RECOMBITEK® LYME VACCINE

CLEAR PROTECTION
CLEAR CONFIDENCE

Canine Lyme disease protection

Pure, targeted protection with the RECOMBITEK® Lyme vaccine: the only nonadjuvanted canine Lyme disease vaccine.

RECOMBITEK® lyme

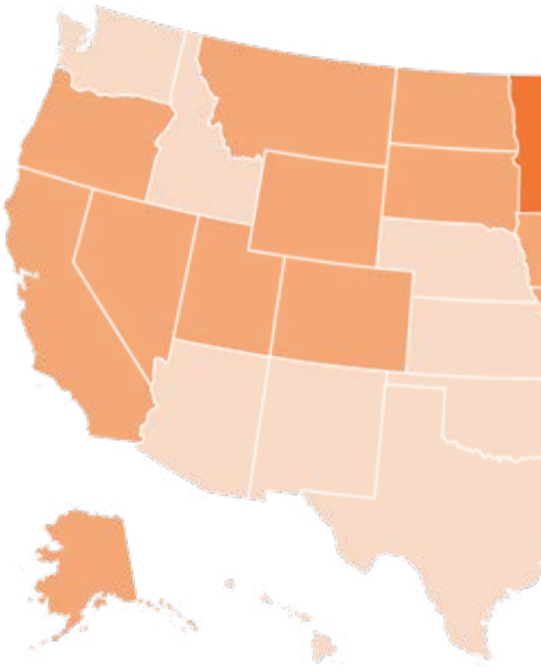
Lyme disease: the threat against dogs continues to rise

- Lyme disease is the most common tick-borne disease of dogs and humans in the northern hemisphere[1]
- The spread of Lyme disease over the past several decades has been linked to several changes in land use patterns, climate, and other host factors[2]
- For example, suburban development in the northeastern United States has brought people, deer, rodents and ticks closer together[2]
- A positive correlation between Lyme disease incidence in humans and seroprevalence in dogs has been demonstrated[3]
- Diagnosis of Lyme disease is difficult: Most *Borrelia burgdorferi* seropositive dogs show no clinical signs, and infected dogs do not typically present acutely[4]

Lyme disease is on the move

Lyme disease has been detected in dogs in all 50 states and is common in the Northeast, upper Midwest, Mid-Atlantic and West Coast.[2]

- Infection is common in the Northeastern, upper Midwestern and West Coast states[5]
- In endemic areas, regional seroprevalence in dogs ranges from 1.4% in the West to as high as 13.3% in the Northeast[5]
- Lyme disease is transmitted from the bite of the black-legged tick (or deer tick)—*Ixodes scapularis* in the Northeast and Midwest, and *Ixodes pacificus* on the West Coast[6]



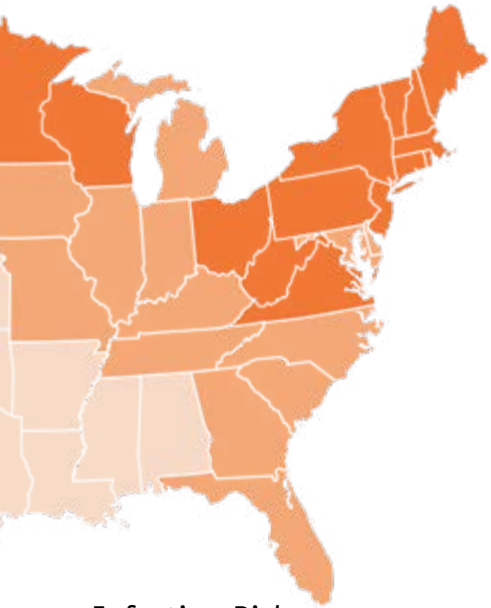
CAPC, Companion Animal Parasite Council

WING THREAT

Lyme disease mode of transmisson

- *B. burgdorferi*, the causative agent of Lyme disease, is transmitted by ticks
- Transmission of *B. burgdorferi* typically occurs 36 to 48 hours or more after tick attachment[7]
- Outer surface protein A (OspA), the predominant surface protein expressed on *B. burgdorferi*, is involved in the attachment of spirochetes to the tick's midgut[8]
- During feeding, the warmth of the new environment causes spirochetes to downregulate their expression of OspA and start expressing OspC; spirochetes then migrate from the midgut to the salivary glands and subsequently infect the mammalian host[8]
- The OspA lipoprotein is highly conserved between *B. burgdorferi* species in the US; this homogeneity makes it an ideal vaccine target[9]
- OspC exhibits much greater heterogenicity than OspA: **Over 30 distinct OspC phyletic types** have been identified, and immune responses elicited by OspC epitopes are phyletic–specific[10]

