

A portfolio of advanced vaccines for the well-being of canine family members



# Prevention to the power of 2... **That's Protection** <sup>SHARED</sup>

**2** **Critical Indications**  
protect against mortality  
and shedding

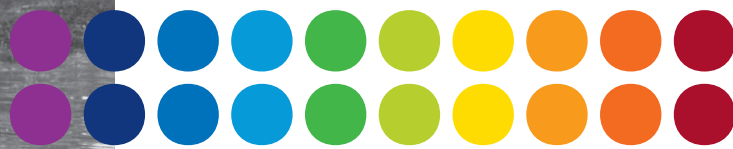
**Nobivac<sup>®</sup>:Lepto<sub>4</sub>**  
and Nobivac<sup>®</sup>: Canine 1-DAPPv+L<sub>4</sub>

**2** Induces borreliacidal  
antibodies **against**  
**Key OspA and OspC**  
and aids in the prevention of  
subclinical arthritis and other  
signs of Lyme disease

**Nobivac<sup>®</sup>:Lyme**

# Facts about Leptospirosis and Lyme Disease

- About 50 million US households own dogs—an estimated 78 million canine pets<sup>1,2</sup>
  - Only about half of household dogs are protected from parasitic diseases<sup>2</sup>
  - 56% of potential dog owners also have children<sup>3</sup>
- Reported cases of zoonotic diseases are on the rise, and are expected to continue to rise<sup>2,4-8</sup>
  - One out of every 16 dogs tests positive for Lyme disease, and the incidence is growing<sup>4,5,9</sup>
  - The CDC reports more than 30,000 cases of human Lyme disease annually, up from 19,931 in 2006<sup>4,5</sup>
  - The prevalence of canine leptospirosis has increased in recent years, and as many as 8.2% of dogs are shedding leptospires, some asymptotically<sup>8</sup>
  - Weather changes, population growth, and habitat encroachment have all increased human and canine exposure to pathogens and their carriers<sup>8,10</sup>



# Leptospirosis presents multiple threats to your patients

## Dogs at risk

Dogs at greatest risk for developing leptospirosis include those with<sup>8</sup>:

- Access to ponds, lakes, streams, or standing water
- Exposure to urine from other infected animals, including:
  - Other dogs in crowded shelters or other pet care facilities
  - Wildlife (eg, rodents, raccoons, opossum, deer), either through direct contact with urine or through contaminated water

## Morbidity threats

As leptospirosis progresses, it can result in<sup>8,11</sup>:

- Leptospiremia
  - Leptospire can multiply in the bloodstream and spread to many tissues and organs
- Vascular damage/thrombocytopenia
  - Can lead to kidney failure and interfere with liver function
  - Contributes to coagulopathy abnormalities and hemorrhages
- Severe kidney and liver damage
  - Acute renal failure occurs in 80%-90% of dogs with severe clinical signs<sup>11</sup>
  - Acute hepatic dysfunction or chronic hepatitis have been caused by specific serovars

