A randomized non-inferiority study evaluating the efficacy of two commercially available teat sealants in dairy cows.

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INTRODUCTION

Subclinical intramammary infection acquired during the dry period can contribute to decreased production and milk quality (Gonçalves et al., 2018). Failure of formation of a keratin plug early in the dry period leaves the teat at risk to acquire a new IMI (Dingwell et al., 2004). Internal teat sealants (**ITS**) at dry-off have been shown to reduce the risk of acquiring a new IMI during the dry period (Vasquez et al., 2018; Winder et al., 2019).

OBJECTIVE

The objective was to compare a new ITS (ShutOut [**SO**], Merck Animal Health, Madison, NJ) to the first product on the market (Orbeseal [**ORB**], Zoetis, Parsippany, NJ) in a trial evaluating quarter-level intramammary infection (IMI) dynamics over the dry period and cow-level health events through 120 DIM.

MATERIALS AND METHODS

This study was conducted on six commercial dairy farms in IA and MN. Eligible cows were cultured prior to dry-off with 500 mg cloxacillin benzathine (Orbenin DC, Merck & Co., Rahway, NJ, USA) and again after calving. Generalized linear mixed models were used to build univariable and multivariable models exploring the relationship between explanatory variables of interest and IMI at enrollment, IMI at 1-14 DIM, cured IMI risk, and new IMI risk (**NIMI**). A non-inferiority analysis evaluated the effect of ITS treatment on quarter-level dry period NIMI risk, with an a priori margin of non-inferiority established at 5%. The null hypothesis tested was that risk of NIMI for SO was ≥+5% than the NIMI risk for ORB, thus asserting that SO is inferior to ORB. Generalized linear mixed models were used to assess the risk of clinical mastitis, culling, and death before 120 DIM. Kaplan-Meier curves were developed to show the incidence of clinical mastitis, culling, and death. The effect of treatment on milk yield and $\log_e$ SCC were analyzed using repeated measures models.

This study concludes that the new ITS (ShutOut) is not inferior to the original product (Orbeseal) at preventing new IMI during the dry period in dairy cattle. Additionally, no differences were detected between other quarter and cow-level parameters.

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RESULTS

There were 418 cows enrolled in the ORB group and 404 in the SO group. Risk difference estimates and 95% CI were determined from generalized linear mixed models in R. Final models included random intercepts for 'cow, herd, and cow within herd' for IMI at Dry Off (IMI at DO); 'cow and herd' for IMI at Post-Fresh (IMI at PF) and Cure IMI Risk; and 'cow' for New IMI Risk. Fixed-effect covariates included in the final model due to evidence for confounding when using the 10% change in estimate approach were: 'lactation' for IMI at DO and 'herd' for New IMI Risk. No fixed-effect covariates were included for IMI at PF and Cure IMI Risk.

Adjusted dry period new IMI risk in the ORB group was 33.1% versus 31.5% for the SO group. The risk difference (SO minus ORB) was determined to be -1.6% (95% CI: -1.8, -1.37). A margin of noninferiority for risk difference of +5% was specified *a priori*. The lower and upper limits of the 2-sided 95% CI for the risk difference of new IMI risk were below the margin of inferiority, indicating that ShutOut was not inferior to Orbeseal.

Estimated least square means (plus 95% CI's) of test-day log SCC by month fresh during the first 100 d of lactation were compared using repeated measures analysis for cows receiving ORB vs SO at dry-off (Graph A). There were no covariates included in the analysis. Repeated measures analysis did not determine an effect of treatment or treatment by month fresh interaction, but there was a difference detected between months fresh (P=0.008). Kaplan-Meier curves were developed to show the incidence of clinical mastitis (Graph B). No difference in mastitis incidence was detected (P=0.49).

TABLE 1. Final generalized linear mixed models (logistic regression) estimating the effect of internal teat sealant group on quarter level dry period IMI dynamics.

	Adjusted risk (%)	Risk Difference (%)	95% CI of Risk Difference	*P*-value
IMI at Dry Off				
Orbeseal	32.5			
ShutOut	29.9	-2.6	-2.8, -2.4	0.25
IMI at Post-Fresh				
Orbeseal	34.1			
ShutOut	31.5	-2.6	-2.81, -2.39	0.26
Cure IMI Risk				
Orbeseal	95.9			
ShutOut	96.7	0.8	0.007, 1.59	0.58
New IMI Risk				
Orbeseal	33.1			
ShutOut	31.5	-1.6	-1.8, -1.37	0.54

FIGURE 1. Non-inferiority hypothesis test for new intramammary risk difference between ShutOut and Orbeseal.