CAPC 2024 Canine Lyme Disease Prevalence Map



CLEAR PROTECTION CONFIDENCE

OspA is the only vaccine antigen necessary to block transmission of *B. burgdorferi* from the tick to the dog.[11]

The only vaccine that contains lipidated OspA in a nonadjuvanted formulation

RECOMBITEK® LYME VACCINE:

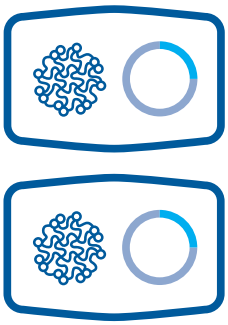
Purifying OspA for the RECOMBITEK Lyme Vaccine

1. DNA of *Borrelia burgdorferi* spirochete with genetic code of OspA is fragmented by restriction enzymes.
2. Plasmid vector (free-floating DNA) is selected.
3. OspA DNA sequence is inserted into plasmid vector, creating recombinant plasmid.
4. Recombinant plasmid is inserted in host *E. coli*.

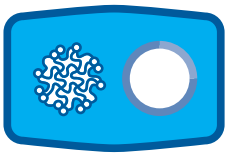
Nonadjuvanted formulation

- RECOMBITEK Lyme is the only nonadjuvanted canine Lyme vaccine
- RECOMBITEK Lyme contains a highly purified lipidated OspA[12]
- RECOMBITEK Lyme uses only a pure protein without an adjuvant to stimulate immunity
- Unlike RECOMBITEK Lyme, whole-cell bacterin canine Lyme vaccines and the chimeric recombinant canine Lyme vaccine contain adjuvants to enhance the immune response[5]
  - Sensitization to an adjuvant may contribute to hypersensitivity reactions[13]
- Whole-cell bacterin Lyme vaccine contains more than 100 *B. burgdorferi* lipoproteins, inducing host inflammatory responses that may lead to pathologic changes responsible for the inflammation associated with infection[14,15]

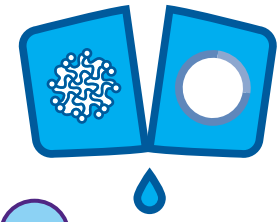
TARGETED, PURE PROTECTION



5 *E. coli* containing the recombinant plasmid multiplies in culture.



6 Recombinant plasmid directs *E. coli* to produce OspA.

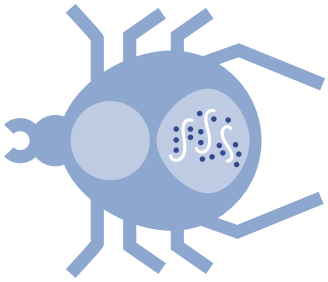


7 *E. coli* is lysed; OspA is extracted and purified.

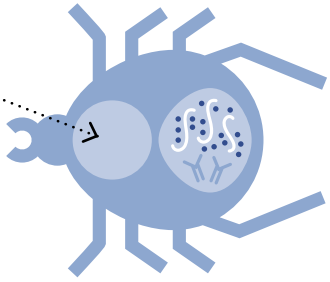
8 Purified OspA is used to manufacture RECOMBITEK Lyme vaccine. (No adjuvant is needed.)

What happens when an infected tick bites a dog protected by the RECOMBITEK Lyme vaccine?

In the unfed tick, *B. burgdorferi* expresses OspA in the tick midgut.



As the tick feeds, OspA antibodies in the dog's blood enter the midgut and bind to OspA on the surface of *B. burgdorferi*.



