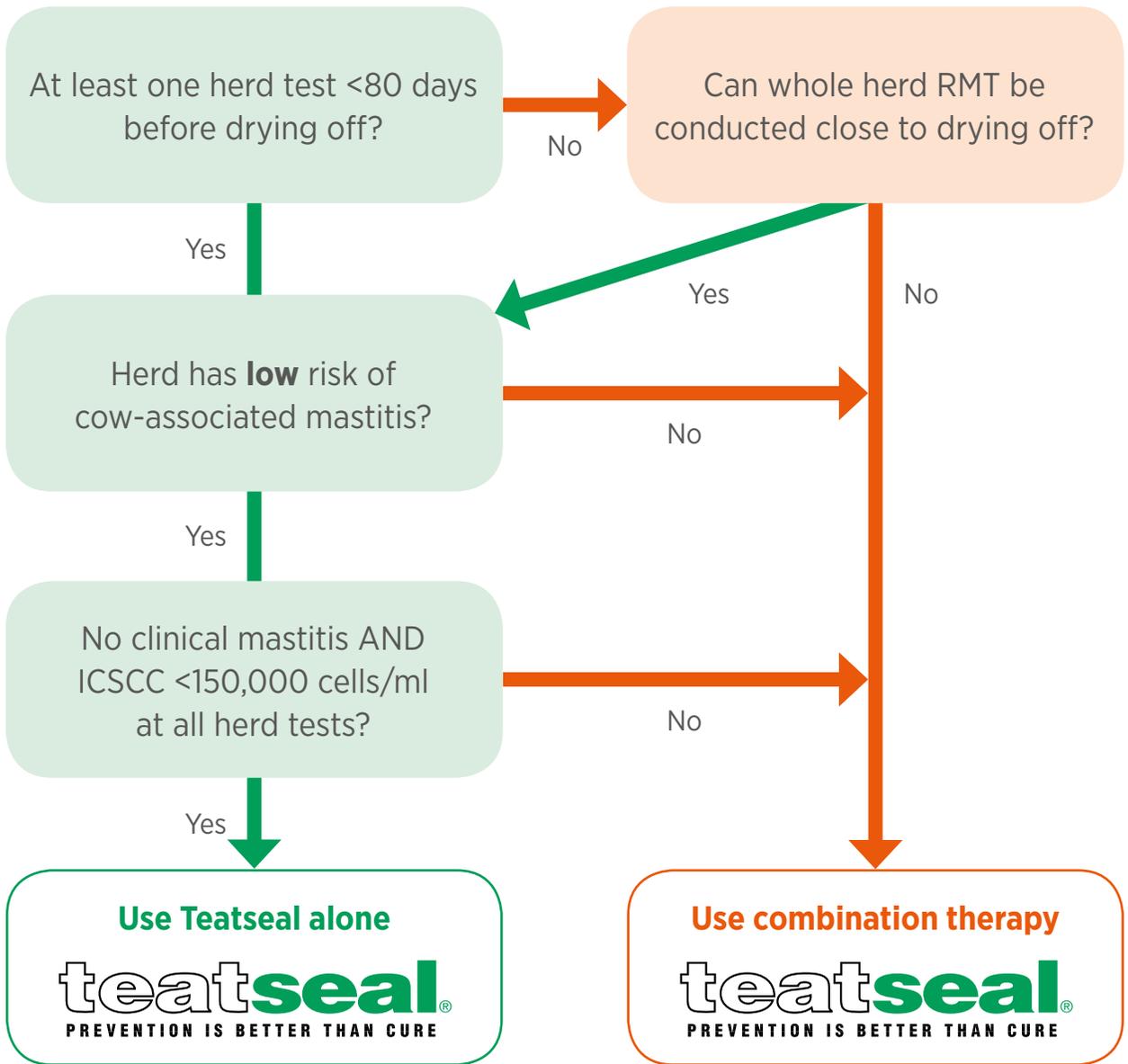


FIGURE 2. DAIRY NZ DECISION MAKING GRAPH – SMARTSAMM TECHNOTE 14.²

| | | Risk of mastitis by cow-associated bacteria e.g. <i>Staph. aureus</i> | | |
|--|------|---|---------|---------|
| | | COW STATUS | LOW | HIGH |
| Risk of mastitis by environmental bacteria e.g. <i>Strep. uberis</i> | LOW | Uninfected cows ¹ | ITS | DCT |
| | LOW | Infected cows ² | DCT | DCT |
| Risk of mastitis by environmental bacteria e.g. <i>Strep. uberis</i> | HIGH | Uninfected cows ¹ | ITS | DCT+ITS |
| | HIGH | Infected cows ² | DCT+ITS | DCT+ITS |

¹ Individual cow SCC <150 at 3 or more herd tests in lactation and no clinical mastitis.

² Individual cow SCC >150 at 1 or more herd tests in lactation and/or clinical mastitis in previous dry period or lactation.

TABLE 1. SELECTION CRITERIA AND SUMMARISED RESULTS OF NINE STUDIES COMPARING THE PERFORMANCE OF TEATSEAL TO OTHER TREATMENTS OR NO TREATMENT.

| | SCC at enrolment (cells/ml) | # herd tests | Interval from last herd test to drying off (days) | Treatments | Cows with dry period CM | Cows with new dry period IMI | Cows with postpartum CM |
|---|--|----------------------|---|---|---|--|--|
| Lacy-Hulbert <i>et al.</i> 2016⁴ | Cows <250,000 Heifers <150,000 | 3 | >110d | Negative control, Teatseal, ABDCT, ABDCT + TS | 4.4% 1.0% 0.0% 0.0% | 50.6% ^a 6.4% ^c 15.1% ^b 5.1% ^c | 11.7% ^a 4.4% ^b 3.6% ^b 3.4% ^b |
| Kromker <i>et al.</i> 2014⁵ | Geometric mean <50,000 | Last 3 monthly tests | <30d | Teatseal, Negative control at the quarter level (within cow) | NA | 3.5% ^a 10.5% ^b | 2 cases 2 cases |
| Bradley <i>et al.</i> 2010⁶ | <200,000 | Last 3 monthly tests | <30d | Teatseal, ABDCT + TS | OR = 0.89 (NS) | 226 quarters 220 quarters | OR = 0.89 (NS) |
| Berry and Hillerton 2002⁷ | <200,000 | All monthly | <30d | Teatseal, Negative control | 0.0% ^a 2.9% ^b | 10.7% ^a 30.9% ^b | 15 cases ^a 52 cases ^b |
| Huxley <i>et al.</i> 2002⁸ | <200,000 | All monthly | <30d | Teatseal, ABDCT | 0 cases 2 cases | Major pathogens: OR = 0.66 ^a | 10.6% 12.8% |
| Woolford <i>et al.</i> 1998⁹ | <200,000 | 1 | <4 weeks | Negative control, Teatseal, ABDCT, ABDCT + TS | 3.4% ^a 10-fold reduction ^b 10-fold reduction ^b 10-fold reduction ^b | 16.1% ^a 2.5% ^b 2.7% ^b 2.0% ^b | 33 cases ^a 11 cases ^b 16 cases ^c 15 cases ^c |
| Bhutto <i>et al.</i> 2016¹⁰ (organic farms) | Randomly allocated despite SCC Mean = 560,000 & 762,000 | N/A | N/A | TS vs NT | N/A | Less likely to have IMI at calving (p <0.001) | 24% vs 45% |
| Laven and Lawrence 2008¹¹ | <150,000 | Not stated | Not stated | TS vs NT | N/A | N/A | 6.4% vs 10.2% RR =0.55 (95% CI=0.27-1.12) |
| Sanford <i>et al.</i> 2006¹² | N/A | N/A | N/A | TS vs cloxacillin | N/A | Environmental IMI: OR = 0.54 (p=0.06) | N/A |

NT = no treatment, DCT = cephalonium, TS = Teatseal
 NS = No significant difference
 Superscript letters denote within-trial differences that are statistically significant (p<0.05).
 Note: in all studies, cows with a history of clinical mastitis in the preceding lactation were not eligible for Teatseal alone. Zoetis also recommends this.