## Spreading disease

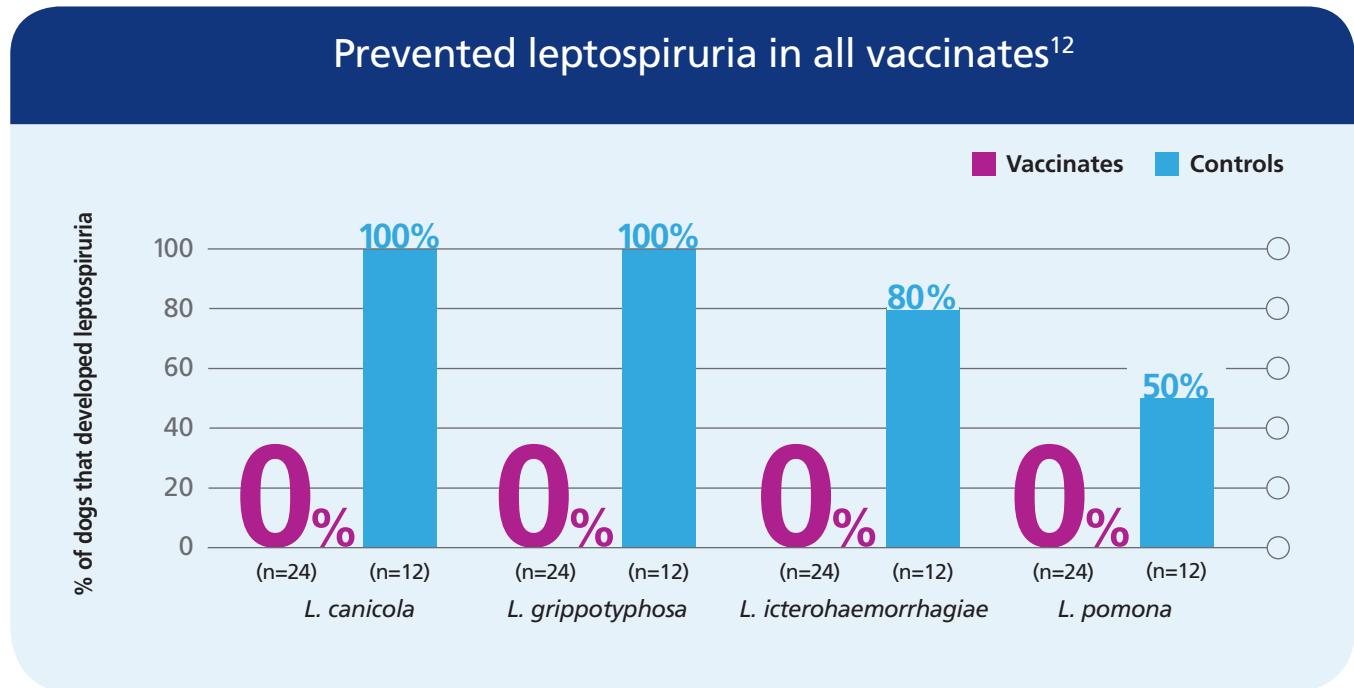
- Leptospiruria<sup>8</sup>
  - Infected dogs can enter a carrier state
  - Organisms may persist in the kidney and be shed in the urine for weeks to months



OTHER DOGS MAY BECOME INFECTED

## 2 critical indications

### 1. SHEDDING: defense against urinary shedding caused by 4 key *Leptospira* serovars



A key objective of vaccination is to prevent urinary shedding of leptospires, which has potential zoonotic risk<sup>8,12</sup>:

- 0% of dogs vaccinated with Nobivac<sup>®</sup> Canine 1-DAPPv+L<sub>4</sub> developed leptospiuria
- All of the control dogs challenged with *L. canicola* and *L. grippityphosa*, 80% of control dogs challenged with *L. icterohaemorrhagiae*, and 50% of control dogs challenged with *L. pomona* developed leptospiuria

Nobivac Lepto<sub>4</sub> prevents leptospiuria associated with

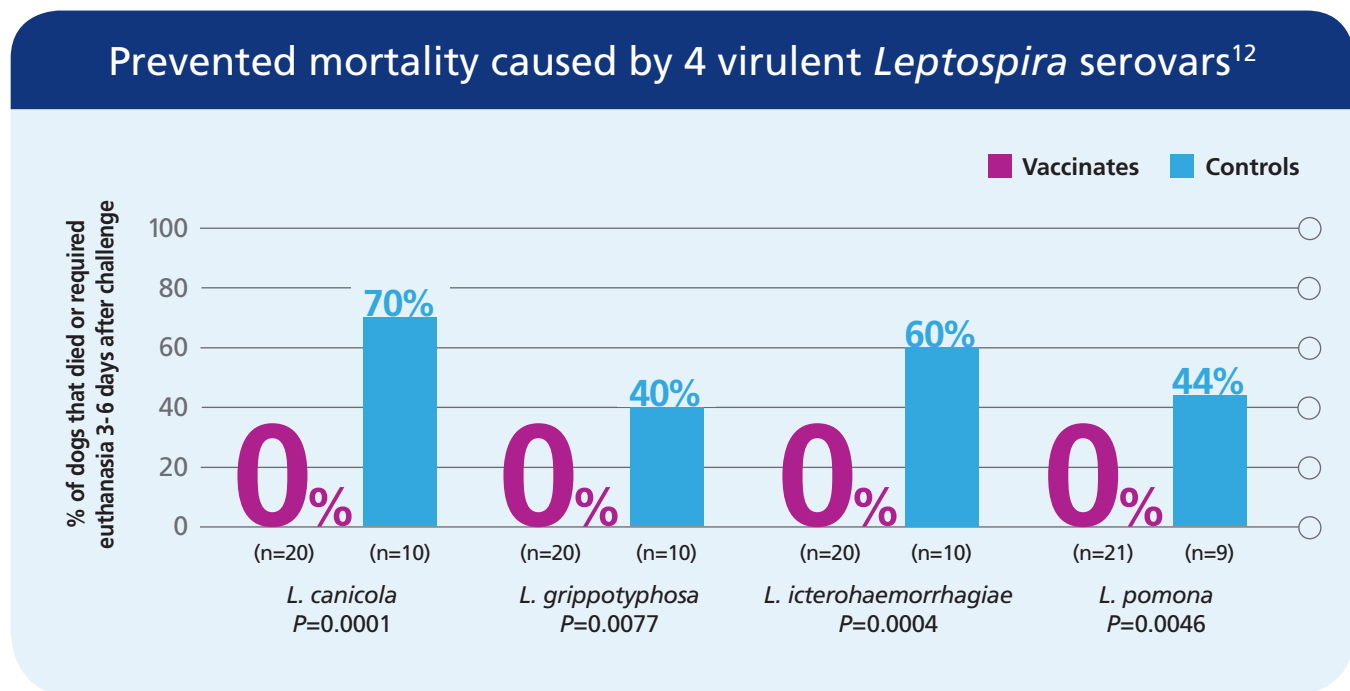
- *L. grippityphosa*
- *L. canicola*
- *L. icterohaemorrhagiae*