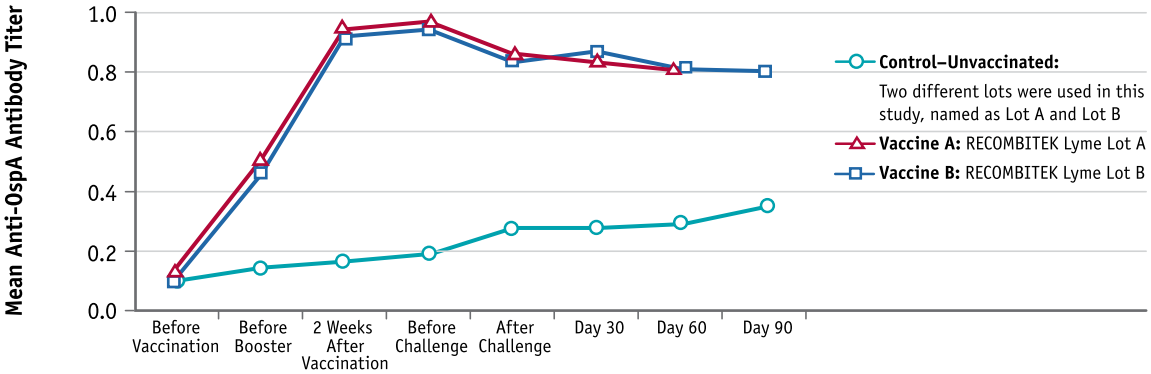
B. burgdorferi growth is arrested, migration to the salivary gland is blocked, and transmission is prevented.

PROVEN EFFICACY

The RECOMBITEK Lyme vaccine blocked infection before transmission could occur[11]

- Randomized, blinded, controlled study designed to mimic natural tick challenge
- 100% of control dogs infected post-challenge
- Efficacy of the RECOMBITEK Lyme vaccine was determined by:
  - Serology (ELISA*)
  - Recovery of the infectious agent via skin biopsy culture, PCR analysis, Western Blot analysis and tick xenodiagnosis

The RECOMBITEK Lyme vaccine induced a robust antibody response

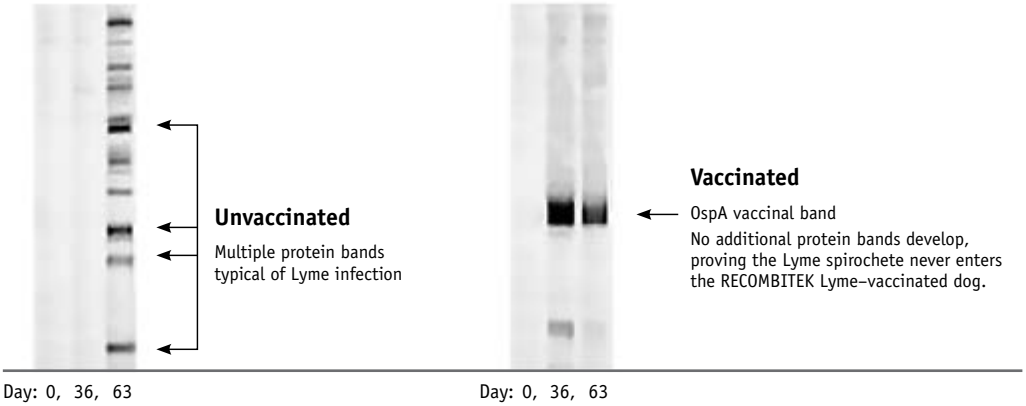


- Relative to controls, vaccinates responded with significantly high levels of anti-OspA antibodies that were maintained throughout the study
- Vaccinates showed no booster effect after challenge, demonstrating solid immunity
- The unvaccinated control group had low titers that increased in response to challenge and were maintained throughout the study

American Animal Hospital Association (AAHA) recommendation: Vaccination for Lyme borreliosis should be considered for dogs that live within or travel to regions with emerging or endemic Lyme disease.[16]

