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Dry cow therapy with a non-antibiotic intramammary teat seal - a review

Fiona Crispie,[1,2] **James Flynn,**[2] **R. Paul Ross,**[1,3] **Colin Hill**[4,3] and **William J. Meaney**[2]

[1] Teagasc, Dairy Products Research Centre, Moorepark, Fermoy, Co Cork,
[2] Teagasc, Dairy Production Research Centre, Moorepark, Fermoy, Co Cork,
[3] Alimentary Pharmabiotic Centre, University College Cork,
[4] Department of Microbiology, University College Cork.

Dry cow antibiotic therapy is used to eliminate existing intramammary infections and to prevent new infections in the dry period. It is implemented as part of a total management system known as the 'Five-Point Plan' for mastitis control. Recent public concerns over the widespread prophylactic use of antibiotics, coupled with an increasing interest in organic farming, have lead to a re-evaluation of the treatment of cows at drying-off. As a result, attention has focussed on the use of novel alternatives to antibiotic therapy at the end of lactation. One such therapy involves the application of a non-antibiotic bismuth-based intramammary teat seal designed for use in cows with low cell counts at the end of lactation. Like the keratin plug that forms naturally in teats of cows that have been dried-off, teat seal forms a physical barrier to invading pathogens. To date, a number of independent studies have shown that teat seal is as effective as traditional dry cow antibiotic products in preventing the occurrence of new infection during the dry period in cows with somatic cell counts of $\leq$200,000 cells ml^{-1} at drying-off. This paper reviews the efficacy of teat seal in preventing dry period mastitis in both conventional and organic dairying systems.

Introduction

Mastitis continues to be one of the greatest problems faced by the dairy industry. Over 137 different organisms have been identified as being causative agents of bovine mastitis, including bacteria, viruses, mycoplasma, yeasts and algae (Watts, 1988). However, most of the mastitis cases in the UK and Ireland are caused by one of the following bacterial pathogens: *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus uberis*, *Strepococcus dysgalactiae* and *Streptococcus agalactiae* (Bradley, 2002). Mastitis continues to be the most economically important disease of dairy cattle, due to the expense of antibiotic treatment, along with the associated costs of decreased milk production and decreased fertility or, in cases where antibiotic treatment is ineffective, culling or death (Bradley, 2002). Indeed, mastitis is believed to be the most common cause of death amongst lactating cows, with a death rate of 0.6% (Bradley and Green, 2001). Overall, clinical mastitis has been estimated to cost the UK dairy industry £168 million annually (Bradley, 2002) and the worldwide costs have been estimated to be $1.5 to $2.0 billion per annum (Wells *et al.*, 1998).

Although about 20 to 35% of clinical mastitis cases are of unknown aetiology (Wellenberg *et al.*, 2002), it is widely accepted that bovine mastitis is mainly bacterial in origin. It can be classified as contagious or environmental (Blowey and Edmondson, 1995). In the former case, it is caused by organisms such as *S. aureus*, *Strep. dysgalactiae* and *Strep. agalactiae*, which are all adapted to survive in the udder, causing subclinical infections. Environmental pathogens such as *Strep. uberis* or enterobacteriaciae like *E. coli* are not well-adapted to survive within the udder and, instead, they multiply rapidly following invasion, evoke a swift immune response and are eliminated (Bradley, 2002).

The advent of antibiotics in the 1940s led to hopes that mastitis would be eradicated quickly and easily. However, it was not

Corresponding author:
W.J. Meaney
Teagasc Dairy Production Centre,
Moorepark, Fermoy, Co Cork,
Republic of Ireland.
Tel: +353 25 42285
Fax: +353 25 42340
E-mail: bmeaney@moorepark.teagasc.ie

Abbreviations

DCT	dry cow therapy
DIM	days in milking
GRAS	generally regarded as safe
IMI	intramammary infection
SCC	somatic cell count
TS	teat seal

until the 1960s, following the introduction of a 'Five-Point Plan' developed initially in the UK (Smith *et al.*, 1967), that any success was achieved in the control of clinical and subclinical mastitis (Berry and Hillerton, 2002a). The plan suggested that control of the disease could be achieved by using the following five strategies:

- Routine maintenance of milking machines.
- Post-milking teat disinfection.
- Rapid identification and treatment of clinical cases.
- Routine whole herd antibiotic dry cow therapy.
- Culling of chronically infected cows.

