



Responsible Use of Antimicrobials in Dry Cow Strategies

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WHAT IS RESPONSIBLE USE?

The Responsible Use of medicines means: “using medicines as little as possible and as much as necessary”.

Little as possible

- ✓ Reduce risk of disease challenge by
 - Good farm management including ventilation, nutrition, access to fresh water, hygiene
 - Biosecurity
 - Farm health planning
 - Vaccination programmes
- ✓ Medicines must not be used as a substitute for good farm management

As much as necessary

- ✓ For antibiotics, diagnosis and prescription by vet
- ✓ Purchased from authorised supplier
- ✓ Follow label and vet instructions
- ✓ Correct dose
- ✓ Full course
- ✓ Observe the withdrawal period

INTRODUCTION

Facts about RUMA

(RESPONSIBLE USE OF MEDICINES IN AGRICULTURE ALLIANCE)

What is RUMA?

RUMA was established in November 1997 to promote the highest standards of food safety, animal health and animal welfare in the British livestock industry. It is a unique independent non-profit group involving organisations that represent all the stages of the food chain from 'farm to fork'. This reflects the importance of traceability, transparency and accountability in all stages of the chain: from primary food production, through processing, manufacturing and retailing to the final consumer. Its membership includes organisations representing interests in agriculture, veterinary practice, animal medicines industry, farm assurance, training, retailers, consumers and animal welfare interests.

RUMA aims to produce a co-ordinated and integrated approach to best practice animal medicine use. It has an established communications network with government departments and many non-governmental organisations.

Amongst its aims is to communicate practical strategies by which the need for use of antimicrobials might be reduced without adversely affecting either the welfare of animals, or the viability of a business, and provide guidance on how antimicrobials can be used responsibly when this is necessary for animal health and welfare.

What are the Aims of RUMA?

The main aims of RUMA are to:-

- a) Identify issues of scientific and public concern in the areas of public health, animal health, animal welfare and the environment which relate to animal medicine use.
- b) Provide an informed consensus view on the identified issues, developed by discussion and consultation.
- c) Establish and communicate guidelines which describe "best practice" in the use of medicines.
- d) Advise industry in the implementation of "best practice", especially in the development of codes of practice and assurance schemes.
- e) Communicate and to consult on:
 - i) The effective use of animal medicines.

- ii) The regulation of livestock production and use of medicines.
- f) Promote the appropriate use of authorised medicines for disease prevention and control.
- g) Liaise with National Authorities including DEFRA, Veterinary Medicines Directorate (VMD) and Food Standards Agency (FSA).
- h) Identify practical strategies to sustain responsible use of medicines.

How Does RUMA Achieve its Aims?

Chiefly through the publication of the RUMA Guidelines for the responsible use of medicines, including antimicrobials, for all the major food producing species such as dairy and beef cattle, sheep, pigs, poultry and fish. These are all working documents and built up from the contributions from member organisations. Available free of charge from the RUMA website www.ruma.org.uk, they are continually reviewed and updated in the light of new developments.

Contact

For more information on RUMA please go to the RUMA website www.ruma.org.uk or contact the Secretary General by email at rumasec@btinternet.com.

Classification of Animal Medicines

- POM-V (prescription only medicine - veterinarians): prescribed by a veterinary surgeon and supplied by a veterinary surgeon or a pharmacist against a veterinary surgeon's prescription;
- POM-VPS (prescription only medicine - veterinary surgeons, pharmacists and Suitably Qualified Persons (SQP)): prescribed by a veterinary surgeon, a pharmacist or a SQP and supplied by these professionals;
- NFA-VPS (non-food animal - veterinary surgeons, pharmacists and SQPs): no prescription required - supplied by a veterinary surgeon, a pharmacist or a SQP;
- AVM-GSL (authorised veterinary medicine - general sales list): no prescription required - can be supplied by any retailer.

All antimicrobial veterinary medicines are classified POM-V.