ACCURACY OF SOMATIC CELL COUNT, RAPID MASTITIS TEST AND ELECTRICAL CONDUCTIVITY USED ALONE AND IN COMBINATION FOR MAKING DRY COW THERAPY DECISIONS AT DRYING OFF

The most accurate method of determining IMI status is to perform microbiology on every quarter of every cow, which is of course rarely feasible. We therefore rely on indirect tests, in particular somatic cell count (SCC) data from herd testing, which has become the industry standard. However, many farmers do not complete three or four herd tests for the season, and many do not herd test at all.

To help veterinarians challenged by incomplete information, Zoetis commissioned a pilot study that evaluated various tests used alone or in combination for determining IMI status and compared them against the gold standard of microbiology. This study, conducted by Cognosco and published in the *New Zealand Veterinary Journal*¹, has provided clinically-relevant information on how veterinarians can make dry cow therapy decisions in the absence of regular herd testing. This research update shares some of the results from this study.

METHOD

The objective was to evaluate the diagnostic value of the following tests used alone or in combination, using microbiology as the gold standard:

- Maximum SCC from the preceding lactation's herd tests
- SCC of only the most recent herd test
- RMT at the cow and quarter level
- Electrical conductivity at the cow and quarter level

Eligible cows were selected from three autumn-calving herds that had performed regular herd testing through the lactation. Cows were excluded if they had clinical mastitis on the day of testing or if they were systemically unwell or had been treated in the previous 14 days with antibiotics or anti-inflammatories.

Quarter milk samples were tested at drying off using RMT and an electrical conductivity meter and duplicate quarter milk samples were collected for bacteriology. RMT results were scored on a scale of 0–3, where 0=no thickening, trace=slight thickening, 1=distinct thickening but not gel formation, 2=immediate thickening followed by gel formation and 3=immediate gel formation. In addition to electrical conductivity, each quarter was assigned an inter-quarter ratio by dividing the electrical conductivity value of each quarter within a cow by the lowest quarter value obtained from within the same cow. RMT and electrical conductivity were assessed at both the quarter level and at the cow level while herd test SCC remained a cow-level variable. Cow-level RMT was calculated using two techniques: assigning the cow the highest quarter-level RMT score and by taking the number of quarters with a score \geq trace. Cow-level electrical conductivity and inter-quarter ratio were calculated by taking the highest quarter-level result.

The tests were evaluated for the presence of IMI by any pathogen and IMI by major pathogens (*Staph. aureus*, *Strep. uberis*, *Strep. dysgalactiae*, *Strep. agalactiae*, *Arcanobacterium pyogenes*, yeast, *Escherichia coli*, *Klebsiella* spp. or *Serratia* spp).

Among other assessments, the area under the receiver operator characteristic curve (AUC) was calculated for each diagnostic test. The receiver operator characteristic curve is a plot of sensitivity versus the false positive rate for several different cut points of a diagnostic test. AUC can take a value between 0 and 1, with values between 0.5 and 1.0 indicating a test that performs better than random chance and a value of 1.0 indicating a perfect test. The cut point with the maximum sum of sensitivity and specificity was deemed the optimal cut-point for each diagnostic test.

RESULTS

Analysis was conducted on data from 153 cows (609 quarters). IMI with any pathogen was found in 62/153 (40.5%) of cows and 99/609 (16.3%) of quarters, with coagulase negative staphylococci predominating. IMI with major pathogens was found in 7/153 (4.6%) of cows and 8/609 (1.3 %) of quarters.

All tests were more accurate at predicting IMI with a major pathogen than with any pathogen. There was no significant difference in overall accuracy between the last SCC, the maximum SCC of the season's herd test data and RMT at predicting IMI with a major pathogen or any pathogen (Tables 2 and 3). Electrical conductivity was numerically less accurate at the cow and quarter levels for predicting IMI with a major pathogen or any pathogen. Combining RMT or electrical conductivity with SCC in series or in parallel improved the accuracy slightly (data not shown).

INTERPRETATION

This study showed that using SCC information from only the last herd test SCC was as accurate as using the highest SCC from any herd test of the lactation. This indicates that a single herd test may be sufficient for making dry cow therapy decisions. However, veterinarians should consider how stable the herd's infection prevalence is and how close to drying off the herd test is performed. Examining the effect of the timing of the herd test was not an objective of the present study. Previous research showed that herd test data collected more than 80 days prior to drying off performed poorly for predicting infection status at drying off.³

For herds that do not herd test, RMT at dry off had comparable accuracy to SCC but it requires a skilled operator who can competently and consistently grade the RMT.

Combinations of tests in parallel or series did not improve outcomes sufficiently to justify the time and/or cost.

The improved accuracy of the tests with regard to major pathogen IMI was interesting and possibly related to the more significant inflammation associated with major pathogens.

Veterinarians should interpret this study in light of its limitations and apply it according to the individual circumstances of their farms. It was a pilot study and therefore limited in scale. There were only seven cows with major pathogen infections at drying off. The optimal cut point for each test was selected based on receiver operator characteristic curves, but the ideal cut point depends on the objectives and priorities of the farmer and veterinarian and is a trade-off between minimising antimicrobial consumption and avoiding misclassification of truly infected cows. It is worth noting that 90% of major pathogen IMIs in cows that were treated with an internal teat sealant alone at drying off self-cured over the dry period.³ Zoetis encourages veterinarians to read the full study report, which contains more information than presented in this summary and is available at SciQuest.