More recently, EU milk hygiene directives imposed strict limits on the somatic cell count (SCC) of bulk tank milk and they have ensured that the guidelines laid down in the Five-Point Plan are followed, improving milk quality and production (Berry and Hillerton, 2002a; Bradley, 2002). While there have been enormous improvements in milk quality, recent evidence suggests that the frequency of mastitis due to environmental pathogens or to minor pathogens like coagulase-negative staphylococci and *Corynebacterium bovis* is increasing rapidly (Schukken *et al.*, 1989; Myllys *et al.*, 1998). These data, allied with increasing consumer fears over the widespread and often indiscriminate use of antibiotics, have lead to the conclusion amongst many people working in the dairy industry (including those engaged in research on mastitis) that a re-assessment of existing treatments and development of novel treatments are essential, if current standards are to be improved or even maintained.

Factors predisposing to mastitis

Several factors have conspired to ensure that mastitis has not been completely controlled to date. Firstly, in the dairy industry emphasis is often placed on breeding cows for increased milk production (Burton *et al.*, 2001). A negative correlation exists between milk production capacity and resistance to mastitis; this is attributed, in part, to the increased metabolic stresses associated with the synthesis and secretion of milk (Pyörälä, 2002). The nutritional status of the cow is also an important factor in determining susceptibility to infections: deficiencies of selenium, copper, zinc or vitamin E levels can predispose the cow to infection (Pyörälä, 2002). Milking machines are often the cause of problems, as they can induce changes in the width of the teat duct, increasing the risk of colonisation of the teat duct and new intramammary infections (Pyörälä, 2002). Invasion by environmental pathogens such as *Strep. uberis* and *E. coli* almost certainly occurs at or soon after milking or if there is any teat damage. Surprisingly, even though animal husbandry practices have improved greatly, there has been no reduction in the number of environmental infections. Probably the greatest problem in treating mastitis is the plethora of pathogens that can cause mastitis - if protection or immunity is enhanced against one pathogen, it doesn't protect against another (Sordillo and Streicher, 2002).

Dry cow therapy

During the dry period (i.e., the time between the last milking of one lactation and calving at the start of the next), the mammary gland undergoes a series of changes that influence the cow's resistance to bacterial infection. Even the length of the dry period can affect udder health (Green *et al.*, 2002). Additionally, it is well known that the presence of infection during the dry period can have profound effects on cow health and productivity after calving, often resulting in decreased milk yield and milk of poor quality from the infected quarters. Dry period infections may have persisted from the previous lactation or they may be new infections acquired during the dry period. Indeed, new infections during the dry period have been shown to occur at up to 10 times the rate of new infections during lactation, with *E. coli* or *Strep. uberis* being the most common causative agents. However, clinical mastitis is rare during the dry period, probably due to high concentrations of lactoferrin and leucocytes in the mammary gland at this time. Nonetheless, while dry period infections may not present as clinical cases during the dry period, there is a high risk that subclinical cases will become clinical after calving (Green *et al.*, 2002).

Antibiotic therapy

The use of antibiotics for the treatment of mastitis in the 1950s led to the development of dry cow therapy (Bramley and Dodd, 1984). It is used to eliminate existing intramammary infections (IMI) and to prevent new infections during the dry period (Bramley and Dodd, 1984). Ideally, dry cow therapy will achieve high initial concentrations of antibiotic throughout the udder, resulting in a swift kill of existing pathogens, followed by a prolonged period of release of the antibiotic to prevent new infections (Green *et al.*, 2002). The antibiotic should then be readily milked out following calving. While normally very effective, dry cow antibiotic therapy has some disadvantages, including the appearance of residues in the milk when treated cows calve. As a result, milk is normally withheld for a period of time following calving, with concomitant economic losses (Craven, 1987). Additionally, there is mounting concern over the indiscriminate overuse of antibiotics, as it may contribute to the alarming increase in resistance to antibiotics that many microorganisms have evolved (WHO, 1994). Such claims have been fiercely debated. Even after 30 years of use, resistance to cloxacillin has not been detected in bovine isolates of *S. aureus* (Booth, 1997). Regardless of the concerns, or their veracity, dry cow antibiotic therapy remains a cornerstone of mastitis treatment.