Veterinary Surgeons

Introduction

1. RUMA is a unique independent non-profit group involving organisations that represent all the stages of the food chain from 'farm to fork'. Amongst its aims is to communicate practical strategies by which the need for use of antibiotics and other antimicrobials might be reduced without adversely affecting either the welfare of animals, or the viability of a business, and provide guidance on how antibiotics and other antimicrobials can be used responsibly when this is necessary for animal health and welfare.

2. This guideline should be read together with the comprehensive RUMA guidelines for the responsible use of antimicrobials in cattle and other livestock.

Background

3. Dry cow therapy (DCT) is an essential part of a dairy farmer's routine to ensure the health and welfare of his/her cows.

4. The dry cow period is a high risk time for acquisition of new bacterial infections.

5. While there is no evidence of change in resistance patterns in animals or humans arising due to antibiotic use in intra mammary preparations, the current concerns over the use of antibiotics and possible implications with antimicrobial resistance mean it is timely to review the current practice to treat all cows at the end of lactation to both prevent new infections and treat any existing infections.

6. It is timely also to review the current situation in dairy farming particularly with regards the incidence of intra mammary infections, monitoring tools and the availability of products that were not available when recommendations such as the Five Point Plan were developed in the 1960s. The Five Point Plan recommended the use of antibiotics at the end of lactation in all dairy cows to treat existing infections and prevent new infections occurring during the risk periods when cows were non-lactating. Current RUMA guidelines recommend that there should be a strategy for drying off policies at the individual cow level.

7. Recent research has shown that it is still the case that doing nothing results in a significant number of new infections during the dry period and any existing sub clinical infections may not self-cure and will be present at the start of the next lactation (Berry and Hillerton 2002). This applies even with a lower level of intra mammary infections in the national herd and good management during the dry period and at calving.

8. More recently non antibiotic internal and external teat sealants have been developed. The internal teat sealants have been shown to be as effective as dry cow antibiotics in preventing new infections during the dry period. They do not have any therapeutic effect so any existing infections would not resolve unless there was a self-cure. External teat sealants are not as effective and require frequent reapplication (Hemling et al 2000).

9. Dry cow antibiotic therapy of the non-lactating mammary gland is currently (January 2015) used on more than 95% of cows in UK dairy farms.

10. It is used both therapeutically (to treat infections present at the end of the lactation) and prophylactically (to prevent new infections occurring over the dry period, primarily at the start of the dry period) with the combined aim of reducing the prevalence of infections present at calving (Neave et al. 1966; Smith et al., 1967c.)

11. Dry cow antibiotic therapy was first used in the early 1950s to prevent *Trueperella* (formerly *Corynebacterium*) *pyogenes* infections, known as summer mastitis (Pearson 1950 and 1951). These infections were common during the dry period and often resulted in the death of affected animals or, at the very least, a non-productive quarter, which economically was a disaster.

12. Earlier research had highlighted the dry period as a risk in terms of acquisition of many new infections including coliforms and *T. pyogenes* (Murphy and Hanson, 1943; Neave et al., 1950). There are two major risk periods to acquiring new infections during the dry period

- at the start of the dry period when the mammary gland is involuting; and
- at the end of the dry period just prior to calving when the mammary gland is undergoing colostrogenesis.

13. The highest risk period is at the start of the dry period when the udder undergoes involution and is 20 times more susceptible to new infections. Antibiotic treatment was shown to minimise this risk period (Neave et al. 1950).

14. Following from this work, dry cow antibiotic therapy was adopted as one of the recommendations in the mastitis control plan (later called the 'Five point plan') of the National Institute for Research in Dairying (NIRD)/ Central Veterinary Laboratory (Neave et al. 1966; Smith et al., 1967c). Over a three year period the use of dry cow antibiotic therapy (DCT) resulted in a 20% reduction in sub-clinically infected quarters (Wilson and Kingwell, 1975). In the UK, Antibiotic formulations in a long acting oil base in tubes to be inserted into the teat at the end of lactation were developed and used here and in Australia, New Zealand and the USA. However, the Nordic countries took a different approach and commonly used systemically injected antibiotics, usually intra muscular, and often selected only cows known to have intramammary infections, i.e. therapeutic use only.

