

Technical Bulletin



Equivalence Study of Two Internal Teat Sealants*

*This technical bulletin is a brief summary of Rowe SM, Godden SM, Nydam DV, et al. Randomized equivalence study comparing the efficacy of two commercial teat sealants in dairy cows. *J Dairy Sci* 2020. doi: 10.3168/jds.2019-17884 (e-pub ahead of print).

Objective

To evaluate Lockout® (bismuth subnitrate) by comparing it directly to Orbesal® (bismuth subnitrate) in a randomized, positively controlled equivalence clinical trial during the dry period and the first 100 days of lactation utilizing health indicators.

Results

Intramammary Infection (IMI) at Dry-Off and at 1–13 Days in Milk (DIM)		
	Crude Quarter-Level Prevalence – Dry-off, %	Quarter-Level Prevalence – 1–13 DIM, %
LOCKOUT	22.9	12.0
ORBESEAL	21.1	13.5

Effect of Internal Teat Sealant Group on Dry-Period New IMI Risk and IMI Cure Risk		
	Crude Dry Period New IMI Risk, %	Crude Dry Period IMI Cure Risk, %
LOCKOUT	10.4	94.0
ORBESEAL	11.6	91.6

Effect of Internal Teat Sealant Group on Clinical Mastitis and Culling/Death During First 100 Days of Lactation		
	Crude 100-Day Clinical Mastitis Risk, %	100-Day Culling or Death Risk, %
LOCKOUT	19.0	10.3
ORBESEAL	18.9	10.8

Effect of Internal Teat Sealant Group on Milk Yield and Somatic Cell Counts (SCC) During the First 100 Days of Lactation		
	Estimated Marginal Means for Milk Yield, kg	Marginal Mean SCC on the Linear Scale, Units of 103 Cells/mL
Lockout® (bismuth subnitrate)	43	71
Orbeseal® (bismuth subnitrate)	43	67

Conclusion

- LOCKOUT in this multi-site, multi-herd equivalence clinical trial performed as well as ORBESEAL for health indicators during the dry period and during the first 100 days of lactation.
- Producers should consider using LOCKOUT as part of a dry cow therapy program.

Purpose

- To optimize udder health in early lactation, it is important to prevent new intramammary infections (IMI) during the dry period. The keratin plug is an important component of protecting against new IMI; however, the keratin plug may take weeks to form, and may be expelled in response to intramammary pressure late in the dry period. To reduce this risk, producers utilize an internal teat sealant (ITS) in the teat canal and teat cistern. In multiple studies, ORBESEAL has been shown to reduce IMI during the dry period when used in conjunction with a dry cow therapy antibiotic, thereby reducing somatic cell count (SCC) and clinical mastitis risk in early lactation.
- The objective of this study was to evaluate LOCKOUT, by comparing it to ORBESEAL in a multi-site, randomized, positively controlled equivalence clinical trial, for health indicators during the dry period and during the first 100 days of lactation.

Study Design

Study Herds: There were five herds from three study sites (New York = 1, Minnesota = 2, California = 2). Selected herds were of sufficient size to dry off a minimum of 15 cows per week and were on a monthly Dairy Herd Improvement Association (DHIA) testing schedule, including individual SCC and milk production, and consistently recorded clinical mastitis and culling events.

Enrollment and Randomization: Eligible cows required at least three functional quarters, an expected dry period length of 30 to 90 days, no history of recent antibiotic treatment, no clinical mastitis, not lame and not in poor body condition.

Treatments: Cows were block-randomized into two groups, “ORBESEAL” and “LOCKOUT,” with treatment group name indicating which ITS would be used in enrolled quarters at the time of dry-off. An arbitrary decision was made to use a block size of 18, with 11 unique blocks, coinciding with the approximate number of cows dried off in the study dairies each week. All study animals were treated with Dry-Clox® (cloxacillin benzathine) prior to ITS infusion.

Follow-up During the Dry Period and Post Calving: Farm staff, responsible for detecting clinical mastitis and other disease events during the dry period and early lactation, were masked to treatment status of cows at dry-off. However, it was possible for parlor staff to determine treatment group for the first few milkings due to the white or blue color of the teat sealant present in foremilk. Duplicate milk samples were collected from each quarter at dry-off and at 1–13

days in milk (DIM). Samples were collected for all herds pre-milking except for Farms C and E, whose samples were collected post milking and were immediately chilled on ice and transported to the site laboratory for storage. Somatic cell count and milk yield data were measured at monthly intervals, following the regular DHIA schedule.

