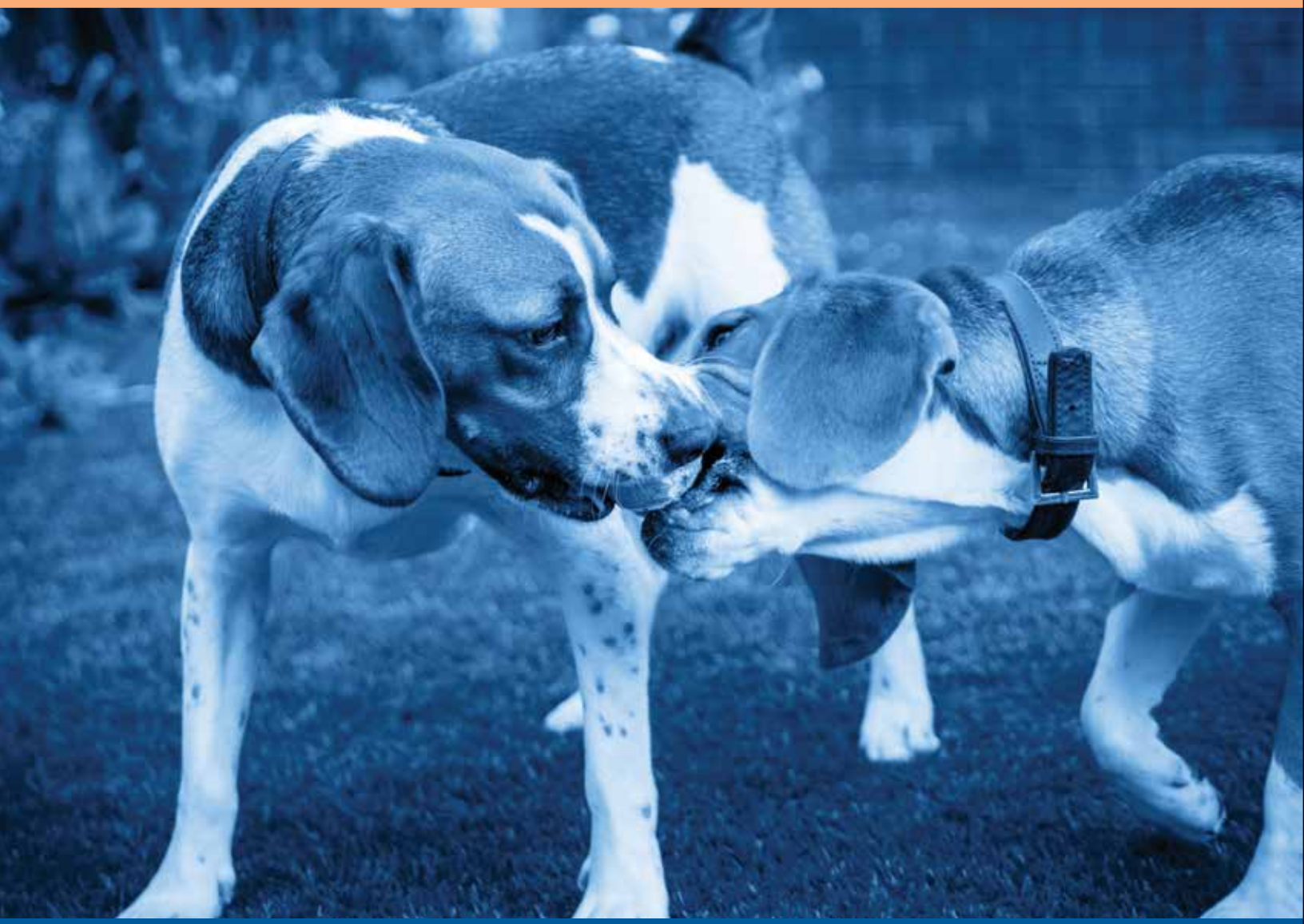
Technical Bulletin



Comparative onset of immunity of oral and intranasal vaccines against challenge with *Bordetella bronchiseptica*

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Title: **Comparative onset of immunity of oral and intranasal vaccines against challenge with *Bordetella bronchiseptica***

Maya M Scott-Garrard, Yu-Wei Chiang, Frederic David. *Vet Rec Open*. 2018;5:e000285.