Nobivac Lepto<sub>4</sub> aids in the prevention of leptospiuria associated with

- *L. pomona*

## 2. MORTALITY: the only leptospirosis vaccine indicated to aid in the prevention of disease and mortality

- Protection for dogs facing the most severe challenges



- No dogs vaccinated with Nobivac® Canine 1-DAPPv+L<sub>4</sub> died or required euthanasia
- 54% mortality and euthanasia in control groups, reflecting the severity of challenge

Clinical efficacy results showed that Nobivac Canine 1-DAPPv+L<sub>4</sub> also prevented<sup>12</sup>

- Leptospiemia
  - More than 85% of vaccinates had no leptospiremia; leptospire were cleared quickly from the blood in those that did
  - By contrast, all control dogs had leptospiremia, and it lasted significantly longer, by days
- Liver dysfunction
  - Serum levels of bilirubin and AST\* remained at normal levels in significantly more vaccinates
- Thrombocytopenia
  - Platelet counts remained in the normal range

AVAILABLE IN 2 CONVENIENT FORMS:

**Nobivac Lepto<sub>4</sub>**  
**Nobivac Canine 1-DAPPv+L<sub>4</sub>**  
**combination vaccine** for the same critical  
 indications concerning shedding and mortality

\*AST = aspartate aminotransferase.

**Nobivac® Lepto<sub>4</sub>**

Because life is precious

## Unmatched protection<sup>12</sup>

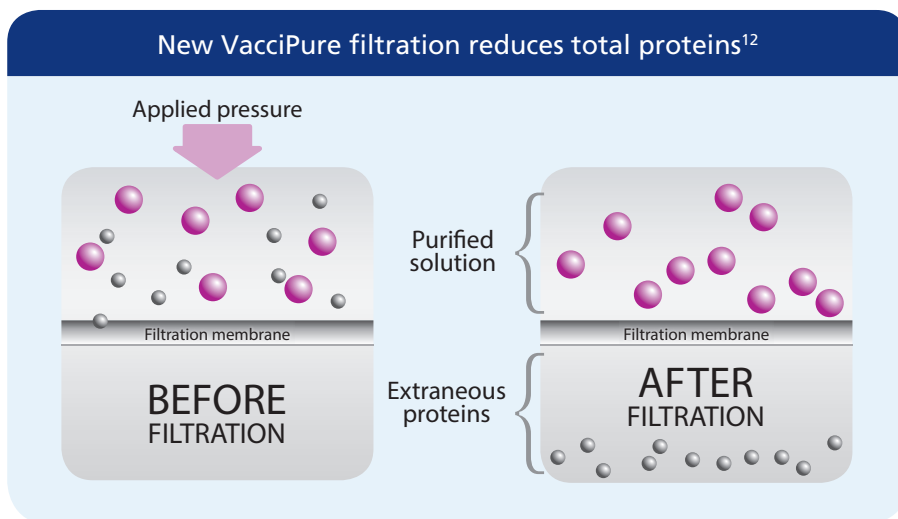
Nobivac Lepto<sub>4</sub> is the clear choice when compared with other 4-way leptospirosis vaccines.