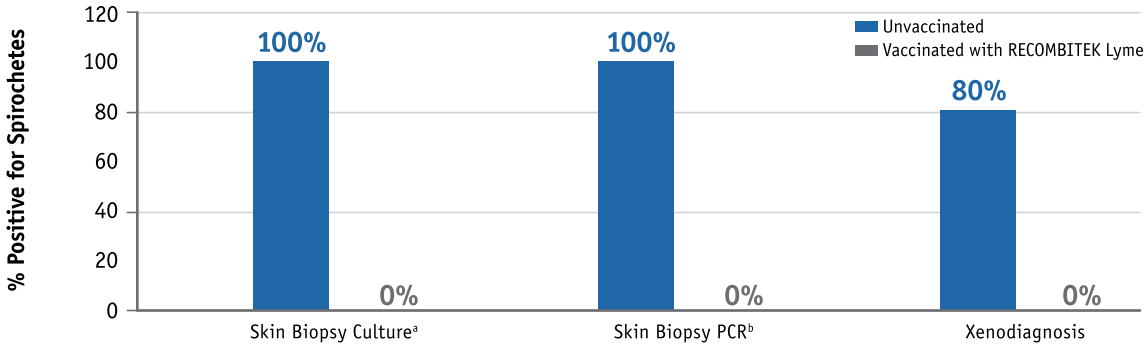
*ELISA= enzyme-linked immunosorbent assay

The RECOMBITEK Lyme vaccine prevented infection in the face of challenge



- All controls (10/10) had antibodies characteristic of infection with *B. burgdorferi* after challenge (day 63), whereas no antibodies developed to antigens that are specific for infection to *B. burgdorferi* in the vaccinates
- Vaccinated dogs demonstrated an OspA antibody pattern following vaccination (day 36) and tick challenge (day 63)
- This confirms that no infection occurred in the vaccinated dogs following challenge with ticks infected with *B. burgdorferi*

No evidence of infection in dogs vaccinated with the RECOMBITEK Lyme vaccine



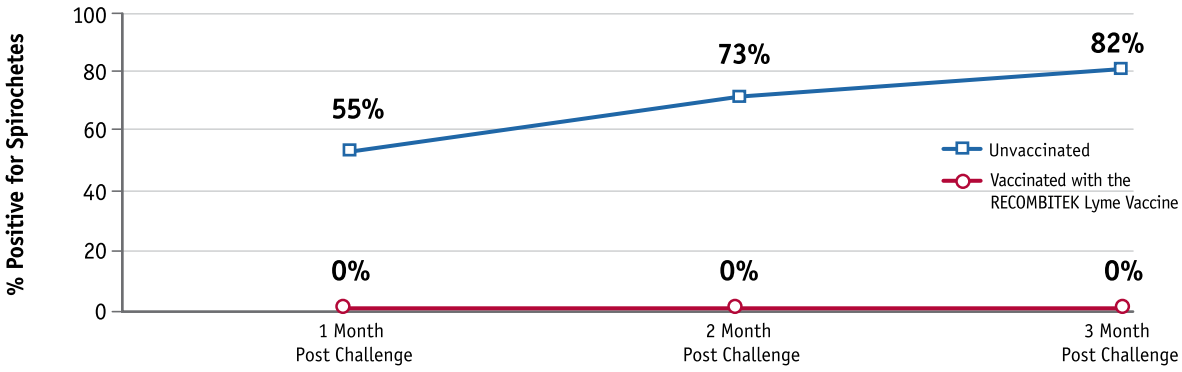
[a] Post challenge days 30, 60, and 90
[b] Post challenge days 30 and 60

- In contrast to the unvaccinated group, vaccinates had no isolation of spirochetes on skin biopsy, and had no positive PCR results after challenge for up to 3 months and 60 days, respectively
- Xenodiagnosis demonstrated that all ticks recovered from vaccinated dogs were negative for *B. burgdorferi,* whereas 80% of ticks were positive for *B. burgdorferi* in unvaccinated controls

PROVEN 1-YEAR IMMUNITY AND

The RECOMBITEK Lyme vaccine demonstrated long-lasting protection in a live-tick challenge 366 days after vaccination[17]

- Duration of immunity and safety for RECOMBITEK Lyme was evaluated in a randomized, blinded, placebo-controlled study
- Dogs were challenged by exposure to naturally infected ticks 1 year (366 days) after initial vaccination series (2 doses administered, 3 weeks apart)
- Spirochete reisolation from skin biopsies was used to assess vaccine efficacy at monthly intervals for 3 months after challenge



- Spirochetes were reisolated from 82% of the unvaccinated dogs at 3 months post challenge, whereas none of the vaccinated dogs had spirochete reisolation at any assessed time
- None of the vaccinated dogs had clinical signs of Lyme disease, whereas 18% of unvaccinated control animals showed clinical signs during the study
- No general adverse reactions to the vaccine were noted at any time during the study
- No vaccinates showed any signs of infection after challenge in both efficacy and duration-of-immunity study[a]