Limiting therapy to infected cows or to infected quarters (selective dry cow therapy) is one method by which the use of antibiotics is reduced (Bratlie, 1972; Browning *et al.*, 1990). However, several investigations have shown that the incidence of new intramammary infections increases when uninfected dry cows are left untreated. A recent study by Berry and Hillerton (2002a) compared the effects of dry cow treatment and no

treatment on the incidence of new IMIs and clinical mastitis within two low-cell-count herds and two herds undergoing conversion to organic farming. They demonstrated that there was a significant reduction in the incidence of clinical mastitis during the dry period in cows that had been treated with an antibiotic when compared to untreated cows (Berry and Hillerton, 2002a). In addition, there were also significantly more IMIs present at calving in the untreated groups in all four herds. Fifty *per cent* of new infections that occurred at calving were caused by *S. aureus*, a microorganism that is particularly difficult to treat effectively with antibiotics (Berry and Hillerton, 2002a). Thus, it appears that antibiotic treatment is necessary during the dry period, unless new alternatives can be developed (Berry, 2002; Berry and Hillerton, 2002a).

Teat seals

A keratin plug forms naturally in the teat canal after drying-off and appears to be a major defensive mechanism against infection. It has been reported that the rate of closure of teat canals after drying-off varies greatly from cow to cow (Williamson *et al.*, 1995), with 50% of teats still 'open' 10 days after drying-off. This delay may lead to an increase in new infections, as 97% of clinical dry period IMIs occur in open quarters (Williamson *et al.*, 1995). Thus, the concept of using artificial teat seals as a barrier to prevent new IMIs was developed. Given the current public concerns over the blanket use of antibiotics in farm animals, it is hardly surprising that the idea of using teat seals as a prophylactic treatment for mastitis has gained popularity. Quarters with external seals have been shown to have a lower level of new IMI during the dry period than do unsealed quarters, but the existing external seals are ineffective as a long-term treatment (Leslie *et al.*, 1999; Hemling *et al.*, 2000). Much greater success has been achieved with internal seals. A teat seal containing bismuth subnitrate was developed in the 1970s and was shown to be effective at preventing new dry period infections in an artificial challenge study (Meaney, 1977). This product resulted in a 90% reduction of new IMI during the dry period, and remained lodged in the lower teat for at least three to four weeks following drying-off (Figure 1). Subsequently, a commercial combination product comprised of a short-acting antibiotic and a bismuth subnitrate seal was developed and has been available in Ireland since that
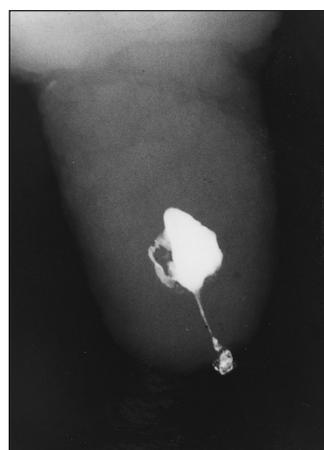

Figure 1. X-ray plate illustrating the appearance and position of teat seal in the teat sinus, teat canal, and teat orifice.

time (Osmonds Teat Seal, Cross Vetpharm Group Ltd., Dublin, Ireland). Thus, sealing the teats of uninfected cows at the end of lactation was proposed as an acceptable alternative to blanket treatment with antibiotics. However, the abundance of new antibiotics developed in the 1970s resulted in limited interest in the use of internal teat seals, despite promising results obtained with their use (Meaney, 1977).