Study Summary

Methods

Investigators compared the clinical efficacy of an intranasal *Bordetella bronchiseptica* (*Bb*) vaccine with a more recently developed avirulent, modified-live oral vaccine against *Bb*—one of the primary causative agents of canine infectious respiratory disease complex (CIRDC). Vaccine efficacy was evaluated using a range of criteria, yet the incidence of spontaneous coughing served as the primary assessment. Healthy beagles (8 weeks of age) were randomized to receive either RECOMBITEK® Oral Bordetella, an intranasal *Bb* vaccine*, or placebo vaccine, followed by postvaccination challenge with virulent *Bb* via aerosolization.

Results

Dogs in both the RECOMBITEK Oral Bordetella and intranasal vaccine groups had significantly lower incidence of disease (defined as spontaneous cough for 2 or more consecutive days), compared with dogs in the placebo group (0% vs 88.9%, respectively; $P<0.0001$) with a 100% preventable fraction following postvaccination challenge.

Conclusions

Data from this randomized, placebo controlled, blinded study demonstrated that RECOMBITEK Oral Bordetella provided protection against disease† caused by *Bb* equivalent to the intranasal vaccine 7 days after vaccination.

This is the first published study of an oral *Bb* vaccine to demonstrate onset of immunity at 1 week after vaccination; previous studies assessed onset of immunity at 3-4 weeks after administration.[1,2]

*Nobivac® Intra-Trac®$_3$ (canine adenovirus type 2, parainfluenza, *B. bronchiseptica*, modified-live virus and avirulent live culture vaccine)
†Disease defined as a spontaneous cough for two or more consecutive days

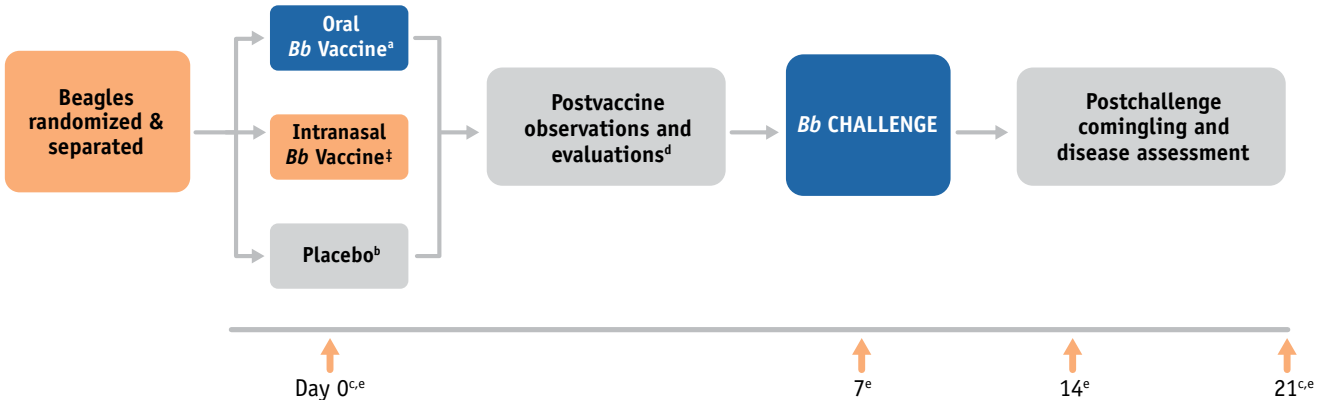
Study Details

Investigators conducted a randomized, placebo controlled, vaccination-challenge study to compare the efficacy of a newly-developed oral vaccine with an established intranasal vaccine against *B. bronchiseptica* challenge 7 days after vaccination. Thirty one days prior to vaccination, all dogs were screened and determined to be serologically negative for antibodies to *Bb* and to be negative for the presence of *Bb* by tracheal culture. Dogs were tested again on Day 0 and any serologically or culture positive dogs were excluded. Eight-week old beagles were randomized to receive either 1 mL of RECOMBITEK Oral Bordetella (avirulent modified-live culture; n=10), 1 mL of an intranasal *B. bronchiseptica* vaccine (0.5 mL/nostril; n=10), or 1 mL placebo (oral, n=9). The two groups of vaccinated dogs were housed in separate isolation rooms to prevent cross-shedding prior to challenge, and were observed after vaccination (3 days) for possible vaccine-related adverse events.