Concerns over antibiotics used during the dry period

15. Concerns were raised over the long standing recommendation of administering antibiotics to all cows (Olsen 1975). The Nordic countries had already started to use a more selective approach to treatment of cows using extensive laboratory and field back up but such facilities were not available or affordable in the UK.

16. The widespread use of DCT was criticised as possible indiscriminate use of antibiotics in uninfected cows. There was also speculation that this may lead to the development of antibiotic resistance in both animal and human populations due to overuse or possible residues (Bratlie, 1972). However, to date there is no direct evidence to support either of these hypotheses with regards the use of antibiotic dry cow therapy (IDF antimicrobial resistance statement).

17. Scientists and veterinary organisations from other countries have also queried the need for dry cow therapy on all cows (Macmillian at al., 1983; Browning et al 1984; Kirk et al., 1994).

Current situation

18. In 2002 a re-examination of selective dry cow treatment in four UK herds was published (Berry and Hillerton 2002). This study examined the need for dry cow therapy on all cows in four herds - two with low somatic cell counts and no *Streptococcus agalactiae* or *Staphylococcus aureus* and two herds with low somatic cell counts and undergoing conversion to organic status. Cows were randomly allocated to either dry cow antibiotic in all quarters or no treatment at drying off. Clinical cases of mastitis during the dry period were observed in untreated cows and there were significantly fewer new intramammary infections and clinical cases in quarters of treated cows compared with untreated cows. There was no difference between the herds and management with regards the new infections acquired during the dry period.

19. This highlighted that the dry period still presents a major risk for acquisition of new infections in cows left untreated at drying off, even in herds with a low level of intramammary infections and good management.

Non-antibiotic alternatives for use during the dry period

20. External teat sealants of various types and formulations, with the aim of sealing the teat end during the dry period, have been tried. They have had limited success in reducing the incidence of new infections acquired during the dry period and persistence of material on the teat (Timms et al 1997; Hemling et al., 2000).

21. Internal teat sealants were first used in 1977 (Meaney 1977). An internal teat sealant, comprising the dense salt, bismuth subnitrate, in a paraffin base inserted via the teat canal into each quarter, demonstrated equivalent protection of the mammary gland to new infections compared with long-acting antibiotics at drying off (Woolford, 1998). It was noted that hygiene when inserting this teat sealant was crucial as the teat sealant has no anti-bacterial activity. This product appeared to protect those quarters where an effective teat plug was slow in forming after the cessation of milking and to provide protection during the last few weeks of the dry period. Subsequent studies, under a variety of conditions, have shown this teat sealant to be equivalent to DCT in terms of protection against new infections in the dry period and significantly superior to no antibiotic treatment (Berry and Hillerton, 2002, Huxley et al., 2002, Berry and Hillerton, 2007, Parker et al., 2007, Parker et al., 2008, Bradley et al., 2010). Some studies have used pre-partum heifers where infection status was not known (Parker et al., 2007 and 2008) and others used both uninfected and infected quarters (Berry and Hillerton 2002). All showed no adverse effects from using an internal teat sealant in infected quarters during the dry period. The teat sealant contains no known

antimicrobial active product. The addition of internal teat sealant with an antibiotic, was shown to significantly reduce new infections, compared with an antibiotic alone in longer dry periods. As the dry period lengths were longer than the claim of activity for the antibiotic, it would be assumed that this was due to protection prior to calving by the internal teat sealant (Berry and Hillerton 2007).

22. This teat sealant was launched as OrbeSeal™ (Boviseal in Ireland and Teat Seal in New Zealand) and the registration data state it can be used as a sole product at drying off in low somatic cell count uninfected cows. Other internal teat sealants have been launched and are now registered in the UK and other internal teat sealants are available in other countries. Internal teat sealants are the only products available that have been shown to be effective in preventing acquisition of new infections throughout the entire dry period. They are an essential component of selective dry cow therapy.

