

VANGUARD[®] crLyme Frequently Asked Questions

Lyme Disease:

How prevalent is canine Lyme disease in the U.S.?

According to the Baker Institute for Animal Health at Cornell University, Lyme disease is the most common arthropod-borne disease in dogs in the U.S.¹ The Banfield State of Pet Health™ 2014 Report cites that the prevalence of Lyme disease in dogs has increased by 21 percent since 2009.² Additionally, data available on the Companion Animal Parasite Council website indicates that 1 in 16 dogs or ~251,000 of the ~4.1 million dogs tested for Lyme disease had a positive result in 2015. They anticipate that only 30% of test results are reported; therefore, the total number of positive tests could actually be closer to 800,000.³

Is Lyme disease confined to the Northeastern region of the United States?

According to the Companion Animal Parasite Council (CAPC), infection with *Borrelia burgdorferi*, the causative agent of Lyme disease in dogs, is common in the Northeastern, upper Midwestern and West Coast states.⁴ Lyme disease in dogs is also a concern in portions of Southern Canada and throughout most of Europe.

Is Lyme disease spreading into areas of the United States where it hasn't been seen with any frequency in the past?

A recent study by the CDC revealed that the ticks that carry and transmit Lyme disease have spread across the United States. These ticks are now found in 49% of the counties in the US. As infected ticks move into new areas they transmit Lyme disease to small mammals which can then serve as reservoirs for the Lyme disease spirochetes. When uninfected ticks feed on these infected mammals they acquire the Lyme disease spirochetes and can subsequently transmit the bacterium to other mammals. This can result in an increased risk of Lyme disease in dogs.⁵

When dogs from areas currently considered non-endemic for Lyme travel to endemic areas what steps can be taken to minimize their risk of contracting Lyme disease?

All dogs that travel to Lyme endemic areas are at risk of infection. This risk can be minimized with good preventive practices such as avoidance of tick habitats (such as wooded areas, overgrown shrubs, leaf litter, wood piles and areas that may be frequented by mice and wildlife), careful examination and removal of any ticks every 24 hours, the use of tick control products and vaccination to help prevent Lyme disease.

What are outer surface proteins? What are they important to consider with Lyme disease in dogs?

Outer surface proteins, commonly abbreviated as Osp, are found on the outer membrane of *Borrelia burgdorferi* spirochetes. OspA and OspC are two of these proteins that are believed to play critical roles in host infection and antibody response.

What is OspA?

OspA is an outer surface protein produced by *B. burgdorferi* while they reside in the midgut of an unfed tick. OspA is thought to play an important role in helping the spirochetes survive the harsh conditions found there. It is very important to note that shortly after a tick begins ingesting blood any *B. burgdorferi* spirochetes it is carrying will stop producing OspA.

What is OspC?

OspC is an outer surface protein expressed by *B. burgdorferi* both in the tick, where upregulation begins in conjunction with the ingestion of a blood meal, and in the dog. OspC is required for spirochete attachment to the tick salivary gland and is also required for mammalian infection to occur.

What do the terms “OspA type” or “OspC type” mean?

The word "type" is used to differentiate different variants of the OspA and OspC proteins. In N. America, *B. burgdorferi* strains all produce a single OspA type. In contrast, more than 30 types of OspC exist worldwide. Only a subset of these types have been found in N. America. Approximately 11 OspC types have been detected in Lyme infected dogs in N. America.⁶

What are the clinical signs of Lyme disease in dogs?

The clinical signs of Lyme disease can and do vary greatly among individual dogs. These signs may consist of fever, lameness, swelling in the joints, swollen lymph nodes, lethargy and loss of appetite. Additionally, dogs with Lyme disease frequently develop subclinical arthritis and inflammation that is not readily apparent during a routine examination.

What is the underlying cause of the clinical signs associated with canine Lyme disease?