Efficacy of teat seal in cows with low cell counts

Recently, a reformulated version of the seal (Teatseal; Bimeda (NZ) Ltd., Auckland, New Zealand) was examined for its ability to prevent the development of new IMIs during the dry period and of clinical mastitis during the following lactation (Woolford *et al.*, 1998). Four weeks before drying-off, cows were screened on the basis of SCC and bacteriology. Only cows with an SCC of <200,000 cells/ml and with at least three uninfected quarters were chosen as experimental subjects. Thus, the final selection comprised 528 cows. A within-udder design was then used wherein the rate of new IMIs was compared between adjacent quarters of each cow. This ensured that treatments were evaluated within each cow selected for the study. Udder quarters were treated at drying-off with one of the following treatments: 505 quarters with teat seal (TS:"Teatseal"; Bimeda NZ Ltd); 505 quarters with TS plus antibiotic (600mg benzathine cloxacillin in an aqueous base, Osmonds "Teatseal 1", CrossVetpharm Group, followed immediately by an infusion of teat seal); 528 quarters with antibiotic (250mg cephalonium: Cepravin Dry Cow; Mallinkrodt Veterinary Ltd, Wellington, New Zealand) alone and 528 quarters served as untreated controls. Relative to the control group, the three groups that received an infusion of TS, TS plus antibiotic or antibiotic only showed a 10-fold reduction in new clinical IMIs during the dry

TABLE 1: Number of new intramammary infections (IMIs) over the dry period and at calving in udder quarters of untreated cows (negative control) and of cows treated with a dry cow antibiotic (positive control), teat seal, or teat seal plus antibiotic (Adapted from Woolford *et al.,* 1998)

Experimental group	Negative control	Positive control	Teat seal	Teat seal + antibiotic
Total quarters treated	528	528	505	505
New dry period clinical IMIs	18	2*	1*	2*
New IMIs at calving	67	12*	12*	8*
Total new IMIs	85	14*	13*	10*
% of quarters infected	16.1	2.7*	2.5*	2.0*

*The difference between any of the three treated groups and the negative control group was significant (p < 0.01) in all cases.

period. A similar reduction was seen in the incidence of new IMIs at calving. The infusion of an antibiotic together with the seal did not achieve any extra reduction in new IMIs (Woolford *et al.*, 1998); the quarters treated with antibiotic had approximately the same level of infection in the dry period and at calving as the other two treated groups (Table 1). The incidence of new clinical mastitis in the first two months of lactation was similar in the three treated groups (Woolford *et al.*, 1998). Importantly, the seal appeared to remain lodged in the teat canal for up to 100 days of the dry period and was particularly effective at reducing the incidence of infection caused by *Strep. uberis*, the predominant mastitis-causing organism in New Zealand (Woolford *et al.*, 1998). Thus, these authors concluded that teat seal was as effective as a long-acting antibiotic in preventing mastitis both during the dry period and during the first 60 days of lactation.

A similar independent study (Huxley *et al.*, 2002). was undertaken in the UK where the efficacy of a dry cow antibiotic containing cephalosporin was compared to teat seal. The cows chosen for this study did not have any sign of clinical disease, had four functioning quarters, and had been free of anti-inflammatory and antibiotic treatment for at least 30 days.

TABLE 2: Number of IMIs acquired during the dry period, listed by causative organism (Adapted from Huxley *et al.*, 2002)[1].		
Causative organism	**Group A (Teat seal) No of quarters=928**	**Group B (Antibiotic) No of quarters=940**
Coagulase-positive staphylococci	10	7
Streptococcus spp.	24	26
Escherichia coli	13*	42*
All enterobacteriaceae	17*	55*
All major pathogens	103*	145*
All minor pathogens	218	224

[1]Numbers within rows marked with * differ significantly (p<0.01) between treatments.

FIGURE 2. Rate of new infection after inoculation with 1,200 cfu *Strep. dysgalactiae*.