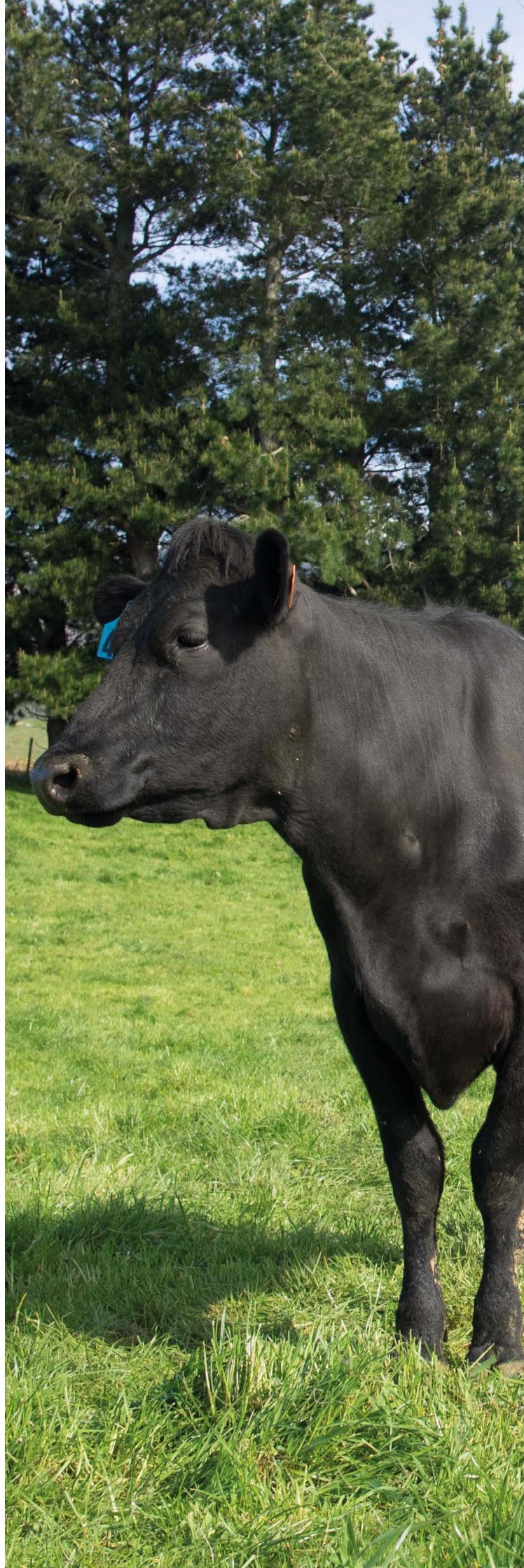


TABLE 2: TEST CUT-POINT THAT OPTIMISED SENSITIVITY (SE) AND SPECIFICITY (SP), WITH AREA UNDER THE RECEIVER OPERATOR CHARACTERISTIC CURVE (AUC), FOR INDIRECT PREDICTORS OF INTRAMAMMARY INFECTION, AT THE COW (N=153) AND QUARTER (N=595) LEVELS, WHEN COMPARED TO MICROBIOLOGICAL CULTURE OF ANY PATHOGEN AS A GOLD STANDARD.

| Variable | Cut-point | AUC (95% CI) | Se | Sp |
|--------------------------|-------------------------------|------------------|------|------|
| Cow-level | | | | |
| Last SCC ^a | ≥77x10 ³ cells/ml | 0.69 (0.60-0.78) | 0.57 | 0.79 |
| Highest SCC ^b | ≥110x10 ³ cells/ml | 0.64 (0.55-0.73) | 0.63 | 0.64 |
| RMT ^c | ≥1 quarter | 0.63 (0.54-0.71) | 0.71 | 0.57 |
| Max RMT ^d | score ≥trace | 0.69 (0.60-0.77) | 0.71 | 0.57 |
| EC IQR ^e | ≥1.37 | 0.62 (0.53-0.72) | 0.39 | 0.85 |
| Mean EC | ≥5.5 mS/cm | 0.58 (0.48-0.67) | 0.47 | 0.70 |
| Quarter-level | | | | |
| RMT | score ≥trace | 0.63 (0.58-0.68) | 0.46 | 0.78 |
| EC | ≥5.1 mS/cm | 0.57 (0.51-0.64) | 0.68 | 0.47 |
| EC IQR | ≥1.14 | 0.58 (0.52-0.64) | 0.48 | 0.66 |

- a. Somatic cell count at the last herd test of the lactation.
- b. The highest SCC at any herd test of the lactation.
- c. Number of quarters at or above the cut point.
- d. The highest RMT score of the cow's quarters.
- e. Maximum inter-quarter electrical conductivity ratio.

TABLE 3: TEST CUT-POINT THAT OPTIMISED SENSITIVITY (SE) AND SPECIFICITY (SP), WITH AREA UNDER THE RECEIVER OPERATOR CHARACTERISTIC CURVE (AUC), FOR INDIRECT PREDICTORS OF INTRAMAMMARY INFECTION, AT THE COW (N=153) AND QUARTER (N=595) LEVELS, WHEN COMPARED TO MICROBIOLOGICAL CULTURE OF A MAJOR PATHOGEN AS A GOLD STANDARD.

| Variable | Cut-point | AUC (95% CI) | Se | Sp |
|--------------------------|-------------------------------|------------------|------|------|
| Cow-level | | | | |
| Last SCC ^a | ≥150x10 ³ cells/ml | 0.78 (0.58-0.98) | 0.71 | 0.80 |
| Highest SCC ^b | ≥148x10 ³ cells/ml | 0.79 (0.66-0.92) | 0.86 | 0.65 |
| RMT ^c | ≥1 quarter | 0.75 (0.65-0.85) | 1.00 | 0.49 |
| Max RMT ^d | score ≥trace | 0.83 (0.72-0.94) | 1.00 | 0.49 |
| EC IQR ^e | ≥1.47 | 0.72 (0.47-0.98) | 0.71 | 0.86 |
| Mean EC | ≥7.0 mS/cm | 0.40 (0.12-0.69) | 0.14 | 0.98 |
| Quarter-level | | | | |
| RMT | score ≥trace | 0.91 (0.86-0.97) | 1.00 | 0.75 |
| EC | ≥56.2 mS/cm | 0.47 (0.17-0.76) | 0.38 | 0.84 |
| EC IQR | ≥1.30 | 0.52 (0.28-0.76) | 0.38 | 0.85 |

- a. Somatic cell count at the last herd test of the lactation.
- b. The highest SCC at any herd test of the lactation.
- c. Number of quarters at or above the cut point.
- d. The highest RMT score of the cow's quarters.
- e. Maximum inter-quarter electrical conductivity ratio.



SECTION 2

TEATSEAL ALONE IN COWS

TEATSEAL IN UNINFECTED COWS

Teatseal provides proven protection against new infections during the dry period when administered alone to uninfected cows.

Teatseal has been repeatedly shown to provide protection against new intramammary infections (IMI) during the dry period when administered alone to uninfected cows (Table 4).

SmartSAMB Technote 14 recommends that internal teat sealants may be used alone in cows that:

- have not exceeded a herd test somatic cell count of 150,000 cells/ml at one or more of at least three herd tests for the lactation
- have not had a case of clinical mastitis
- come from a farm with a low risk of cow-associated mastitis.²

Zoetis-sponsored independent research has shown that a single herd test, provided it is conducted within 80 days of drying off, is as accurate as multiple herd tests at predicting IMI status. For herds that do not perform herd testing, the rapid mastitis test is equally accurate, provided it is performed correctly.