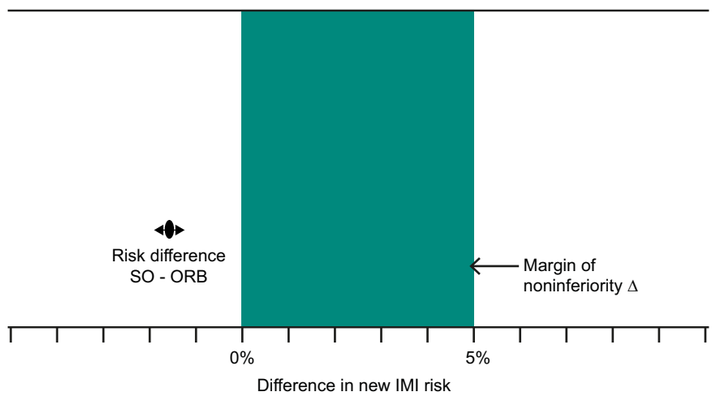
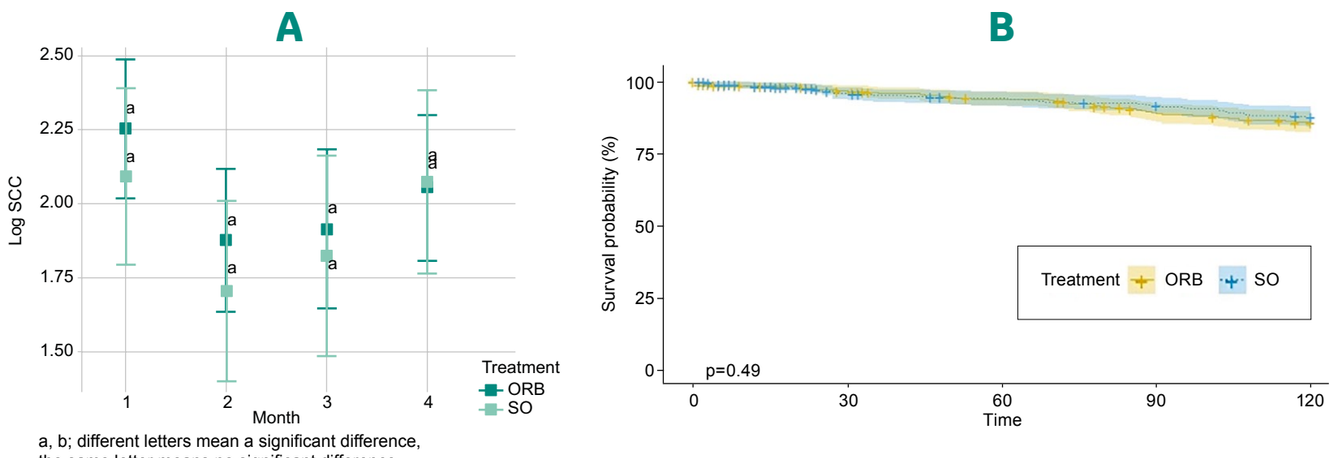


FIGURE 2. Least square mean estimates of log SCC by month fresh (A); B-Kaplan-Meier curve showing incidence of mastitis (B).



a, b; different letters mean a significant difference, the same letter means no significant difference.

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REFERENCES

Gonçalves, J. L., Kamphuis, C., Martins, C., Barreiro, J. R., Tomazi, T., Gameiro, A. H., Hogeveen, H, and dos Santos, M. V. 2018. Bovine subclinical mastitis reduces milk yield and economic return. Live Sci, 210, 25-32. doi:https://doi.org/10.1016/j.livsci.2018.01.016.

Dingwell, R. T., Leslie, K. E., Schukken, K. E., Sargeant, Y. H., Timms, J. M., Duffield, L. L., Keefe, G. P., Kelton, D. F., Lissemore, K. D., and Conklin, J. 2004. Association of cow and quarter-level factors at drying-off with new intramammary infections during the dry period. Prev Vet Med, 63(1-2), 75-89. doi:http://doi.org/10.1016/j.prevmed.2004.01.012.

Vasquez, A. K., Nydam, D. V., Foditsch, C., Wieland, M., Lynch, R., Eicker, S., and Virkler, P. D. 2018. Use of a culture-independent on-farm algorithm to guide the use of selective dry-cow antibiotic therapy. J Dairy Sci, 101(6), 5345-5361. doi:https://doi.org/10.3168/jds.2017-13807

Winder, C. B., Sargeant, J. M., Hu, D., Wang, C., Kelton, D. F., Leblanc, S. J., . . . O'Connor, A. M. 2019. Comparative efficacy of teat sealants given prepartum for prevention of intramammary infections and clinical mastitis: a systematic review and network meta-analysis. Anim Health Res Rev, 20(2), 182-198. doi:https://doi.org/10.1017/S1466252319000276.

MSD Animal Health