There is no simple answer to this question but it has been suggested that it may be the body's own immune response to *B. burgdorferi* migration into tissues, joints, organs and the central nervous system that causes harm.⁷

What are the potential long-term health issues associated with Lyme disease in dogs?

Because *B. burgdorferi* spirochetes can move throughout the body they can cause long-term problems in both organs and joints. If the infection is not treated early enough chronic conditions affecting the kidneys, heart, joints and/or central nervous system can develop. Such conditions can be difficult to treat and may be irreversible. Prevention remains the most reliable method for dog owners to be confident their pet is protected.

Is there a risk of transmission of Lyme disease from an infected dog to a person?

Ticks that are brought into the home by pets can be a potential source of human infection; however, it is much more common for people to become exposed during outdoor activities.

What are the current treatment recommendations for Lyme infected dogs?

Treatment for dogs with positive serological tests for Lyme disease has been and remains a controversial topic. When the decision is made to use antibiotics, doxycycline

is most commonly used at a total dose of 10mg/kg/day. Some practitioners may elect to dose twice daily while others will dose on a once daily basis.⁸ In addition to doxycycline other antibiotics have been shown to be effective as well.

How is Lyme disease diagnosed in dogs?

There are several diagnostic assays that can be used to determine if your dog has been exposed or is actively infected with the Lyme disease spirochetes. In the United States many dogs are screened on an annual basis for exposure using an in-clinic point of care test called IDEXX SNAP[®]4Dx[®] Plus. The Lyme disease portion of this simple, qualitative, blood-based test screens for antibodies that recognize a peptide called C6. The C6 peptide used in the test is derived from a highly conserved segment of the VlsE protein. VlsE is a surface protein that the Lyme disease spirochetes produce during infection in mammals. This test can yield a positive result starting approximately 21 days postinfection.⁹ A quantitative C6 test is also available that can precisely measure the levels of antibody to C6.

Another widely used test is the AccuPlex[®] 4 test which measures antibody levels to multiple surface proteins of *B. burgdorferi* including: OspA, OspC and OspF. OspF is specifically produced during late stage infection. This test recognizes both antibodies elicited due to vaccination and those induced by natural infection. In the event of a positive AccuPlex[®] test Zoetis' VMIPS group recommends follow-up quantitative C₆ testing.

Western blotting or immunoblotting is a reference laboratory run test that can be used. It can also help distinguish between vaccination induced antibody responses and those from natural infection. However, western blotting is laborious and can be costly. Other methods of testing are also available but are less commonly used due to concerns about specificity and their inability to differentiate between antibody responses stimulated by natural infection from vaccination.

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VANGUARD[®] crLyme:

What is VANGUARD[®] crLyme? What is it indicated for?

VANGUARD[®] crLyme is indicated in healthy dogs 8 weeks of age or older to aid in the prevention of clinical disease and subclinical arthritis associated with *B. burgdorferi* infection. Dogs should receive two doses administered three weeks apart and annual revaccination thereafter. The vaccine is to be delivered subcutaneously.

Why are two doses of VANGUARD[®] crLyme recommended even for dogs that have previously been vaccinated for Lyme disease?

VANGUARD[®] crLyme is unique in that it contains antigenic material derived from a broad array of OspC types. Other Lyme disease vaccines on the market either lack OspC or contain only a single OspC type protein. Dogs that are exposed to *B. burgdorferi* that produce OspC types that are not included in these vaccines may not have antibody that can target these other OspC proteins.

What is the significance of the name “crLyme”?

The “c” stands for chimeric and the “r” stands for recombinant. A chimeric protein is one that contains segments of several different proteins joined together to form a single hybrid protein. To

make a chimeric protein, the DNA sequences that encode the desired segments to be included are “recombined” into a piece of DNA referred to as a “recombinant”. The chimeric recombinant OspC component of crLyme is a unique in that it consists of regions of seven diverse OspC types that have been demonstrated to stimulate antibody production in mammals.

What are the benefits of recombinant vaccines?