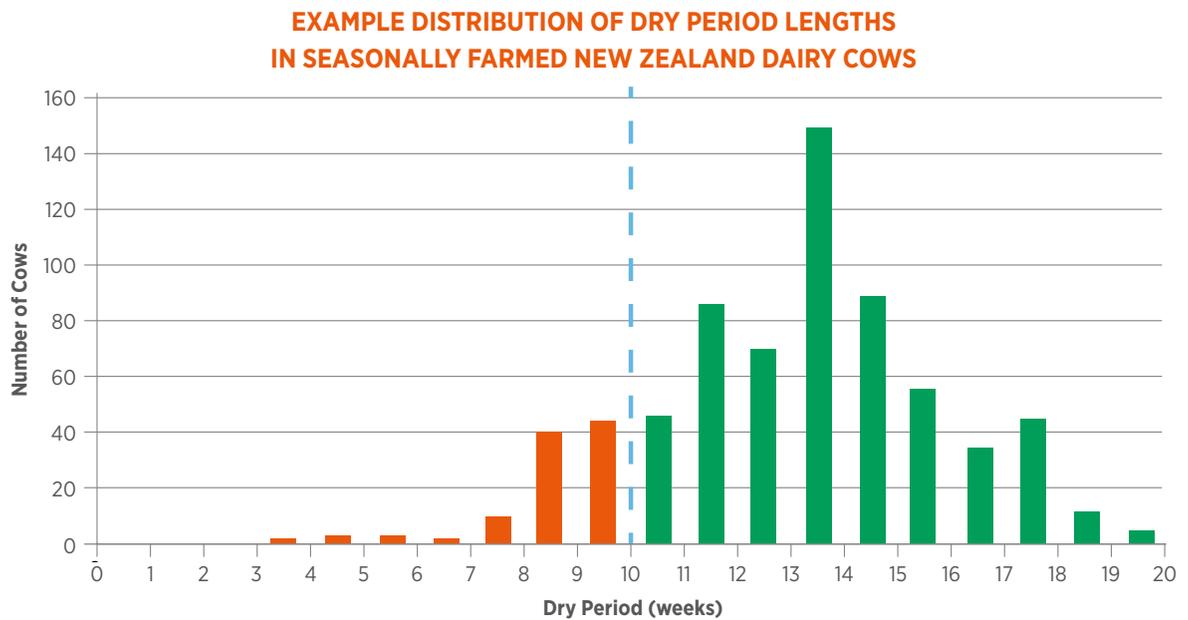
TABLE 4. MEASURING THE PROPORTION OF COWS INFECTED WITH A MAJOR PATHOGEN AT DRYING OFF AND TREATED WITH TEATSEAL THAT UNDERWENT BACTERIOLOGICAL CURE OVER THE DRY PERIOD.

| | Study 1 ⁸ | Study 2 ⁶ | Study 3 ³ | | |
|---|------------------------|---------------------------|----------------------|------------------------|------------------------|
| | | | 3a | 3b | 3c |
| Cow selection criteria | SCC < 200,000 No CM | SCC < 200,000 No CM | SCC < 200,000 | SCC < 200,000 No CM | SCC < 200,000 No CM |
| Comparator | Cephalonium | Cephalonium + Teatseal | N/A | N/A | N/A |
| Teatseal cure of major pathogens | 63% | 100% | 73% | 93% | 94% |
| Comparator cure of major pathogens | 70% | 100% | N/A | N/A | N/A |

Prevention of new intramammary infections leads to a significant reduction in the incidence of clinical mastitis during the dry period, through calving and into lactation.

Large numbers of cows in New Zealand have dry periods that are longer than the protective period of any dry cow antibiotic. Teatseal provides long lasting protection over the dry period. See the Teatseal retention study for more information.

The schematic below shows an example distribution of dry period lengths on a New Zealand farm. New Zealand studies have shown an average dry period of approximately 13 weeks.¹³⁻¹⁵ The blue line shows the protective period of the longest acting dry cow antibiotic.



Given that many cows are unprotected by ABDCT for at least part of the dry period, Teatseal should be used to cover the critical pre-calving period when the teat canal may open.

META-ANALYSIS OF TEATSEAL® STUDIES¹⁶

Teatseal has been the subject of a number of NZ and overseas studies in the last several years. In this paper, Dr Rabiee and Professor Lean have applied the most robust scientific approach available to analyse the overall impact of Teatseal – used alone or in combination with antibiotic dry cow therapy - on intramammary infections (IMI), clinical mastitis (CM) and somatic cell counts (SCC) in lactating dairy cows.

METHOD

A literature search was performed using a variety of search terms and sources. Studies that fitted quality criteria and reported the relevant data were included in the meta-analysis. The results are reported as Relative Risk (RR) and number needed to treat (NNT).

RESULTS

A total of 17 IMI and 21 CM trials were included in the meta-analysis. Other teat sealants were not excluded from the analysis; however, all studies eligible for inclusion used Teatseal.

RR: Relative risk, the risk of IMI or CM in cows that were treated with Teatseal divided by the risk of IMI or CM in non-Teatsealed cows.

NNT: The number of cows that need to be treated to prevent one new IMI or one case of CM.

| | RR | NNT |
|--|------|-----|
| Clinical mastitis | | |
| Teatseal vs no treatment (7 studies) | 0.52 | 13 |
| Teatseal in combination vs antibiotic alone (14 studies) | 0.71 | 21 |
| IMI | | |
| Teatseal vs no treatment (4 studies) | 0.27 | 7 |
| Teatseal in combination vs antibiotic DCT alone (13 studies) | 0.75 | 20 |

p<0.001 for all RRs.

Milk SCC

The analysis of the pooled data from three studies showed no statistically significant difference in linear score of milk SCC. However the low number of studies that included milk SCC data meant that further investigation into this effect is warranted.

CONCLUSION

A robust meta-analysis of all trials showed that Teatseal, either alone or in combination, significantly reduces the incidence of IMI and clinical mastitis in lactating dairy cows.



THE USE OF TEATSEAL ALONE COMPARED TO ANTIBIOTIC OR COMBINATION DRY COW THERAPY IN UNINFECTED COWS

Bradley *et al.* 2010⁶

A UK study enrolled 433 low SCC cows in 6 commercial dairy herds. The cows were allocated into the high SCC infected group or the low SCC uninfected group based on clinical mastitis and monthly herd test data. The uninfected cows were then randomly allocated so that ipsilateral quarters were dried off using either Teatseal alone or Teatseal plus a cephalonium dry cow product. Quarter milk samples were collected at dry off and post calving for bacteriology and SCC. The cows were monitored for clinical mastitis throughout the study period.

RESULTS

There was no significant difference in the incidence of new IMI or clinical mastitis between the treatment groups. There was therefore no benefit to adding cephalonium dry cow therapy to Teatseal in uninfected cows.



Huxley *et al.* 2002⁸

A UK study enrolled 505 cows with ISCC <200,000 cells/ml at any routine herd test and no history of mastitis in the current lactation. They were randomly divided into two groups: one group (202 cows) received Teatseal alone, and one group (203 cows) received long acting cephalonium dry cow therapy. Milk cultures were taken at drying off, calving and from any mastitis cases during the trial period.

RESULTS

The incidence of new IMI caused by *E. coli*, Enterobacteriaceae and all major pathogens combined was significantly lower in quarters treated with Teatseal. There was no significant difference in the incidence or severity of clinical mastitis or the dry period cure rate between the two groups.

Lacy-Hulbert *et al.* 2016⁴

A study performed in Southland in 2015 enrolled 929 cows from two herds, one wintered in a barn system, and one on fodder beet. The low SCC cows in each herd (ISCC <250,000 at three herd tests, no clinical mastitis) were assigned to one of four treatments: no treatment (NT), Teatseal (TS) alone, TS+ABDCT and ABDCT alone. The high SCC cows were assigned to one of two treatments: ABDCT alone or ABDCT + TS. Quarter milk samples were tested at drying off, at calving and again within four days of calving. SCC data was used from herd testing in both seasons, and clinical mastitis was recorded.

