

## 1. Mastitis in the Dry Period – a brief summary:

“Mastitis is one of the most important problems in the dairy industry, causing economic loss and milk quality reduction. Mastitis is mainly caused by bacterial intramammary infection (IMI)”.<sup>1</sup>

There are broadly speaking two different types of cell wall types among bacteria, gram-positive and gram-negative. It is estimated that around “40% of clinical mastitis cases are caused by gram-negative bacteria”<sup>2</sup>.

## 2. The Limitations of Antibiotics in the dry period:

Many antibiotics, including most of those routinely used in the dry period, are relatively ineffective against gram-negative bacteria. The Merck Manual states that while “numerous commercial [antibiotic] products are available and include Penicillin, Cloxacillin, Cephapirin, Ceftiofur or Novobiocin ... most commercial dry cow antibiotics have little or no activity against gram-negative pathogens, and their administration at the start of the dry period will not be effective against new infections that begin during the periparturient period.”<sup>3</sup>

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<sup>1</sup> Leelahapongsathon, Kansuda, et al. "Factors in dry period associated with intramammary infection and subsequent clinical mastitis in early postpartum cows." *Asian-Australasian journal of animal sciences* 29.4 (2016): 580.

<sup>2</sup> Hogan, Joe, and K. Larry Smith. "Coliform mastitis." *Veterinary research* 34.5 (2003):507519.

<sup>3</sup> From The Merck Veterinary Manual, online version. Alexandra Winter, ed. Copyright © 2022 Merck & Co., Inc., Rahway, NJ, USA and its affiliates. All rights reserved. Used with permission. Available at: <https://www.merckvetmanual.com/reproductive-system/mastitis-in-large-animals/mastitis-in-cattle>. Accessed October 5, 2022.

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By way of an example, “Cloxacillin [a popular antibiotic in the dry period] is active against most Gram-positive cocci, but *E. faecalis* is relatively resistant ..., Enterobacteriaceae [this family include *Salmonella*, *Escherichia coli*, *Klebsiella*, and *Shigella*] and *Ps. Aeruginosa* are resistant, as are Gram-negative anaerobes.”<sup>4</sup>

Unlike gram-positive bacteria, gram-negative bacteria have a unique outer membrane consisting of a complex lipopolysaccharide. The structure of the outer membrane provides gram-negatives with an extra layer of protection, as a result, they are often environmental.

### 3. The Need for a Teat Sealant:

Given the foregoing limitations of antibiotics it is widely acknowledged that, “Prevention of infections through reduction of exposure is the cornerstone of mastitis control on dairy farms.”<sup>5</sup>

“With few exceptions, mastitis occurs when microbes enter the teat via the teat canal.”<sup>6</sup>

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<sup>4</sup> Bush, Karen. "Beta-lactam antibiotics: Penicillins." Antibiotic and chemotherapy, (2010): 200-225

<sup>5</sup> Schukken, Ynte, et al. "The “other” gram-negative bacteria in mastitis: *Klebsiella*, *Serratia*, and more." Veterinary Clinics: Food Animal Practice 28.2 (2012): 239-256.

<sup>6</sup> From The Merck Veterinary Manual, online version. Alexandra Winter, ed. Copyright © 2022 Merck & Co., Inc., Rahway, NJ, USA and its affiliates. All rights reserved. Used with permission. Available at: <https://www.merckvetmanual.com/reproductive-system/mastitis-in-large-animals/mastitis-in-cattle>. Accessed October 5, 2022.

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An internal teat sealant is an “inert”<sup>7</sup> malleable paste infused into the teat to “protect cows from new mastitis infections during the dry period by providing a safe antibiotic-free physical barrier between the udder and the environment”.<sup>8</sup>

The intention of a teat sealant has simply been to lock out bacteria and help prevent new infections. Teat sealants containing Bismuth Subnitrate are uniformly described as “inert” nonantibiotic products that act as a physical barrier to the colonization of bacteria through the teat canal during the dry period.<sup>9</sup>

Internal teat sealants can be used with or without antibiotics.

#### **4. The Problem:**

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Conventional Bismuth Subnitrate Teat Sealants (Conventional Teat Sealants) have been the dairy industry’s tool of choice for 20 years in reducing the incidence of mastitis during the dry period. The problem, however, is that Conventional Teat Sealants are intrinsically flawed. Conventional Teat Sealants have been carefully formulated to be “inert”<sup>10</sup> and exhibit little, or no, demonstrable antimicrobial activity.

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<sup>7</sup> <https://www2.zoetisus.com/products/dairy/orbeseal-teat-sealant?>

<sup>8</sup> <https://www2.zoetisus.com/products/dairy/orbeseal-teat-sealant?>

<sup>9</sup> (Meaney et al., 2001; Codex Alimentarius, 2016)

<sup>10</sup> Notcovich, S., et al. "Effect of bismuth subnitrate on in vitro growth of major mastitis pathogens." *Journal of dairy science* 103.8 (2020): 7249-7259.

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Due to their inert, yet sticky nature, these Conventional Teat Sealants have the potential to acquire microbes from the environment, during or post infusion. These pathogens are then able to exploit the sealant.

Disturbingly , under certain circumstances microbial growth can be sustained within the sealant, i.e. bacteria can use the sealant paste as a medium for growth. When testing such a product, MCS, an independent, accredited, microbiological laboratory reported, “The data shows that the growth of the organisms is sustained within the product, and the preservative system has negligible effect on the organisms introduced.” <sup>11</sup>

Conventional Teat Sealants fail one of the most basic adequacy of preservations tests<sup>12</sup>.

On farm, this serious shortcoming is known (at least by the drug companies) and documented. **“Multiple case of Pseudomonas mastitis occurred in several herds” <sup>13</sup> after the introduction of a Conventional Teat Sealant in New Zealand. The outbreak was traced back to syringes becoming contaminated prior to infusion.** Given the results of the laboratory tests this is not surprising.

Antibiotics will not necessarily redress the shortcoming. The bacteria that were demonstrated to exploit Conventional Teat Sealants were of the gram-negative types that are also a weakness for many antibiotics.

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<sup>11</sup> MCS Laboratory email communication dated 28 April 2021.

<sup>12</sup> Efficacy of Antimicrobial Preservation (European Pharmacopoeia) TmPh1.

<sup>13</sup> Sanford, Carolyn Jane. *Innovative dry cow therapy*. 2006. PhD Thesis

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## 5. The Solution - The LactoSeal Advantage:

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LactoSeal is just like a Conventional Bismuth Subnitrate Teat Sealant but it is further impregnated with Phenoxyethanol, a powerful, yet safe, GRAS (Generally Regarded As Safe) listed, antimicrobial.

“Phenoxyethanol has a broad range of antimicrobial activity, but the greatest activity is against gram-negative organisms. It is particularly effective against *Pseudomonas aeruginosa*...”<sup>14</sup>

LactoSeal’s secondary antimicrobial protection inhibits gram-negative and gram-positive bacteria within, or on, the sealant, making it much more difficult for bacteria to exploit the sealant.

LactoSeal can be used just like any Conventional Teat Sealant without any change of protocol.

Howard Marginson PhD DIC

Zelpharma Ltd – 11 Oct 2022

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<sup>14</sup> REV, EXPERT PANEL COSMET INGREDIENT. "Final report on the safety assessment of phenoxyethanol." *Journal of the American College of Toxicology* 9 (1990): 259-278.