Seven days after vaccination, all of the dogs were challenged with 2 virulent *Bb* strains via aerosolization in a closed chamber. Dogs of different groups were comingled after challenge and were randomized to two pens so that each vaccination group was represented in each pen.

Investigators involved with clinical observations, sample collection, and laboratory analyses were blinded to group assignment for each dog. Treatment assignments were revealed only after study completion (*Figure 1*).

Figure 1. **Study Design**



[a]The RECOMBITEK Oral Bordetella group received a monovalent, avirulent, modified-live, industrial scale, prelicense serial at the target commercial dose

[b]Dogs in the placebo group received sterile water

[c]Tracheal swabs were collected prior to vaccination (day 0) and on the final day of the of the study (day 21)

[d]Daily clinical observations, rectal temp

[e]Serum samples collected on days 0, 7 (prior to challenge), 14, and 21

During the 2-week postchallenge observation period:

- Dogs were observed for spontaneous cough, malaise (appearance of generalized illness, weakness or fatigue), nasal discharge, ocular discharge and other signs of respiratory infection. Rectal temperatures were recorded daily
- Primary outcome for this study was active disease due to *Bb* (defined as spontaneous cough lasting 2 or more consecutive days)

‡This group received Nobivac® Intra-Trac®$_3$, a commercial canine adenovirus type 2, parainfluenza, *B. bronchiseptica*, modified-live virus and avirulent live culture vaccine.

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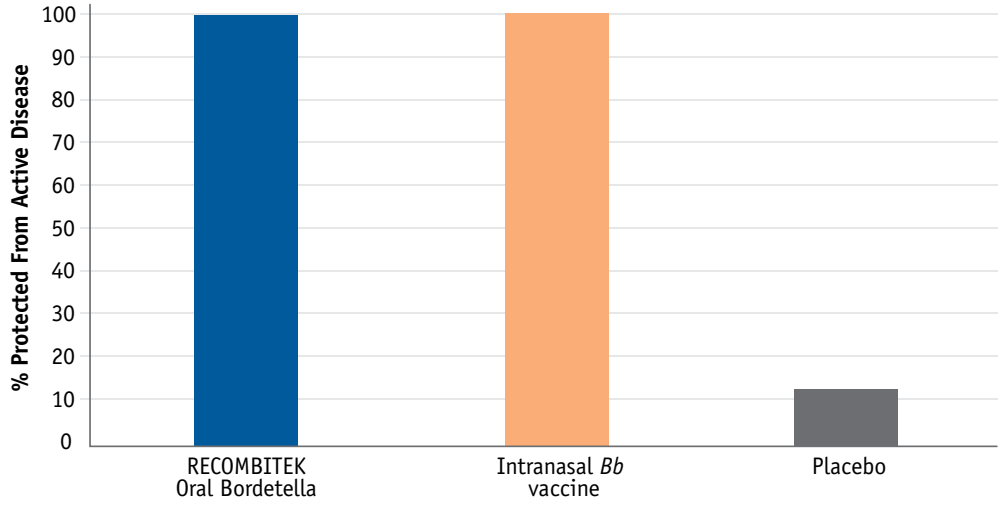
Study Results and Conclusions

Vaccination with either RECOMBITEK Oral Bordetella or an intranasal vaccine is effective in preventing disease 7 days after vaccination, when compared to dogs vaccinated with a placebo.

- No dogs in either the oral or intranasal vaccine groups developed active *Bb* infection,† while 88.9% of dogs in the placebo group developed *Bb* infection ($P<0.0001$) (*Figure 2*)
- The prevented fraction was 1.00 (95% CI, 0.67 to 1.00) in both oral and intranasal vaccine groups

Figure 2.



RECOMBITEK® oral bordetella

†Disease defined as a spontaneous cough for two or more consecutive days

References: 1. Ellis JA, Gow SO, Waldner CL et al. Comparative efficacy of intranasal and oral vaccines against Bordetella bronchiseptica in dogs. *The Veterinary Journal*. 2016;212:71-77. **2.** Larson LJ, Thiel BE, Sharp P, Schultz RD. A comparative study of protective immunity provided by oral, intranasal and parenteral canine Bordetella bronchiseptica vaccines. *Intern J Appl Res Vet Med*. 2013;11(3):153-160.