[a] Infection with *B. burgdorferi* does not always produce clinical signs in dogs[8]

STRONG IMMUNOGENICITY

The RECOMBITEK Lyme vaccine features a uniquely constructed OspA antigen that provides strong immunogenicity[12]

- Natural spirochete-associated OspA is lipidated at the N-terminus of the amino acid sequence[18]
- Lipidation has been demonstrated as a determinant of immunogenicity for OspA[12]

Lipidation assessment of the OspA antigen of 2 recombinant canine Lyme vaccines[12]

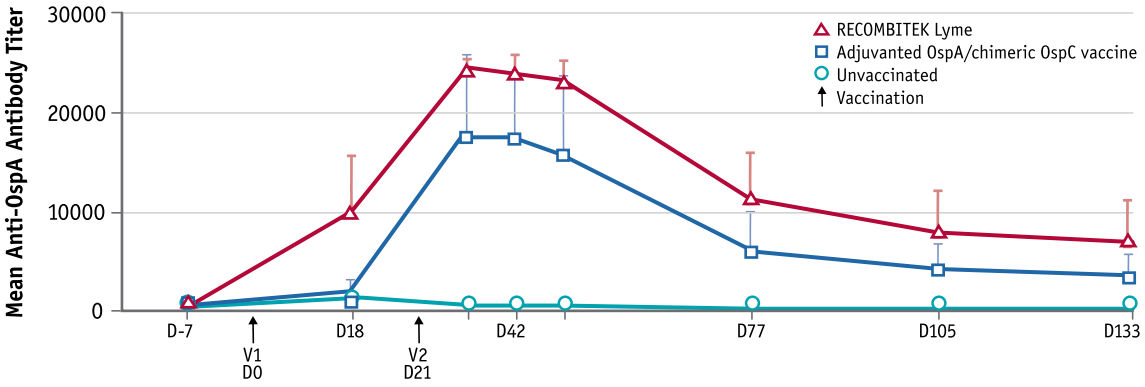
The RECOMBITEK Lyme vaccine	Adjuvanted OspA/chimeric OspC vaccine
A mix of bi- and tri-lipidated forms	Non-lipidated
Molecular weight of 418 kDa; diameter: 18 nm	Molecular weight of 34 kDa; diameter: 6.4 nm

- Recombinant OspA lipidation and subsequent micelle formation might account for higher immunogenic profile of recombinant OspA compared with adjuvanted OspA/chimeric OspC vaccine[12]

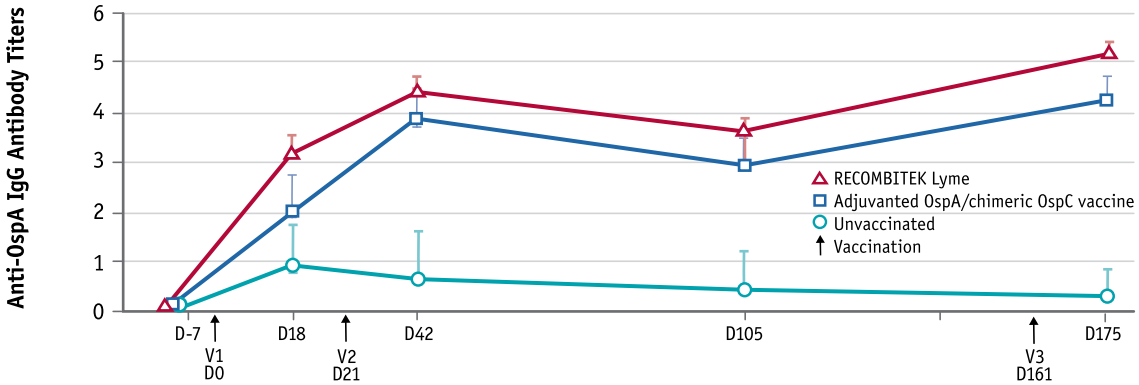
ROBUST, HOMOGENEOUS, AND

Serological response and borreliacidal activity of the RECOMBITEK Lyme vaccine and adjuvanted OspA/chimeric OspC vaccine[12]

The RECOMBITEK Lyme vaccine produces a greater and more homogenous anti-OspA humoral response