RESULTS

In both cases, cows with NT had a significant risk of new IMI at calving, approximately threefold that of cows receiving any intervention. In the low SCC cows, cows treated with either TS alone or ABDCT+TS had a significantly decreased risk of new IMI at calving compared to cows treated with ABDCT alone. The authors concluded “For cows receiving teat sealant alone, the level of protection was almost the same as a combination of dry cow and teat sealant, and for some measures, was better than dry cow treatment alone.”



SECTION 3

COMBO THERAPY

COMBO THERAPY: TEATSEAL PLUS ANTIBIOTIC DRY COW THERAPY

The use of combination therapy, instilling both an appropriate antibiotic such as Orbenin Enduro, with Teatseal, provides both cure and protection to cows that are infected at drying off. The popularity of this approach is due to the greatly increased chances of calving a low SCC, uninfected cow.

Bates *et al.* 2016¹³

A 2014 study investigated the effect of combo therapy on cows of different dry period lengths. A 600 cow herd in South Canterbury was enrolled. To be eligible cows required data from at least three of four herd tests. Cows were excluded if they had teat end pathology, had been treated with antibiotic therapy within the last 30 days or were being induced the following spring.

Cows were randomly allocated to one of two treatments applied at the cow level. 593 cows were enrolled, 289 in the cephalonium group and 304 in the combo group.

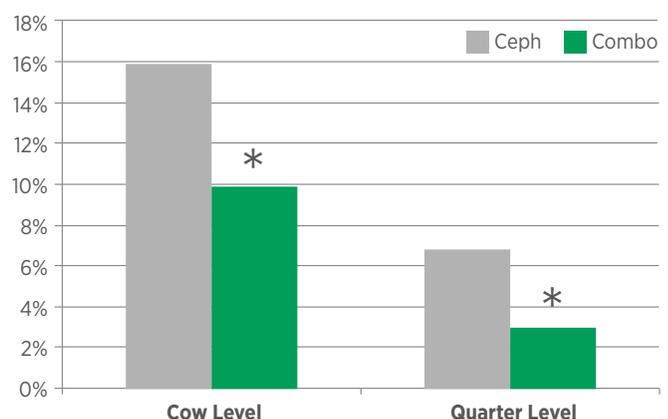
RESULTS

The mean dry period length was 93 days and the mean SCC at enrolment was 147,000 cells/ml. There were no recorded cases of mastitis during the dry period in either treatment group.

ADDING TEATSEAL TO CEPHALONIUM DRY COW THERAPY:

- Reduced the prevalence of subclinical mastitis at the first herd test of the subsequent lactation.
- Reduced the hazard of clinical mastitis in the first 100 days at both the cow and quarter level. Hazard ratios (95% CI) = 0.60 (0.39–0.98) and 0.41 (0.23–0.74) respectively).

INCIDENCE OF CLINICAL MASTITIS IN FIRST 100 DAYS OF LACTATION



* Results statistically significant ($p < 0.05$)

Age was associated with subclinical and clinical mastitis but dry period length was not.



Bradley *et al.* 2010⁶

This study examined the effect of adding Teatseal to high cell count cows treated with cephalonium dry cow therapy, and the effect of using combination dry cow therapy in low SCC cows. 890 cows were enrolled from 6 herds. Adding Teatseal to cephalonium dry cow therapy in infected cows resulted in:

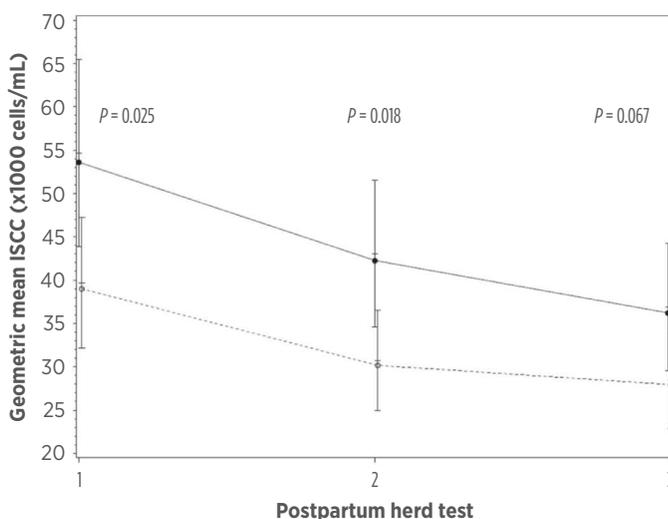
- Odds ratio of 1.40 (95% credibility interval = 1.03–1.90) of being pathogen free post-calving.
- Odds ratio of 0.68 (95% credibility interval = 0.48–0.98) of having clinical mastitis in the first 100 days of lactation.

An Australian study treated 2080 cows from eight farms with either Orbenin Enduro, (ABDCT) or a combination of Orbenin Enduro and Teatseal (ABDCT + TS). The cows were randomly allocated and not selected based on previous SCC or mastitis history. After calving they were closely observed for clinical mastitis during the dry period and the first 60 days in milk, with any cases sampled and recorded. Additionally milk samples were taken every 14 days for ISCC testing.

RESULTS

Four cows had a case of clinical mastitis during the dry period. 5% of cows had a case of clinical mastitis in the first 60 days in milk, with 5.7% in the ABDCT group and 4.3% in the ABDCT+TS group but this was not statistically significant (p=0.194.) However, there was a statistically significant (p <0.001) decrease in the likelihood of having a case of subclinical mastitis in the first 60 days in milk (defined as ISCC≥250,000). The odds of an ABDCT cow having a case of subclinical mastitis was 1.9x that of a ABDCT+TS cow.

GEOMETRIC MEAN INDIVIDUAL SCC FOR COWS TREATED WITH ANTIBIOTIC DRY COW THERAPY (SOLID LINE) OR ANTIBIOTIC DRY COW THERAPY PLUS TEATSEAL (DASHED LINE) AT 1 TO 3 HERD TESTS DURING THE FIRST 60 D POSTPARTUM.

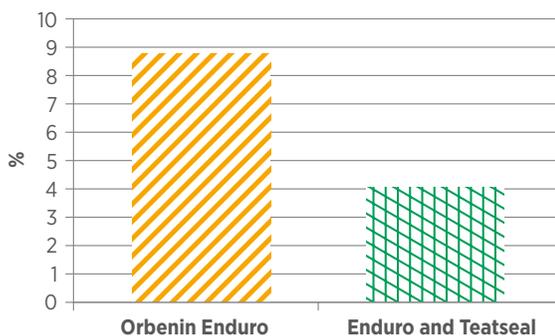


Newton et al. 2008¹⁸

In this 283 cow UK study, quarters were treated with either Orbenin Enduro alone or Orbenin Enduro + Teatseal, where the cow had an SCC of >200,000 cells/mL.

- Quarters that received Orbenin Enduro + Teatseal had a 50% reduction in the incidence of clinical mastitis over the first 100 days of lactation.