23. A vaccination is available STARTVAC® against coliforms and staphylococci species, with claims to strengthen the immunity in cows and heifers. Its claims are as one part of a mastitis prevention programme and require immunisation of the whole herd by reducing the severity and incidence of coliforms and staphylococci species. It has no particular claim for the dry period.

Factors to consider when contemplating selective dry cow antibiotic use

Infection status of the herd

24. The infection status of the herd is a factor to consider when deciding on screening options and setting criteria or levels to use for selection of cows. Herds can have varying levels of bacteria e.g. *Staphylococcus aureus*, *Streptococcus uberis*. In such circumstances, it is advisable to screen cows by

- routine bacteriological monitoring of clinical cases or
- selection of cows at drying off or
- bulk milk sampling at regular intervals and using bulk milk bacteriology or PCR (Polymerase Chain Reaction) to detect bacteria such as *Streptococcus agalactiae*. *Streptococcus agalactiae* rarely survives for long periods outside the udder and detection of this bacterium in a bulk milk sample using PCR indicates infections within the herd.

Herd management

25. Recent work on selective dry cow strategies – no dry cow therapy, antibiotic therapy and internal teat sealants - has been carried out on both organic and conventional herds (Berry and Hillerton, 2001 a and b and Berry et al 2004). Statistical analysis indicated that herd factors and management (including conventional or organic or low somatic cell count) was not a significant risk. All herds are at similar risk to new infections during the dry period with the major risk factor being if cows were left untreated during the dry period.

26. Currently organic herds can use internal teat sealants in all cows at the start of the dry period and apply for a derogation to use antibiotics at the start of the dry period on cows considered to be infected. Usually an elevated somatic cell count is considered to indicate an infection with anything over 200,000 cells per ml considered as indicating an infected cow.

Hygiene at drying off

27. Whatever product is used at drying off an aseptic technique is essential. Even those products containing antibiotics do not protect against all bacteria. Anecdotal and published cases of infections in the dry period attributed to poor infusion technique are available (Milnes and Platter, 2003).

Treatment at cow or quarter level

28. There is some discussion as to whether treatment should be at the whole udder or quarter level but most evidence supports the fact that if one quarter is at risk of infection there is a higher risk in the other three quarters. Thus any dry cow strategy should be applied at the cow not the quarter level.

Dry period length

29. Previous work has demonstrated that a dry period longer than the anticipated length of activity of the dry cow antibiotic is a risk factor for more intramammary infections and clinical incidence in the next lactation (Natzke et al., 1975, Rindsig et al., 1978, Bradley and Green, 2001, Roberts et al., 2003, Berry and Hillerton 2002, Berry and Hillerton 2007). Thus, if using an antibiotic at drying off, the use of a teat sealant in addition to DCT to provide protection for the period beyond the activity of the dry cow antibiotic is advisable.

Infection status at drying off

30. The internal teat sealants available in the UK claim no antimicrobial activity and the recommendation is to use these products in low somatic cell count uninfected quarters, when used alone. Internal teat sealants have been used in cows with quarters infected at drying off with no adverse effects but cure rates are low and more likely attributable to self-cure rather than therapeutic activity of the internal teat sealant.

Selection criteria to use to decide on infection status at the cow level

31. It is generally accepted that a somatic cell count below 200,000 cells per ml at the cow level is indicative of a low probability of being infected (IDF Bulletin 321, IDF Guide to use and interpretation of cell counts 2013). It is also recommended that more than one somatic cell count is used to determine infection status (IDF Bulletin 321, IDF Guide to use and interpretation of cell counts 2013). Using this cell count as a guide along with examination of the udder and teats for any abnormal changes should provide an indicator to the infection status of the udder. For practical purposes selection criteria may use the somatic cell count history and clinical mastitis data for the lactation prior to the dry period (O'Rourke, 2005). Other recognised tests for the detection of subclinical mastitis may also be used e.g. conductivity. It is recommended that cows should have had no clinical cases and all somatic cell counts for that lactation should have been less than 200,000 cells per ml if internal teat sealant is to be used alone. Appendix one in the IDF Bulletin 321 gives examples of the quarter cell counts that obtained within quarters at varying cow cell count levels. Registration work for OrbeSeal™ detected no infections due to major pathogens in quarters, present at both drying off and calving, using the criteria of all cell counts less than 200,000 cells per ml and no clinical infections in the relevant lactation.