Microbiological Culture of Milk Samples: The infection status of each quarter at enrollment and 1–13 DIM was determined using standard bacteriological methods at the three regional laboratories. At the Minnesota and New York laboratories, isolates were identified immediately using the matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF). MALDI-TOF was unavailable in California, so isolates identified there were stored in glycerol and submitted to the Minnesota laboratory. If a glycerol vial failed to yield a single isolate, the original milk sample was re-cultured at the California lab, and the isolate was resubmitted to Minnesota for identification.

Results

Enrollment: Herd size ranged from 1,050 to 9,200 milking cows, and bulk milk SCC prior to enrollment ranged from 145,000 to 230,000 cells/mL. There were no meaningful differences in herd demographics observed between treatment groups.

Loss to Follow-up: Loss to follow-up was similar between treatment groups during all phases of the study. The final number of quarters at risk of having an IMI at 1–13 DIM for each group was Orbeseal® (bismuth subnitrate) ($n = 1,382$) and Lockout® (bismuth subnitrate) ($n = 1,425$). The final number of cows at risk for clinical mastitis and culling was ORBESEAL ($n = 415$) and LOCKOUT ($n = 419$).

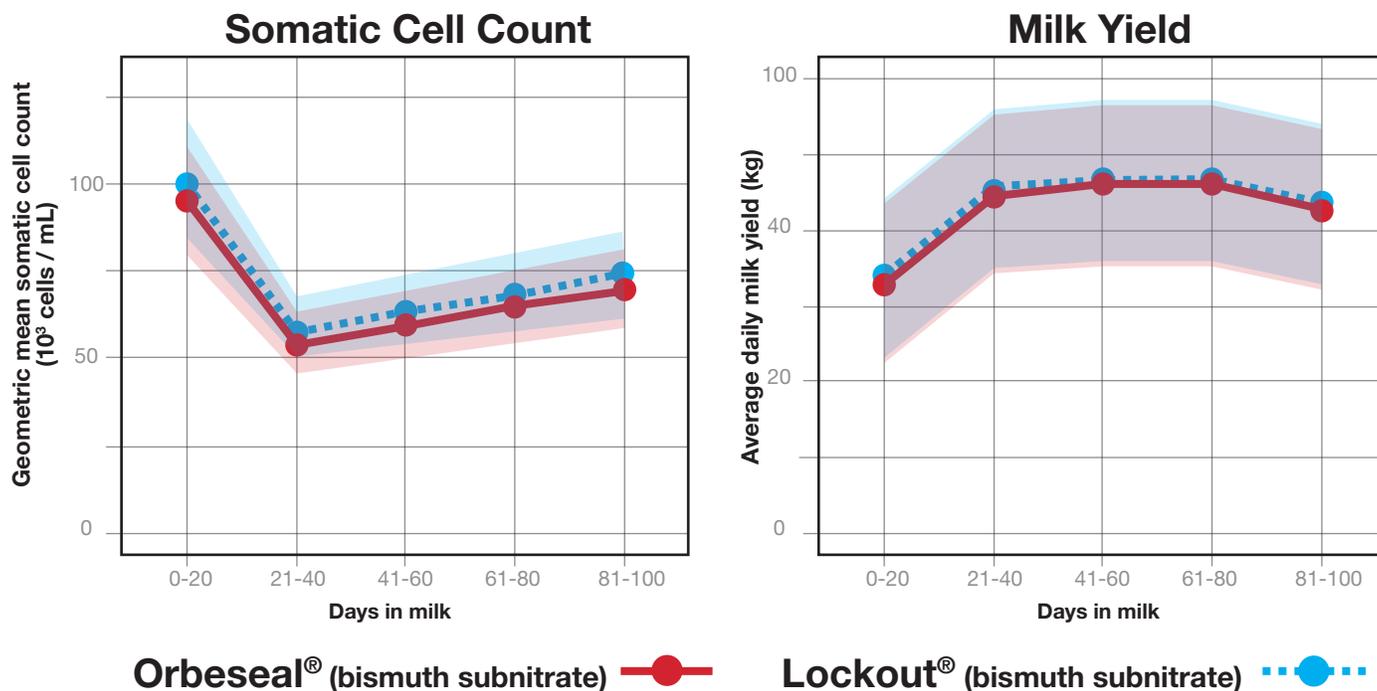
Intramammary Infection at Dry-Off and at 1–13 Days in Milk: The crude quarter-level prevalence of IMI at dry-off was similar in the LOCKOUT (22.9%) and ORBESEAL (21.1%) groups. The quarter-level prevalence of IMI at 1–13 DIM was similar in each group: LOCKOUT (12.0%) to ORBESEAL (13.5%). The final generalized linear mixed model found that LOCKOUT quarters had a similar adjusted IMI risk at 1–13 DIM (14.1%) to ORBESEAL quarters (16.0%, with Risk Difference (RD): -1.9% , 95%; Confidence Interval (CI): $-5.0, 1.2\%$). The majority of cultures yielded no growth at both dry-off (78%) and 1–13 days in milk (87.2%). The most frequently cultured organisms at dry-off were Gram-positive organisms: non-aureus *Staphylococci* (NAS) (15.7%), *Staphylococcus aureus* (0.4%), *Streptococcus* spp. and Strep-like organisms (2.3%), as well as other Gram-positive bacteria (3.9%). Gram-negative organisms represented only 0.5% of the cultures.