% CLINICAL MASTITIS (up to 100 days post-calving)

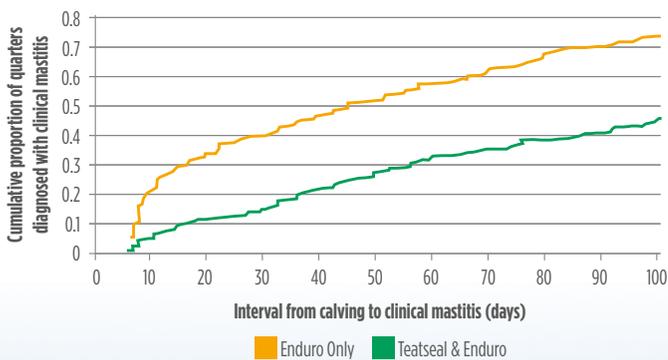


This 2008 Australian study enrolled 2053 cows from 6 seasonally calving herds. Cows received either Orbenin Enduro alone or Orbenin Enduro plus Teatseal.

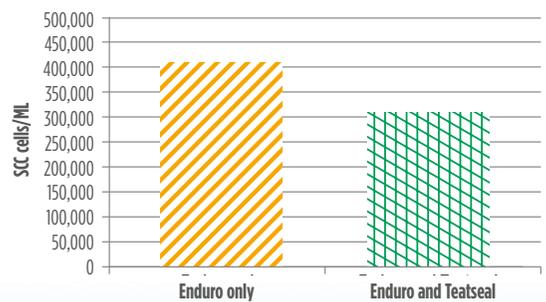
Compared to the Orbenin Enduro alone group, the Enduro + Teatseal group had:

- 70% reduction in the incidence of clinical mastitis within 21 days of calving
- 42% reduction in the incidence of clinical mastitis up to 100 days of lactation
- 20% reduction in the prevalence of subclinical mastitis at the first herd test after calving
- and the mean individual SCC at the first herd test after calving was 100,000 cells/ml lower in the combo group.

QUARTER INFECTION RATE



MEAN SCC POST CALVING





SECTION 4

TEATSEAL IN HEIFERS

TEATSEAL IN HEIFERS

Heifers have been shown to have a higher risk of clinical mastitis in early lactation than older cows. This leaves them at increased risk of having light quarters, teat canal thickening or being culled.

With heifer mastitis incidences exceeding over 25% on many New Zealand farms, the magnitude of the problem and the associated costs become very clear.

Teatseal administered to maiden heifers approximately 4 weeks prior to the planned start of calving dramatically reduces clinical mastitis incidence around calving, thereby reducing the cost and frustration associated with heifer mastitis.

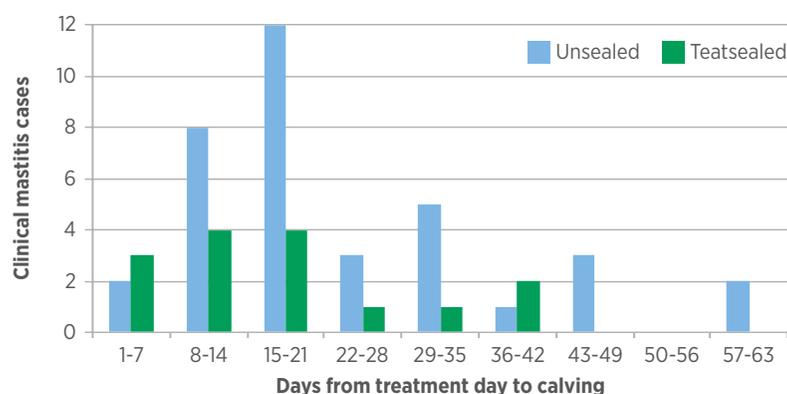
If necessary, Teatseal can be administered closer to calving (1-4 weeks prior to planned start of calving).

Newton, 2012²⁰

A NZ study analysed data from 692 heifers that had received Teatseal in 2 quarters only, with 2 quarters as controls. The heifers were Teatsealed up to 1 day prior to calving with a median pre-calving interval of 20 days.

In heifers that calved at least 7 days after Teatsealing, sealed quarters had only 35% of the risk of clinical mastitis compared to unsealed quarters ($p=0.0015$).

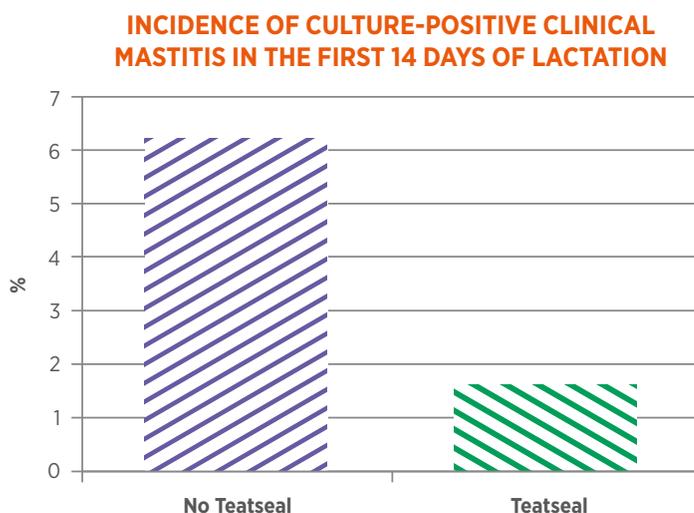
COUNT OF CLINICAL MASTITIS CASES BEFORE 31ST OCTOBER IN QUARTERS TREATED WITH TEATSEAL AT A RANGE OF INTERVALS PRIOR TO CALVING AND UNTREATED QUARTERS



In a 2007 study in the Waikato, 255 heifers were enrolled an average of 31 days before planned start of calving. Milk samples were collected at enrolment, in the first four days of calving from all heifers and additionally from any heifers identified by the farmer as having clinical mastitis.

RESULTS

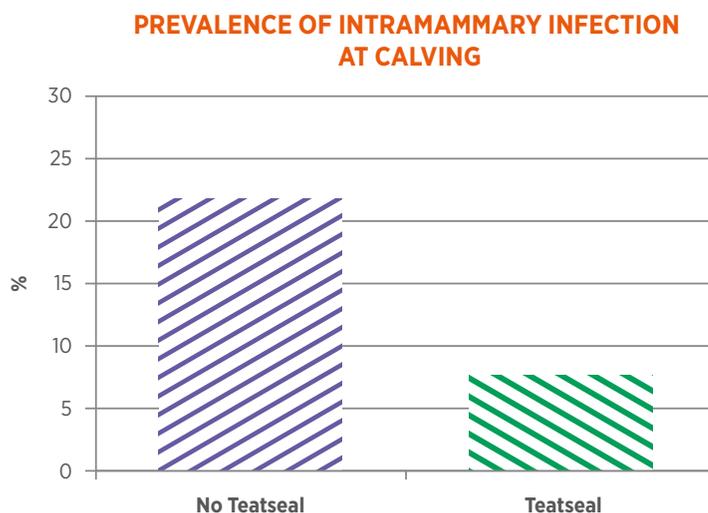
The prevalence of IMI pre-calving was 15.5%. Teatseal reduced the prevalence of an IMI due to *S. uberis* at calving by 84% and of clinical mastitis by 68%.



In 2008, the research was extended, with 1067 heifers enrolled from 30 herds on average 27 days before planned start of calving. Again, milk samples were collected at enrolment, in the first 5 days after calving, and from any clinical mastitis cases.

