### Evolution of BRD metaphylaxis to optimize cost and judicious use practices

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### Abstract

Conventional metaphylactic antimicrobial regimens are applied to populations perceived at elevated risk of developing bovine respiratory disease (BRD). Whisper On Arrival® (WOA) was developed as a chute side tool to individually predict BRD risk for subsequent metaphylaxis decisions. The technology utilizes up to 4 data points to calculate prediction estimates: heart sound, lung sound, body weight and rectal temperature. A multi-site randomized clinical trial consisting of auction market-derived beef calves assessed the WOA technology against a traditional metaphylaxis program. Calves were followed to either a short-term endpoint (50 or 60 days) or closeout. Across all sites, pens allocated to WOA observed a reduction in metaphylactic antimicrobial use by 10% to 43%. Additionally, no significant differences ( $P \le 0.05$ ) in health or performance outcomes were observed compared to the traditional metaphylaxis program.

**Key words:** bovine respiratory disease complex, metaphylaxis, prediction

### Introduction

Bovine respiratory disease (BRD) is the most prevalent health syndrome observed by beef producers in the post-weaning phases of production. The disease complex is composed of multiple factors (environment, pathogens and animal factors) that work in tandem to manifest in clinical or subclinical disease. Multiple risk factors that are common (and sometimes unavoidable) within traditional marketing and procurement activities, have previously been associated with an elevated risk of developing BRD in backgrounding, stocker and feedlot production systems. Additionally, the bovine is highly adept at concealing clinical signs of BRD leading to late treatment administration or failing to recognize disease altogether.

Metaphylaxis has previously been defined as the administration of an antimicrobial to an animal population currently experiencing any level of disease before the onset of blatant illness.4 This management strategy is a proven practice implemented to reduce the overall impact of BRD throughout a given population. Although efficacious, prior work indicates that on average only 20% of animals receiving the metaphylactic antimicrobial observe benefit.2 Therefore, it is plausible that there is unnecessary cost (due to over-administration) associated with the practice of metaphylaxis. Additionally, antimicrobial use in livestock production is constantly in question by consumer and regulatory entities.1 However, removing the practice of metaphylaxis altogether is likely to result in not only negative economic impacts to the producer but also create an animal welfare issue due to withholding antimicrobial therapy to individual animals that could benefit from its effect.

### Whisper On Arrival technology

As mentioned above, metaphylaxis is an effective risk mitigation practice for BRD. However, it is not infallible and is wrought with economic and regulatory challenges. The Whisper On Arrival (WOA) technology was developed to predict the risk of developing BRD among individual animals which informs the user as to which animals may or may not benefit from metaphylactic therapy. Ultimately, this evolution of the practice of metaphylaxis is designed to reduce the cost of the metaphylaxis investment, provide an objective basis for the respective antimicrobial application, and maintain the positive attributes of traditional metaphylactic regimens.

Like a human stress test targeted to estimate the risk of cardiovascular disease, WOA leverages the stress accrued during traditional commerce while capturing multiple points of animal information to predict the risk of a future BRD event. The WOA system is composed of a machine-learning algorithm that utilizes lung sound, heart sound, body weight and rectal temperature at the time of processing to generate the risk prediction for the individual animal. The system is managed chute side and consists of a novel hand-held sound collection device (applied by the user) and a software application. An 8-second heart and lung sound file is collected by the sound collection device while body weight and rectal temperature data can be utilized either at the lot level (recommended) or individually. The user is provided a simple "Treat" or "Do Not Treat" outcome. The sensitivity and specificity of the system can be modified by the user for each incoming lot based upon its perceived BRD risk classification and/or the risk tolerance (or averseness) of the producer.

# Overview of the whisper On Arrival development program

The development of the WOA system consisted of a multi-step program consisting of observational and clinical study efforts combined with customer-experience trials. The Whisper On Arrival machine-learning algorithm was initially generated through a multisite observational study in which the above data (i.e., heart sounds, lung sounds, rectal temperature and body weight) were individually captured on incoming cattle without the application of metaphylaxis. Cattle were followed to closeout and all health, performance, and carcass metrics were used to develop the initial algorithm (data not shown).

The algorithm was then tested in a clinical trial study design. Across 4 sites in Texas (2 sites), Oklahoma, and Nebraska, 5,120 steer calves (in total) at medium- to high-risk of developing BRD were randomly allocated to one of 4 metaphylaxis treatment groups: 1) Negative control, 2) Positive control (100% Tildipirosin), 3) WOA (high threshold), and 4) WOA (low threshold). The 2 WOA thresholds reflect 2 different points of test accuracy: WOA-high reflects high diagnostic test sensitivity and lower specificity while WOA-low reflects low sensitivity and high specificity. The study population was followed to either a short-term timepoint (1 TX site [50 days] and NE site [60 days]) or to closeout (2nd TX site [233 days] and OK site [240 days]). Across all 4 sites, pens whose metaphylactic program was managed by the WOA technology (at both thresholds) displayed no statistical differences in health and performance outcomes compared to the positive control all while reducing metaphylactic antimicrobial usage by 10-43%.3 This reduction in metaphylaxis usage represents a direct cost-savings to the producer.

## Practical application of the WOA technology

The WOA technology presents a novel approach to BRD management and has been shown to provide the user with immediate cost-saving potential while providing additional stakeholders with an objective means of antimicrobial usage. Given the novelty of the system, a thorough site assessment is performed to evaluate labor resources (at processing), potential processing chute challenges, processing time expectations, understanding of hardware application and the user's risk tolerance. Upon initiation of WOA use, oversight and support continue to ensure user acceptance and confidence.

### Conclusion

Metaphylaxis is an important and highly effective BRD management tool. However, evolution of the practice is necessary to address expense management for the producer and judicious antibiotic use practices among the veterinary community, policy stakeholders and the end-consumer. The WOA technology was developed to predict individual animal BRD risk. This information is then used to decide which animals may benefit from BRD metaphylactic drug administration while forgoing therapy to those at reduced risk. The WOA technology has previously demonstrated the ability to maintain the expected benefits of traditional metaphylaxis while significantly reducing antibiotic usage. The reader is encouraged to refer to the full manuscript for additional information.

#### References

1. Baptiste KE, Kyvsgaard NC. Do antimicrobial mass medications work? A systematic review and meta-analysis of randomised clinical trials investigating antimicrobial prophylaxis or metaphylaxis against naturally occurring bovine respiratory disease. *Pathog* Dis 2017;75.

2. DeDonder KD, Apley MD. A review of the expected effects of antimicrobials in bovine respiratory disease treatment and control using outcomes from published randomized clinical trials with negative controls. *Vet Clin North Am Food Anim Prac* 2015;31:97-111, vi.

3. Nickell JS, Hutcheson JP, Renter DG, et al. Comparison of a traditional bovine respiratory disease control regimen with a targeted program based upon individualized risk predictions generated by the Whisper On Arrival technology. *Transl Anim* Sci 2021;5:txab081.

4. Nickell JS, White BJ. Metaphylactic antimicrobial therapy for bovine respiratory disease in stocker and feedlot cattle. Vet Clin North Am Food *Anim Prac* 2010;26:285-301.