Additionally, the selection process specified a SCC level of ≤200,000 cells/ml and freedom from clinical mastitis in the preceding lactation. Using these criteria, 605 cows were selected for the study: of these, 252 were infused with teat seal (Cross Vetpharm Group Ltd., Ireland) and 253 with a long-acting antibiotic preparation (250mg cephalonium, Cepravin Dry Cow, Schering Plough Ltd. UK).
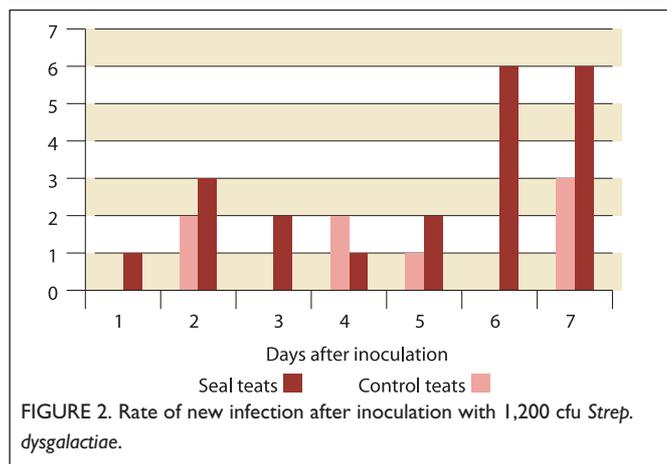
Subsequently, data for dry period IMI were available from 467 quarters (232 teat seal and 235 antibiotic) and data for clinical mastitis were available from 479 quarters (237 teat seal and 242 antibiotic). The results showed that quarters treated with teat seal acquired significantly fewer IMI caused by *E. coli*, by all enterobacteriaceae and by all major pathogens combined during the dry period (Table 2). Despite the significantly greater number of new infections acquired by cows treated with the antibiotic, there was not a significant increase in the development of clinical mastitis in these quarters in the first 100 days of lactation (Huxley *et al.*, 2002). Thus, under UK field conditions, an internal seal was proven to be as effective as an antibiotic, again highlighting the potential of this novel therapy as an effective alternative to antibiotic treatment (Huxley *et al.*, 2002).

In a third study, the efficacy of teat seal in preventing infection following an artificial challenge with *Strep. dysgalactiae* was evaluated by Meaney *et al.* (unpublished data). In this study, 62 infection-free udder quarters in 17 dairy cows were selected at drying-off. Following the last milking of lactation, 31 quarters were infused with teat seal and the remaining 31 were used as untreated controls. Three days after infusion, all teats were inoculated with 1,200 cfu of *Strep. dysgalactiae* into the teat canal to a depth of 17mm. The cows were then observed over the next seven days for signs of clinical mastitis. During this period, 20 clinical cases of mastitis developed in the untreated quarters and eight in the quarters infused with teat seal (Table 3). Additionally, new infections appeared more rapidly in untreated teats than in those infused with teal seal (Figure 2). These data indicate that teat seal provided significant protection (p=0.002) against an artificial challenge with *Strep. dysgalactiae*, supporting the studies using natural challenge (Woolford *et al.*, 1998; Huxley *et al.*, 2002).

Efficacy of teat seal in infected cows

In the studies described above, teat seal was shown to successfully prevent new infections during the dry period both from experimental challenge and from natural exposure (Meaney, 1977; Woolford *et al.*, 1998; Huxley *et al.*, 2002).

TABLE 3: New infections in sealed teats and in unsealed teats of non-lactating cows after inoculation with 1,200 cfu *S. dysgalactiae*.			
Treatment	**Quarters (n)**	**No. of new infections**	**% new infections**
Untreated	31	20	65
Seal	31	8	26

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TABLE 4: Incidence of clinical mastitis in the dry period and new infection status at calving in seven dairy herds (Adapted from Berry and Hillerton, 2002b).				
	New clinical cases in dry period		New IMI at calving	
	Seal	Untreated	Seal	Untreated
No. of quarters at risk	784	812	784	799
No. of new infections	0[a]	10[b]	27[c]	93[d]
Numbers within columns marked with [a,b] or [c,d,] differ significantly (P=0.0011 or P<0.001, respectively) between treatments.				

However, all of the cows in the experiments had low cell counts. This raised the question: would teat seal be equally effective in preventing clinical mastitis in the dry period in cows already infected at drying-off? To address this question, seven dairy herds were recruited for a selective teat seal trial. The herds included two standard dairy herds, two fully commercial organic herds and three herds undergoing conversion to organic status (Berry and Hillerton, 2002b). Uninfected udder quarters of cows in all seven herds were randomly assigned to either teat seal or no treatment (control). Additionally, infected udder quarters in cows in four of the seven herds were also randomly assigned to teat seal or no treatment. Samples were taken from the 398 cows in the trial at one week prior to drying-off, at drying-off, at calving, and approximately one week after calving. As a result of the randomisation process, there were no significant differences in distribution for infection status between the two treatment groups at drying-off. There was, however, a significant difference in the infection status at calving between the two groups (p=0.001), as cows treated with teat seal were 0.27 times less likely to have a new infection at calving than untreated cows (Berry and Hillerton, 2002b). There was also a statistically significant difference in the incidence of clinical mastitis during the dry period. Clinical symptoms were detected in 10 quarters from the untreated group and there was no clinical case in the group treated with teat seal (p=0.001; Berry and Hillerton, 2002b). Again, at calving, the untreated quarters had significantly more new IMI that the treated group (93 and 27 quarters, respectively; p<0.001), although the incidence of the predominant organism causing the new infections, *Strep. uberis*, did not differ between the groups (Table 4). Of the total quarters that were infected at calving, more cases of clinical mastitis arose in the untreated group than in the treated group (p<0.001). Overall, however, the percentage of quarters that developed clinical mastitis in this period did not differ between groups. Thus, the efficacy of teat seal was demonstrated against a variety of environmental challenges, which included cows with a range of cell counts and infections, in both winter housing and summer grazing environments (Berry and Hillerton, 2002b).