RESULTS

Use of Teatseal reduced the risk of any IMI by 74%, and clinical mastitis by 70% in treated quarters.



META-ANALYSIS OF PRECALVING HEIFER MASTITIS INTERVENTIONS

Naqvi *et al.* 2018²³

To compare various precalving interventions for preventing heifer mastitis available to farmers, the authors performed a systematic review and meta-analysis of the literature. Precalving interventions were grouped into antimicrobial therapy, internal teat sealants, teat dips/sprays, vaccines, combinations of these groups and other interventions. A total of 62 studies were included, with 48 entering the meta-analysis, including New Zealand research. The outcome was risk ratio of mastitis, defined as elevated somatic cell count, clinical mastitis or intramammary infection according to each study's design. Internal teat sealants and combinations of interventions were the most effective at reducing the risk of mastitis, with internal teat sealants having a pooled risk ratio of 0.40 (95% CI =0.30 - 0.52). Internal teat sealants were especially effective at preventing environmental mastitis (Table 5). Vaccines were found to be effective for preventing contagious mastitis only.

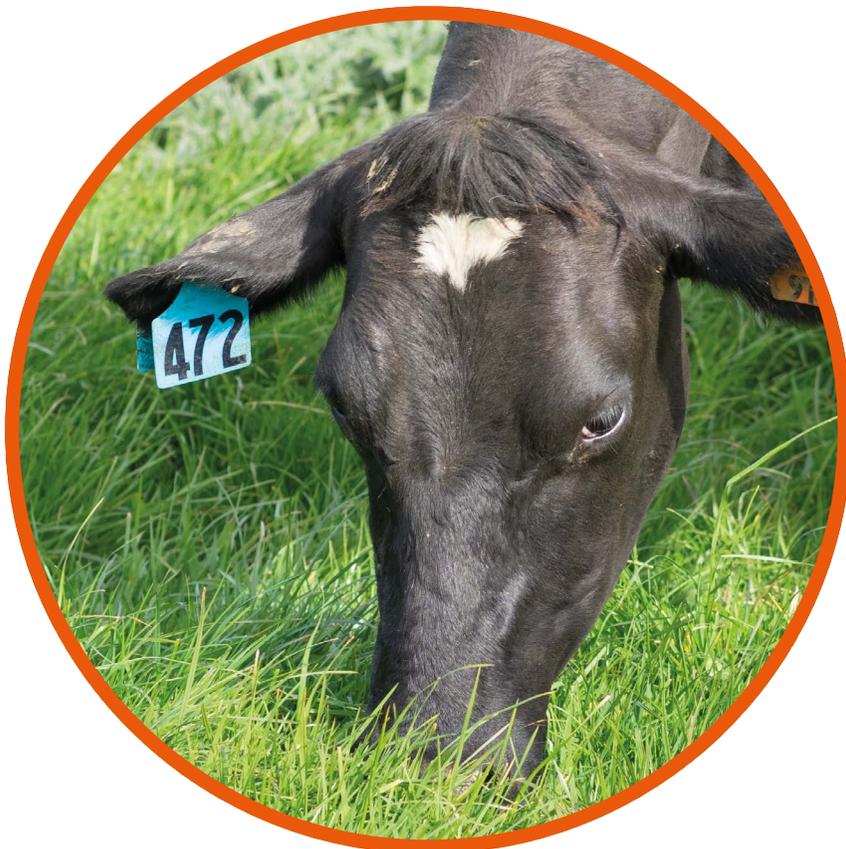


TABLE 5. META-REGRESSION OF RECORDS INCLUDED IN A SYSTEMATIC REVIEW OF PRECALVING TREATMENT FOR IMPROVING UDDER HEALTH IN PRIMIPAROUS DAIRY HEIFERS ON THE TYPE OF TREATMENT ASSESSED IN THE STUDY, STRATIFIED BY TYPE OF PATHOGEN.

| Pathogen and intervention type ^{a,b} | Risk ratio ^c (95% CI) | No. of records | Heterogeneity ^d |
|---|----------------------------------|----------------|--|
| Contagious | | | |
| Antimicrobial | 0.41 (0.34-0.77) | 15 | $f = 0.29$ $Q = 39.36$ $P = 0.025$ |
| Teat sealant | 0.40 (0.22-0.72) | 4 | |
| Teat dips/spray | 1.48 ^e (0.52-4.27) | 1 | |
| Vaccine | 0.56 (0.34-0.92) | 8 | |
| Combination | 0.93 ^e (0.33-1.26) | 1 | |
| Environmental | | | |
| Antimicrobial | 0.58 (0.46-0.74) | 18 | $f = 0.57$ $Q = 71.77$ $P < 0.0001$ |
| Teat sealant | 0.27 ^f (0.15-0.49) | 5 | |
| Teat dips/spray | 0.56 (0.17-1.80) | 3 | |
| Vaccine | 0.78 (0.20-2.98) | 4 | |
| Combination | 0.25 ^f (0.13-0.50) | 2 | |
| CNS | | | |
| Antimicrobial | 0.51 (0.35-0.76) | 15 | $f = 0.89$ $Q = 212.71$ $P < 0.0001$ |
| Teat sealant | 0.46 (0.29-0.73) | 4 | |
| Teat dips/spray | 1.48 (0.31-7.03) | 2 | |
| Vaccine | 0.89 (0.38-2.07) | 4 | |
| Combination | 0.34 ^f (0.21-0.56) | 2 | |
| Other | 0.80 ^e (0.19-3.34) | 1 | |

a. Contagious pathogens include *Staphylococcus aureus* and *Streptococcus agalactiae*. Environmental pathogens include *Escherichia coli* and non-*agalactiae* streptococci.

b. Antimicrobial includes antibiotics as well as antiseptic compounds such as chlorhexidine. Combinations in included studies consisted of teat sealants and antimicrobials; vaccines and antimicrobials; and teat sealants, vaccines, and antimicrobials. Other includes insecticides and management practices such as prepartum milking.

c. Ratio of risk of infection in treated heifers to risk of infection in untreated controls.

d. Residual heterogeneity from meta-regression model attributed to differences in studies. f = statistic to quantify the amount of variation due to study heterogeneity; Q = Cochrane Q statistic for significance.

e. Intervention type within pathogen type stratum did not have enough records for meta-analysis. Risk ratio presented was calculated from the single record within that stratum.

f. Risk ratio was different ($P < 0.05$) from studies assessing antimicrobial effectiveness.