- Anti-OspA antibody response was significantly higher at day 18 in dogs after a single vaccination with the RECOMBITEK Lyme vaccine than in dogs vaccinated with the adjuvanted OspA/chimeric OspC vaccine
- At subsequent time points, the mean anti-OspA antibody titers in dogs vaccinated with the RECOMBITEK Lyme vaccine remained higher than titers in those vaccinated with the adjuvanted OspA/chimeric OspC vaccine (not statistically significant)



- Total IgG titers were significantly higher for RECOMBITEK Lyme vaccinates on days 18, 42, 105, and 175, compared with adjuvanted OspA/chimeric OspC vaccine
- There was a trend of a more consistent anti-OspA (less dispersion) response for the RECOMBITEK Lyme vaccine, compared with adjuvanted OspA/chimeric OspC vaccine, which was significant at day 175

HIGH-AVIDITY RESPONSE

The RECOMBITEK Lyme vaccine elicits a higher-avidity anti-OspA antibody response

- The RECOMBITEK Lyme vaccine generated a significantly higher-avidity response at days 18, 105, and 175, compared with adjuvanted OspA/chimeric OspC vaccine
- Vaccination with the RECOMBITEK Lyme vaccine resulted in the production of large amounts of specific, high-avidity antibodies that increased after each vaccination
- Dogs vaccinated with adjuvanted OspA/chimeric OspC vaccine resulted in the production of specific antibodies with lower avidity that did not increase after subsequent vaccination

The RECOMBITEK Lyme vaccine generates a greater concurrent increase in serum borreliacidal activity

- Post-vaccination borreliacidal activity of sera from dogs receiving the RECOMBITEK Lyme vaccine was consistently and significantly higher on days 18, 35 and 175, compared with activity for dogs that received adjuvanted OspA/chimeric OspC vaccine

Dogs receiving the RECOMBITEK Lyme vaccine had higher levels of anti-OspA antibodies, higher avidity of anti-OspA antibodies, and greater concurrent increase in serum borreliacidal activity compared with dogs that received an adjuvanted OspA/chimeric OspC vaccine

This vaccine is one of a complete line of companion animal vaccines brought to you by Boehringer Ingelheim Animal Health and includes RECOMBITEK® canine vaccines, PUREVAX® feline vaccines and IMRAB® rabies vaccines.

Pet Vaccines Veterinarian Customer Satisfaction Guarantee

In the event that a dog is found to be Lyme positive within 15 months after being properly vaccinated with the RECOMBITEK® Lyme vaccine, Boehringer Ingelheim will support testing with any commercially available test for the detection of exposure to *Borrelia burgdorferi*. Please contact Veterinary Technical Solutions (VeTS) to set up support for testing preemptively. If a positive diagnosis is confirmed, Boehringer will support urinalysis testing and treatment with appropriate antibiotics, such as amoxicillin or doxycycline. More in-depth support will be considered for testing and treatment of definitively diagnosed complications of Lyme disease on a case-by-case basis.

For full details, ask your Representative about our Satisfaction Guarantee for RECOMBITEK canine vaccines or call our Veterinary Technical Solutions team at 1-888-637-4251.

RECOMBITEK® LYME VACCINE MEANS CLEAR PROTECTION, CLEAR CONFIDENCE

Pure, targeted protection with the RECOMBITEK® Lyme vaccine: the only nonadjuvanted canine Lyme disease vaccine.

- Effective protection that blocks *Borrelia burgdorferi* while it's still in the tick[11]
- THE ONLY canine Lyme vaccine that is nonadjuvanted
- THE ONLY recombinant Lyme vaccine that contains lipidated OspA[12]
- Demonstrated 100% efficacy in a single study after one year[17], and has a robust, homogeneous and high-avidity immune response[12,†]

†For advice on revaccination frequency, pet owners are advised to consult their veterinarian.