Teat seals and udder hygiene

Bismuth-based teat seals are biologically inert and the introduction of an internal seal without antibacterial properties into the mammary gland is not risk-free. Undoubtedly, pathogens may be accidentally introduced into the quarter during infusion, or the seal itself may become contaminated, leading to infection. The importance of using teat seal in a hygienic manner and of abiding strictly to the manufacturer's instructions was highlighted recently when a cow in a dairy herd of 150 cows died due to a pseudomonas infection. A subsequent investigation of the sanitary conditions on the farm revealed that tubes of the teat seal (Orbeseal, Pfizer) were stored in a bucket containing water contaminated with *Pseudomonas aeruginosa* (Milnes and Platter, 2003). This consequently led to an outbreak of gangrenous mastitis and, subsequently, the death of one cow. Thus, many farmers may have more confidence in the product if an antibiotic is also incorporated into the treatment. Godden *et al.* (2003) studied the effectiveness of using an internal teat seal with an antibiotic to prevent the acquisition of new dry period IMIs in a North American herd. In order to qualify as eligible for this trial, cows had to have four functional quarters free of clinical mastitis on the day of drying off. Additionally, it was specified that the cows must not have received parenteral or intramammary antibiotic or anti-inflammatory treatment for at least 30 days prior to drying-off. A total of 419 cows were thus selected. Following the final milking, all four quarters were treated with a commercial long-acting dry cow antibiotic (Orbenin DC; Cloxacillin (benzathine), 500mg, Schering Plough Corp., Kenilworth, N.J.). Teat seal (Orbeseal, Pfizer Animal Health, NY) was then randomly assigned to two contralateral quarters (LH/RF or LF/RH) within each cow. The alternate two contralateral quarters served as controls. The seals were removed at the first milking of the new lactation and all quarters were sampled for culture and SCC analysis (Godden *et al.*, 2003). Samples were taken at drying-off, once between one and three days in milking (DIM) and once between six and eight DIM. The proportion of quarters with an IMI present between drying-off and the first three days of the new lactation was 29.1% for the control group (antibiotic only) versus 22.8% for the treated group (teat seal plus antibiotic) - a statistically significant difference (p<0.05). Similarly, between six and eight DIM the proportions of quarters with an IMI were significantly different (p<0.05) at 25.9% for the control group versus 20.6% for the treated group. Thus, quarters treated with Orbeseal had a significantly lower prevalence of IMI caused by all major and minor pathogens, including environmental streptococci, for the first six days of the new lactation (Table 5; Godden *et al.*, 2003). Similarly, treatment with Orbeseal was associated with a significant reduction in the risk of developing a new IMI either from a major pathogen or from environmental streptococci.

TABLE 5: Prevalence of IMI in control (antibiotic only) and treated (seal plus antibiotic) quarters at drying off, 1 to 3 days in milking (DIM) and 6 to 8 DIM (Adapted from Godden *et al.*, 2003).						
Quarters	**IMI present at dry-off**		**IMI present at 1 to 3 DIM**		**IMI present at 6 to 8 DIM**	
	Control (n=828)	Treated (n=834)	Control (n=812)	Treated (n=821)	Control (n=811)	Treated (n=809)
Total qts with IMI	276	259	236	187	210	167
% of all qts with IMI	33.3	31.1	29.1[a]	22.8[b]	25.9[a]	20.6[b]

[a,b] % of all quarters with IMI differ significantly between columns (P<0.05).