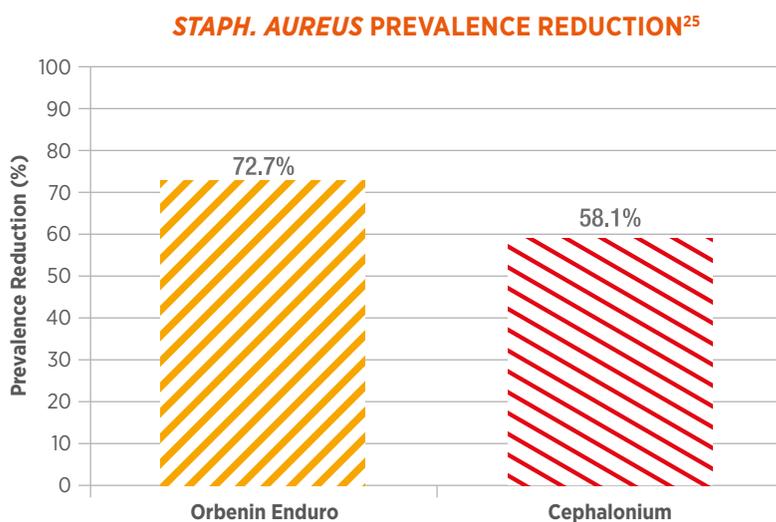
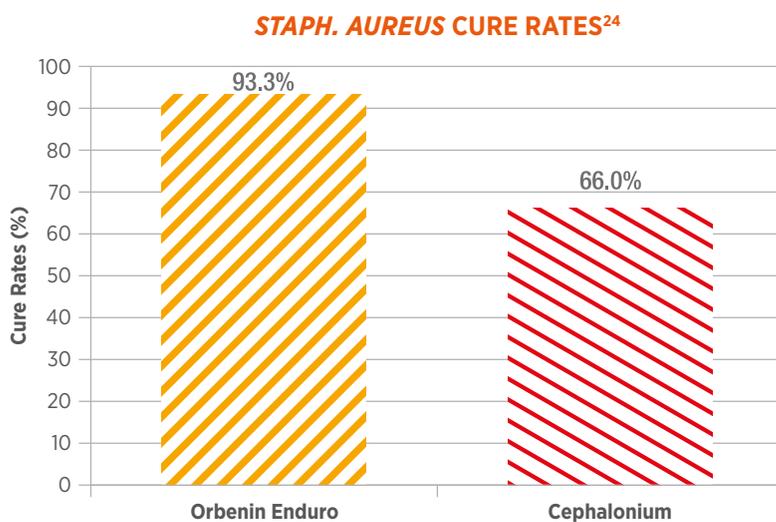
SECTION 5

**ANTIBIOTIC
DRY COW
THERAPY
CURE RATES**

ORBENIN ENDURO

Sol and Sampimon 2005²⁴ & Marco 1995²⁵

Chronically infected cows act as a source of bacteria for other cows in the next lactation and result in higher bulk milk somatic cell counts (BMSCC). Orbenin Enduro has demonstrated a 93% *Staph. aureus* cure rate and 73% prevalence reduction in trial work.



Woolford 2002²⁶

A New Zealand study conducted in the Waikato, using 632 cows from three herds, examined efficacy of teat canal antibiotic infusion at preventing mastitis. Cows were selected for having an ISCC < 200,000 cells and no more than 1 quarter infected with a pathogen at drying off. Orbenin Enduro was used as the positive control. They were sampled for bacteriology at drying off, at calving and monitored for clinical mastitis for the first 8 weeks of lactation. They also examined the percentage of teat canals open at three and six weeks post drying off.

RESULTS

Orbenin Enduro prevented clinical mastitis over the dry period, with only 0.6% of quarters having a case of clinical mastitis during the trial period vs 5.3% of control animals. Only 1.8% of Enduro treated quarters had a new IMI at calving vs. 7.9% of control quarters. Enduro treated quarters had a significantly increased chance of being closed at three weeks.

ORBENIN DC

Pankey *et al.* 1982²⁷

A New Zealand study, conducted in the Waikato, used 1207 cows from 6 herds. They were milked sampled at drying off and again within 21 days of calving. They were randomly assigned to receive either Orbenin DC or a reference product.

RESULTS

The cure rate for Orbenin DC vs *Staph. aureus* was 85.2%; against *Strep. uberis* 77.8%; against *Strep. agalactiae* 92.8%.



SECTION 6

**TEATSEAL
RETENTION
STUDY**

TEATSEAL RETENTION

A 2014 Estendart study examined retention of Teatseal over an extended dry period.²⁸ 84 cows with no history of mastitis in the current lactation were examined and, after screening on teat end scores, udder palpation, and SCC, 45 cows were selected for the trial. The cows were dried off 22 weeks before planned start of calving, and randomly allocated treatment with either Teatseal or a non commercially available test product. Two quarters were treated with Teatseal and two with the reference product per animal, with right/left and fore/rear quarters balanced. Retention was defined as visible Teatseal in either the teat cistern or the streak canal on radiographic image.

The cows' udders were radiographed at 2, 8, 12, 16, and 20 weeks (14, 56, 84, 112, and 140 days).

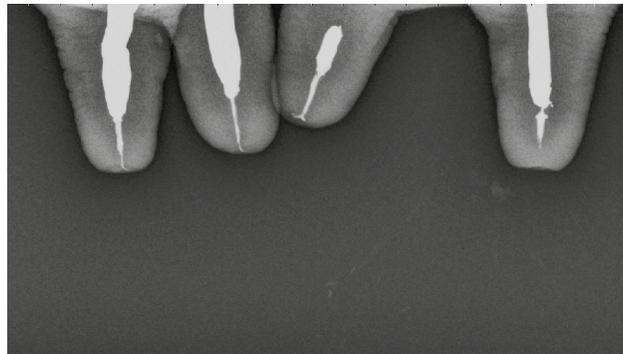
RESULTS

87/90 of Teatsealed quarters (96.7%) retained Teatseal for the full 140 days.

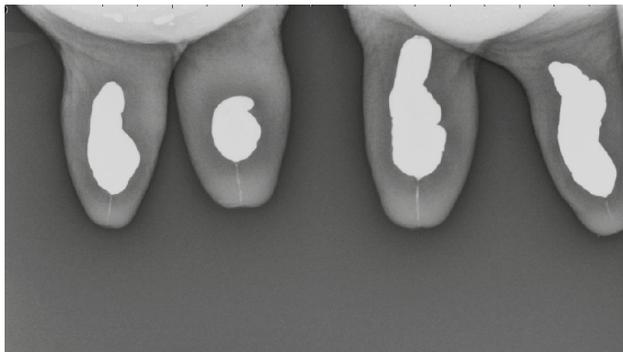
These findings are consistent with other trial work that has looked at Teatseal retention. A New Zealand study found 100% of quarters x-rayed retained some Teatseal in the teat sinus at 100 days post Teatsealing.⁹

| Study Day | Proportion quarters with visible Teatseal |
|-----------|---|
| 0 | 100% |
| 14 | 98.9% |
| 56 | 97.8% |
| 84 | 98.9% |
| 112 | 97.8% |
| 140 | 96.7% |

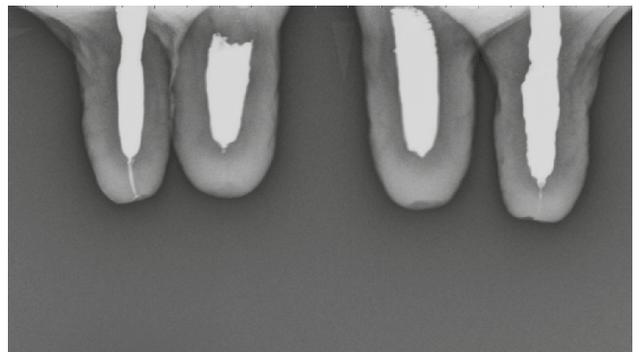
DAY 0*



DAY 84*



DAY 140*



*Selected sample of radiographs based on visual clarity, not necessarily the same cow and results will vary.



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