Recombinant vaccines are also referred to as “subunit” vaccines. Subunit vaccines consist of one more highly purified proteins that are derived from a pathogen that can stimulate immune responses. Subunit vaccines, which contain no extraneous proteins and, are often considered safer with less potential for reactivity.

How does VANGUARD® crLyme differ from other Lyme disease vaccines?

VANGUARD® crLyme, which was designed using an innovative technology, is a high purity vaccine that contains two recombinant proteins: OspA and an OspC chimera. The chimera consists of antigenic regions derived from seven OspC types. The inclusion of epitopes from multiple OspC types stimulates a broader antibody response that can aid in protection against diverse strains of the Lyme disease spirochetes. Prior to VANGUARD® crLyme, only bacterins (whole-cell preparations) or OspA alone vaccines were available.

Is there published research supporting the need to address OspC diversity in Lyme disease vaccine design?

Yes. There is a robust body of scientific literature that highlights the need to address OspC diversity in the design of Lyme disease vaccines.⁶ Bockenstedt et al demonstrated nearly 20 years ago that a single OspC protein can not provide broad protection.¹⁰ To stimulate optimal antibody responses that can target the different OspC types produced by diverse Lyme disease spirochete strains, a multivalent approach is necessary. In contrast to the unique polyvalent nature of the OspC chimeric in VANGUARD® crLyme, whole-cell bacterins contain only one OspC type protein. This compromises the ability of bacterin vaccines to stimulate antibody that can target different OspC proteins.

Which OspC types are included in VANGUARD® crLyme?

This is proprietary and confidential information. The 7 OspC types included in the vaccine have been demonstrated to be present in Lyme infected dogs in North America.⁶ Research has demonstrated that the inclusion of these particular 7 OspC types in the vaccine lead to an effective immune response which helps to prevent dogs in North America from becoming infected with Lyme disease.¹¹

How do we know that the correct OspC types are present in VANGUARD® crLyme?

A laboratory challenge study conducted using field collected ticks from a geographic area known to be endemic for diverse strains of the Lyme disease spirochetes demonstrated that vaccination with VANGUARD® crLyme triggered antibody responses that prevented dogs from becoming infected with *B. burgdorferi*.¹¹

Who developed the new technology used for VANGUARD® crLyme?

Zoetis researchers worked in conjunction with Dr. Richard T. Marconi, from Virginia

Commonwealth University Medical Center, to develop the technology in VANGUARD[®] crLyme.

What studies did Zoetis conduct to support the safety of VANGUARD[®] crLyme?

Zoetis conducted a field safety study including 620 dogs and involving a total of 1,232 vaccine injections using VANGUARD[®] crLyme per label instructions. The study was conducted across 13 different sites. A total of 11 veterinary clinics and 2 breeder facilities participated. Both puppies and adult dogs were represented. Adverse reactions were classified as immediate (<30 minutes) or late (after immediate period ended and continuing for 10 days after injection). All adverse events were mild, and the most common immediate reaction was vocalization at administration (0.73 percent). The most common late reaction was injection site edema (3.81 percent).¹²

VANGUARD[®] crLyme has not been tested in breeding, pregnant or lactating dogs.

Why was injection site edema higher at a single breeder site versus the other twelve sites used in the VANGUARD[®] crLyme safety study?

Injection site edema for VANGUARD[®] crLyme was 3.81% (47/1232 vaccinations). Most of these (38/47) were reported at a single breeder site. These facilities typically used veterinarians or technicians to perform observations for late abnormal health events, as opposed to dog owners. Thus, reports for late abnormal health events were expected to be higher from commercial breeder sites. Notably, no injection site edema was reported at another commercial breeder site used in the study, despite the same pre-study training.¹²

Q26: How is VANGUARD[®] crLyme sold to veterinarians?

VANGUARD[®] crLyme is available in 25- and 50-count packages of ready-to-use, single use glass vials (1 mL solution, no reconstitution necessary). It must be stored in a refrigerator, cannot be frozen and has a shelf life of 24 months.

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