Summary

- BRSV can be resident in adult dairy cows, but subtle adverse effects on milk production can be difficult to detect, often due to the seasonal nature of BRSV infections.
- BRSV seasonality can pose a significant economic threat if vaccination is neglected due to negative diagnostic tests performed during periods of lower BRSV infection.
- A positive-control field research study investigated the impacts of BRSV and INFORCE™ 3 vaccination on the productivity of adult dairy cows.¹

- Overall, BRSV protection provided by INFORCE 3 helped improve estimated dairy income by approximately $36/head during the 315-day study period.
- BRSV protection provided by prepartum vaccination of heifers and cows with INFORCE 3 generated a numerical improvement (non-significant) in milk production for cattle enrolled in the study over a 4-month period (December-March).
- Significant improvements in milk production were observed for cattle enrolled in March (4.9%, P = 0.0225), as well as for cows of parity 3 or greater enrolled during February-March (5.1%, P = 0.0373).

Bovine respiratory syncytial virus (BRSV) infection is typically regarded as a disease limited to young calves due to the severe nature of clinical signs that can occur in young naïve animals. However, evidence suggests that BRSV often remains active in adult cattle and goes undetected since clinical signs in adult animals are far less obvious. Dairy cows that have had previous exposure to BRSV are even more likely to not exhibit signs of infection. The resulting condition for a typical dairy herd is a mild viral manifestation that may cause fever, slight inappetence, and a corresponding decrease in milk production, all without an easily identifiable source of these adversities.

Recent research offers a good example of undetected BRSV infection in adult cows. In a 2011 study, a healthy, well-vaccinated cow herd produced calves that generated BRSV antibody titers even though the cows were vaccinated with a viral respiratory vaccine that did not include a BRSV fraction. This seemingly healthy adult herd with no clinical signs of BRSV infection was passing maternal BRSV antibodies to their calves and also likely serving as sources of viral exposure.
Not only is BRSV difficult to detect in adult cows, natural seasonal fluctuations of BRSV infection can further obscure detection of the virus. A European epidemiological study (temperate climate) found that the highest incidences of BRSV infection occurred in autumn and winter compared to summer or spring. The researchers suggest that a steady, low-level rate of reinfection in seropositive cows throughout the year maintains a reservoir of infectious virus that can manifest more strongly in the fall and winter when environmental conditions favor spread of the virus. Shedding then leads to widespread dissemination through the herd. This form of seasonal high/low prevalence is not uncommon with several other infectious diseases and is often due to depressed immune function associated with increased stressors and physical demands required during certain times of the year. Such patterns should be familiar to most people since several human viral pathogens also tend to follow seasonal prevalence profiles.

The impact of BRSV on the productivity of adult dairy cows (not just young stock) is an emerging area of research interest. Earlier research has demonstrated that BRSV can adversely affect dairy productivity, and that BRSV vaccination of adult cows can generate positive outcomes. In a Pennsylvania study, prepartum vaccination of dairy cows with a product lacking the BRSV component (controls) was compared to vaccination with an identical program that included a BRSV fraction. Compared to controls, first-parity cows that received BRSV vaccination demonstrated greater milk production (3.06 lb/hd/day) during their first 21 weeks of lactation. Conception rates at first insemination were also greatly improved for both first- and second-parity cows that received BRSV protection.

Zoetis researchers recently conducted a study to generate additional insights about BRSV impacts on dairy productivity, and to assess the value of using INFORCE® 3 vaccine to help protect adult cows against BRSV infection.

INFORCE 3

INFORCE 3 is the first and only respiratory vaccine that prevents respiratory disease caused by BRSV while also aiding in the prevention of infectious bovine rhinotracheitis (IBR) and parainfluenza3 virus (PI3). INFORCE 3, developed specifically for needle-free intranasal administration at 1 mL/nostril, has shown excellent efficacy in helping prevent respiratory disease and helping reduce viral shedding. The vaccine contains proprietary temperature-sensitive IBR and PI3, and as well as naturally temperature-sensitive BRSV, so the vaccine strain replicates only in the relatively cool nasal passages. INFORCE 3 helps prime the immune system of cattle so a memory response is generated to subsequent vaccinations and disease challenges.

Dairy herds can benefit from this safe, effective, and novel vaccine. INFORCE 3 is approved for use in all classes of cattle: baby calves, on arrival, at weaning, before moving to group pens, or in prefreshening heifers and cows.

Experiment Design

A positive-control field research study was conducted to investigate the impact of BRSV vaccination using INFORCE 3 on the productivity of adult dairy cows. The study involved 849 Holstein dairy cattle and was conducted at a moderate-sized commercial dairy in California with a prior history of BRSV vaccine use.

Healthy cattle were enrolled in the study over a 4-month period spanning December through March. Exclusion criteria included any animal that was sick, had a somatic cell count (SCC) over 400,000 or a log-linear score over 5, had been dry over 80 days, or had an interval between vaccination and calving under 7 days. Individual enrollments occurred when a heifer or cow was moved to a close-up pen approximately 21 days prior to calving and was vaccinated intranasally with either INFORCE 3 or TSV-2® (similar to INFORCE 3 but lacking the BRSV component), thereby creating 2 overall treatment groups.