Effect of Internal Teat Sealant Group on Dry-Period New IMI Risk and IMI Cure Risk: The final generalized linear mixed model found that LOCKOUT quarters had a similar adjusted dry-period new IMI risk to ORBESEAL quarters (12.4% vs. 13.8%, respectively, with RD: -1.4% , 95%; CI: $-4.3, 1.6\%$). The dry-period IMI cure risk was similar in the LOCKOUT (94.0%) and ORBESEAL (91.6%) groups. The final generalized linear mixed model estimated that LOCKOUT quarters had similar adjusted dry-period cure risk to ORBESEAL quarters (94.4% vs. 91.8%, with RD: $+2.6$, 95%; CI: $-1.8, 7.1\%$).

Effect of Internal Teat Sealant Group on Clinical Mastitis and Culling/Death During the First 100 Days of Lactation: The 100-day clinical mastitis risk in all cows was similar in the LOCKOUT (19.0%) and ORBESEAL (18.9%) groups. The 100-day culling or death risk in all cows was similar in the LOCKOUT (10.3%) and ORBESEAL (10.8%) groups.

Effect of Internal Teat Sealant Group on Milk Yield and Somatic Cell Counts during the First 100 Days of Lactation: In the first 100 days of lactation, there were no significant differences between LOCKOUT and ORBESEAL in SCC and daily milk yield, as seen in Figure 1 (next page).

Figure 1.



Estimated marginal means of test-day somatic cell count and milk yield during the first 100 days of lactation for cows receiving LOCKOUT or ORBESEAL at dry-off. Ninety-five percent confidence intervals are indicated by colored/shaded areas. No statistical interaction was observed between treatment group and days in milk at herd test, which is why the curves are parallel.

Discussion and Conclusion

LOCKOUT performed as well as ORBESEAL in this multi-site, multi-herd, positively controlled equivalence clinical trial during the dry period and during the first 100 days of lactation. The authors concluded that producers should consider using LOCKOUT as part of their dry cow therapy program.

LOCKOUT Withdrawal Information: LOCKOUT requires no milk or pre-slaughter withdrawal when used alone. If dry cow treatment is used in conjunction with LOCKOUT, follow recommended antibiotic withdrawal times per the label.

DRY-CLOX (cloxacillin benzathine) RESIDUE WARNINGS: For use in dry cows only. Not to be used within 30 days of calving. Any animal infused with this product must not be slaughtered for food until 30 days after the latest infusion. Precautions: Because it is a derivative of 6-aminopenicillanic acid, DRY-CLOX has the potential for producing allergic reactions. Such reactions are rare; however, should they occur, the subject should be treated with antihistamines or pressor amines, such as epinephrine.