Antibiotic choice

32. There are a range of antibiotics available for use in current dry cow products and only one product is currently available that contains a Critically Important Antibiotic (CIA) cefquinome, a fourth generation cephalosporin. This antibiotic is only available for animal treatment.

Options for treatment at the start of the dry cow period

33. Use the monitoring results to decide the appropriate treatment for each cow you are drying off

- do nothing and monitor closely for the potential development of mastitis (a health and welfare risk for the cow)
- use an internal teat sealant
- use dry cow antibiotics
- use both an internal teat sealant and antibiotic.

34. Each farm should have a strategy at the cow level for the dry period and this should be discussed with your vet and reviewed regularly.

Individual farm strategies

35. These should take account of various risk factors including

- bulk milk somatic cell count value,
- routine screening for bacteria including *Streptococcus agalactiae*,
- if individual cow somatic cell counts are carried out
- purchase history of the cows.

36. Each farm must be able to identify cows with intra mammary infections from those that are uninfected. Ideally this would be by using bacteriology but this can be time consuming and expensive. A good indicator of intra mammary infection status is using somatic cell counts. It is generally accepted that for on farm management a somatic cell count for the cow level of above 200,000 cells per ml would indicate infection is present in one or more quarters. It is recommended to use more than one somatic cell count to obtain a reliable result on intra mammary infection status (at least three and preferably for the whole lactation). Clinical mastitis history is also a good indicator of risk of intra mammary infection.

37. Ideally cows that would be suitable for an internal teat sealant alone would have had

- somatic cell counts below 200,000 cells per ml for all cell counts
- no clinical cases of mastitis
- no obvious teat lesions at the time of drying off.

38. It is recommended to carry out routine bacteriology on clinical cases and screen bulk milk samples at regular intervals for *Streptococcus agalactiae*, which is very contagious and can cause intra mammary cases, without extremely elevated somatic cell counts. *Streptococcus agalactiae* is the most frequent cause of neonatal death in man but these cases do not usually arise from bovine infections. However, reports from the Nordic countries have highlighted an increase in the prevalence of *Streptococcus agalactiae* cases in dairy cows. While this increase will be multifactorial, contributing factors may be not identifying all cases with routine monitoring and use of selective antibiotics at the end of the dry period in Nordic countries.

39. Remember, antibiotics should be used as little as possible and as much as necessary.

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The Responsible Use of Medicines in Agriculture
Alliance

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RUMA is made up of the following organisations:

Agricultural Industries Confederation (AIC)

AHDB – Dairy (formerly known as Dairy Co)

AHDB – Pigs (formerly known as BPEX) and AHDB – Beef and Lamb (formerly known as EBLEX)

Animal Health Distributors Association (AHDA)

Animal Medicines Training Regulatory Authority (AMTRA)

Assured Food Standards (AFS) better known as Red Tractor Assurance

British Egg Industry Council (BEIC)

British Poultry Council (BPC)

British Retail Consortium (BRC)

British Veterinary Association (BVA)

City and Guilds Land Based Services

Dairy UK

Game Farmers' Association (GFA)

Linking Environment & Farming (LEAF)

National Beef Association (NBA)

National Farmers' Union (NFU)

National Office of Animal Health (NOAH)

National Pig Association (NPA)

National Sheep Association (NSA)

NFU Scotland (NFUS)

Royal Association of British Dairy Farmers (RABDF)

Royal Pharmaceutical Society (RPS)

Royal Society for the Prevention of Cruelty to Animals (RSPCA)

Scottish Salmon Producers' Organisation (SSPO)