References: 1. Karen L. Stasiak, Nicholas A. Cramer, Gavin Z. Chambers, Richard T. Marconi, Serological survey for maternal antibodies to Borreliella burgdorferi and Anaplasma phagocytophilum in dogs from endemic and non-endemic regions of the United States, Veterinary Immunology and Immunopathology, Volume 251, 2022, 110471, ISSN 0165-2427, https://doi.org/10.1016/j.vetimm.2022.110471. **2.** The Centers for Disease Control and Prevention (CDC). Press Kit: Understanding Lyme and other Tickborne Diseases. https://www.cdc.gov/ticks/communication-resources/press-kit.html. Accessed March 3, 2025. **3.** Goel R, Kugeler K. Canine serology as adjunct to human Lyme disease surveillance. *Emerg Infect Dis.* 2011;17(9):1710-1712. **4.** Littman MP, Gerber B, Goldstein RE, et al. ACVIM consensus update on Lyme borreliosis in dogs and cats. *J Vet Intern Med.* 2018;32:887-903. **5.** The Companion Animal Parasite Council (CAPC). Parasites Prevalence Maps. US Canine Positive Lyme Results. https://capcvet.org/maps/#/2024/all-year/lyme-disease/dog/united-states. Accessed March 3, 2025. **6.** The Merck Veterinary Manual website. Overview of Lyme borreliosis. Available at: https://www.merckvetmanual.com/infectious-diseases/lyme-borreliosis/lyme-borreliosis-in-animals. Accessed March 3, 2025. **7.** The Centers for Disease Control and Prevention (CDC). How Lyme Disease Spreads. https://www.cdc.gov/lyme/causes/. Accessed April 2, 2025. **8.** Greene CE, Straubinger RK, Levy SA. Borreliosis. In: Greene CE, ed. *Infectious Diseases of the Dog and Cat.* 4th ed. St. Louis, MO: Saunders, an imprint of Elsevier, Inc.;2012. **9.** Appel MJG: Lyme disease vaccination, in Bonagura JD (ed): *Kirk's Current Veterinary Therapy XIII.* Philadelphia, WB Saunders Co. 1999;256-258. **10.** Rhodes DV, Earnhart CG, Mather TN, Meeus PF, Marconi RT. Identification of *Borrelia burgdorferi* OspC genotypes in canine tissue following tick infestation: Implications for Lyme disease vaccine and diagnostic assay design. *Vet J.* 2013;198(2):412-418. **11.** Conlon JA, et al. Efficacy of a nonadjuvanted, outer surface protein A, recombinant vaccine in dogs after challenge by ticks naturally infected with *Borrelia burgdorferi. Veterinary Therapeutics.* 2000;1:96-107. **12.** Grosenbaugh DA, De Luca K, Durand P-Y, et al. Characterization of recombinant OspA in two different *Borrelia* vaccines with respect to immunological response and its relationship to functional parameters. *BMC Vet Res.* 2018;14:312. **13.** Greene CE, Straubinger RK, Levy SA. Immunoprophylaxis. In: Greene CE, ed. *Infectious Diseases of the Dog and Cat.* 4th ed. St. Louis, MO: Saunders, an imprint of Elsevier, Inc. 2012:1163-1205. **14.** Giambartolomei GH, Dennis VA, Lasater BL, Philipp MT. Induction of pro- and anti-inflammatory cytokines by *Borrelia burgdorferi* lipoproteins in monocytes is mediated by CD14. *Infection and Immunity.* 1999;67(1):140-147. **15.** Appel MJG, Jacobsen RH. CVT Update: Canine Lyme Disease, in Bonagura JD (ed): K*irk's Current Veterinary Therapy XII*, Philadelphia, WB Saunders. 1995;303-309.**16.** American Animal Hospital Association (AAHA). 2022 AAHA Canine Vaccination Guidelines. https://www.aaha.org/aaha-guidelines/2022-aaha-canine-vaccination-guidelines/home/. Accessed March 3, 2025. **17.** Wikle RE, et al. Canine Lyme disease: One-year duration of immunity elicited with a canine OspA monovalent Lyme vaccine. *Intern J Appl Res Vet Med.* 2006;4(1):23-28. **18.** Jiang W, Gorevic PD, Dattwyler RJ, Dunn JJ, Luft BJ. Purification of *Borrelia burgdorferi* outer surface protein A (OspA) and analysis of antibody binding domains. *Clin Diagn Lab Immunol.* 1994;1(4):406-12.

To learn more about the RECOMBITEK vaccines and how they can benefit your patients, contact your Boehringer Ingelheim Representative, call Customer Care at 1-888-637-4251 or Shop on Connect.

Ask your Representative about our Satisfaction Guarantee on the RECOMBITEK canine vaccines.

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