Finally, the proportion of quarters experiencing a clinical mastitis event between drying-off and up to Day 60 of the new lactation was significantly lower (p<0.05) for treated quarters (5.9%) than for control quarters (8.0%) Thus, in some instances, addition of antibiotic to teat seal may increase its efficacy and safety (Godden *et al.*, 2003). The additional protective effect observed by using teat seal plus antibiotic over antibiotic alone may be due to several factors. Firstly, the seal offers a barrier to bacterial entry in the early dry period when the keratin seal may not have formed properly. Secondly, in the late dry period, when the concentration of antibiotic may have fallen below therapeutic levels, the seal persists in its barrier function. Finally, throughout the entire dry period, teat seal provides a barrier against many bacterial species that may be insensitive to the antibiotic being used (Godden *et al.*, 2003).

Discussion

Dry cow therapy was originally developed with the aim of controlling summer mastitis. Its use was rapidly extended to routine use on all cows all year round. More recently, however, the emphasis has changed and in the majority of dairy herds the primary function of DCT is the prevention of new IMIs rather than the treatment of existing IMIs. This is due in part to an increase in organic dairy farming, and also due to attempts to reduce costs in response to lower milk prices. Additionally, in the world of improved milk quality and better udder health one has to question the necessity to treat all cows, irrespective of cell count. Restricted or selective use of dry cow antibiotics would appear to be a good compromise for those concerned about treating cows that do not have intramammary infections at drying-off. Only those cows with an infected gland would be treated, whether in the infected quarter only or in all quarters; in this way, the use of antibiotics would be both targeted and discriminate. Selective dry cow therapy of this type has been shown to be as effective as complete therapy in eliminating existing infections; however, there is still a problem with new infections arising during the dry period. Additionally, selecting treatments at the quarter level proves difficult while infected cows have to be identified quickly, cheaply and accurately. Cell counts, CMT analysis or N-acetyl-ß-D-glucosaminidase (NAGase) tests are sometimes used as confirmatory tests. Bacteriological sampling, however, remains the definitive method of identifying infected quarters and, as this method is both time-consuming and costly, it poses a drawback to selective dry cow therapy. To lower the incidence of mastitis in a herd where selective dry cow therapy is practised, it is necessary to cull older infected cows and prevent new IMI in the younger cows. To this end, teat seal provides an attractive adjunct to both selective and blanket dry cow therapy.

Enhancement of teat sealing formulations may be achieved using non-antibiotic additives like bacteriocins, which are proteins produced by some bacteria that have the ability to kill other organisms (Ryan *et al.*, 1998, 1999; Twomey *et al.*, 2000). Veterinary products used for the treatment or prevention of disease in animals whose tissues and/or products are destined for human consumption may give rise to unwanted or harmful residues. Thus, to maintain consumer confidence, international bodies such as the European Agency for the Evaluation of Medicinal Products (EMEA), Codex Alimentarius and the Food and Drug Administration (FDA) help to evaluate risks and oversee laws relating to the levels and type of residues in milk and dairy products. A non-antibiotic anti-mastitis dry cow formulation containing a bacteriocin derived from a GRAS organism could be of immense benefit to the dairy sector in meeting the rigorous standards imposed by these bodies. Combining the seal with a broad-spectrum bacteriocin provides the physical barrier effect and it localises the anti-microbial inhibitor in the teat sinus. Since the efficacy of the teat seal in preventing mastitis is not dependent on anti-microbial activity throughout the complete mammary gland, then the amount of bacteriocin required per seal treatment will be small relative to antibiotic usage with conventional dry cow therapy. The efficacy of incorporating the bacteriocin lacticin 3147 into teat seal will be reviewed elsewhere (Crispie *et al.*, manuscript in preparation).

Conclusion

Teat seal has been shown to provide a safe, effective alternative to the blanket use of antibiotics at drying-off. Used on its own, teat seal has been shown to be as effective as a long-acting antibiotic in controlling the rate of new infection during the dry period. Importantly, the incorporation of antibiotics or other suitable antimicrobials into teat seal could prevent inadvertent contamination during infusion, thus improving the safety of the product for the untrained user.

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