Treatment assignments, blocking, and randomization were performed at close-up, with enrollees placed into 1 of 6 groups based on parity and treatment. Cows were blocked into 2 groups on the basis of parity number: those initiating their second parity (P2), and those initiating their third parity or greater (P3+). Cows were further sorted into 2 subgroups based on their previous 305-day mature equivalent (305 ME) milk production (<25,000 lb). Since heifers were initiating their first parity (P1), predicted transmitting ability (PTA) estimates were used to form subgroups designated as low- or high-potential
producers. After blocking and sorting by parity and milk production, groups were moved into the close-up pens and randomly assigned to either the INFORCE™ 3 or TSV-2® treatment groups by vaccinating every other cow with the alternate product. Group enrollments/vaccinations occurred on one day each week at the dairy. The enrollment period concluded in late March with approximately 849 adult dairy cattle ultimately enrolled in the study, as shown in Table 1 (INFORCE 3 n=428; TSV-2 n=421). Health events, medical treatments, and reproductive outcomes were also recorded for each enrollee. The economic value of milk produced was calculated based on the California dairy milk price report and the average 4b cheese price over the 315-day span of the study, plus $1.50/100 lb (cwt) for presumed SCC, fat, and protein bonuses, yielding a total value of $17.53 per cwt of milk. Collected data were statistically analyzed using appropriate standard methods, with significance between treatments declared when \( P \leq 0.05 \).

### Results

Over the course of the entire 45-weeks of data collection, no significant overall differences in milk or reproductive parameters were detected between the INFORCE 3 and TSV-2 treatment groups. However, average daily milk production was numerically elevated by 0.65 lb/hd/day (0.83%, \( P = 0.4561 \)) for INFORCE 3 vaccinates (Figure 1). These results suggest that BRSV impacts were not sufficient at this dairy to exert statistically significant milk production effects when the entire 4-month enrollment period was assessed.

In contrast, BRSV vaccination with INFORCE 3 did generate significant milk production differences between treatment groups when evaluated based on the month(s) of vaccination/enrollment.

Average weekly milk production was recorded for each animal beginning at parturition and continuing for 27 to 45 weeks postpartum depending on enrollment date (maximum weeks of data collection: December=46; January=42; February=38; March=34). Health events, medical treatments, and reproductive outcomes were also recorded for each enrollee. The economic value of milk produced was calculated based on the California dairy milk price report and the average 4b cheese price over the 315-day span of the study, plus $1.50/100 lb (cwt) for presumed SCC, fat, and protein bonuses, yielding a total value of $17.53 per cwt of milk.

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### Figure 1 — Average daily milk production (lb/hd) by treatment during the entire study.
Figure 2 summarizes milk production for cattle depending on the month of vaccination. A significant ($P = 0.0225$) average improvement of 3.89 lb/hd/day (4.9%) was observed for all parities of cattle vaccinated with INFORCE™ 3 during the month of March. This productivity response to vaccination in March was consistent with the seasonality aspects of BRSV infection discussed earlier.

Additional analyses further illuminated the effects of vaccination timing, in concert with the lactation experience of cows. Results were analyzed for cattle vaccinated in 2 time periods (December-January and February-March) based on parity. As shown in Figure 3, milk production of INFORCE 3 vaccinates was significantly ($P = 0.0373$) improved by 4.7 lb/hd/day (5.1%) for P3+ cows vaccinated during February and March. Again, these results reinforce the concept that BRSV impacts in adult dairy cattle can be seasonal in expression and detection.

An economic analysis of overall study results was performed (Figure 4). The 0.65 lb/hd/day production advantage for INFORCE 3 vaccinates over the study period (315 days) equated to approximately 205 lb more milk produced per animal. Using the $17.53/cwt value described earlier, calculations reveal that cattle vaccinated for BRSV with INFORCE 3 generated $36 more income per head (computed using all parities and all vaccination months, ignoring the seasonality of BRSV impacts).
Implications
The favorable milk-production outcomes demonstrated by animals vaccinated in March (or February-March) were consistent with the seasonality aspects of BRSV infection mentioned earlier and detected in previous research. The fact that BRSV often poses an undetected threat to adult cows was supported in this study by the non-significant differences for the overall study results compiled using all 4 months of enrolled cattle. However, substantial and significant milk production differences were detected in cattle vaccinated in some months (late winter/early spring at this California dairy), suggesting that BRSV was resident in the dairy population and capable of exerting economic impacts (though often difficult to detect). Furthermore, these results illustrate that BRSV is often lurking in the background microbial flora that will likely infect calves, perpetuating the ongoing risk and economic impact of BRSV at a dairy.

While the overall production improvement of INFORCE™ 3 vaccinates was statistically non-significant, significant distinctions were found during some months, benefits that were diluted in the overall data analysis due to the seasonality of BRSV. This situation illustrates the need to closely evaluate data and not rely solely on overall statistical evaluations, particularly when responses vary over time. The danger for dairy producers is the forfeiture of potential income by failing to vaccinate for BRSV simply because impacts are subtle and/or seasonal. Even with this seasonality factor, BRSV vaccination with INFORCE 3 substantially elevated the income potential of the herd ($36/hd).

Conclusions
BRSV can impede optimal productivity of adult dairy cattle even though the adverse impacts of infection are often seasonal and difficult to detect. In this study, prepartum intranasal BRSV vaccination of dairy heifers and cows with INFORCE 3 supported numerical improvement in overall milk production, with significant production improvements observed in some months (consistent with the seasonal nature of BRSV prevalence). As a result, overall dairy income was enhanced for animals vaccinated with INFORCE 3.

Use of INFORCE 3 in adult dairy cattle offers dairy producers the ability to minimize the adverse impacts of BRSV in their herds. Aggressive BRSV control with INFORCE 3 helps avoid the subtle and seasonal erosion of milk production while also helping limit the potential for economically significant BRSV exposure for calves.
References

1. Data on file, Study Report No. 10PETINF01, Zoetis Inc.
5. Data on file, Study 3131R-60-08-548, Zoetis Inc.