		Nobivac <sup>®</sup> Lepto <sub>4</sub>	VANGUARD <sup>®</sup> L4	RECOMBITEK <sup>®</sup> 4 Lepto	ULTRA <sup>™</sup> Duramune <sup>®</sup> 4L	LEPTOVAX <sup>®</sup> 4
Prevents or aids in the prevention of leptospirosis		✓	✓	✓	✓	✓
Prevents leptospiuria caused by...	<i>Leptospira canicola</i>	✓		✓		
	<i>L. grippityphosa</i>	✓		✓		
	<i>L. icterohaemorrhagiae</i>	✓		✓		
Aids in the prevention of leptospiuria caused by...	<i>L. pomona</i>	✓		✓		
Aids in the prevention of mortality caused by virulent <i>Leptospira</i> serovars		✓				

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## A strategic advance: VacciPure<sup>™</sup> filtration technology<sup>12</sup>

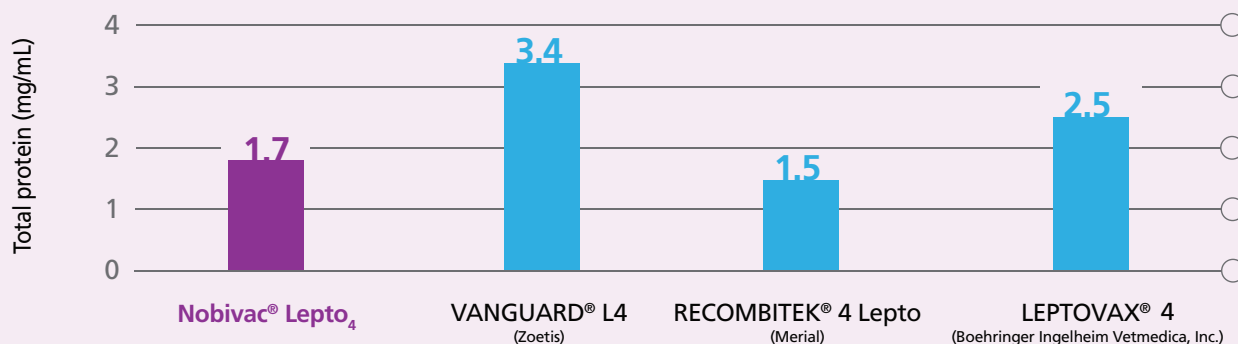
To promote an even higher level of vaccine quality, Merck Animal Health has introduced the special VacciPure filtration process in manufacturing Nobivac Lepto<sub>4</sub> and Nobivac<sup>®</sup> Canine 1-DAPPv+L<sub>4</sub>.



- A porous filtration membrane selectively removes extraneous proteins, salts, and solvents
- The outcome—fewer total proteins and a more purified final product

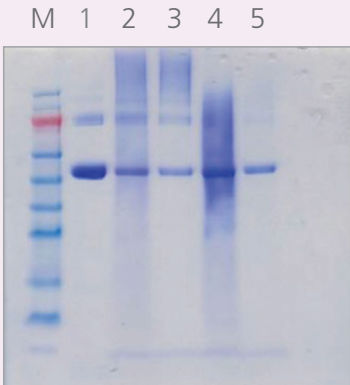
## Reduced total proteins through VacciPure<sup>12</sup>

### Comparison of total protein in leptospirosis vaccines<sup>12</sup>



- Fewer total proteins (TP) means a more purified final product, which may reduce unwanted immune system responses, such as vaccine reactions<sup>12</sup>

### Gel electrophoresis demonstrates comparative purity of Nobivac<sup>®</sup> vaccines<sup>12</sup>



- 1 —○ 1000 µg/mL BSA
- 2 —○ Nobivac<sup>®</sup> Canine 1-DAPPv+L<sub>4</sub>; TP = 6.05 mg/mL
- 3 —○ Nobivac Lepto<sub>4</sub>; TP = 1.66 mg/mL
- 4 —○ Ultra<sup>™</sup> Duramune<sup>®</sup> DAP + 4L; TP = 11.01 mg/mL
- 5 —○ Ultra<sup>™</sup> Duramune<sup>®</sup> 4L; TP = 1.12 mg/mL

## Results of a 749-dog field safety study<sup>12</sup>:

- Well tolerated on subcutaneous administration
  - Most adverse events involved scratching or small swellings at the injection site or lethargy, and were of short duration
  - Less frequently, soreness or vomiting occurred, but resolved within 24 hours
- Proven safe across a variety of breeds and ages

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# Nobivac<sup>®</sup>:Lepto<sub>4</sub>

*Because life is precious*

## Incidence and risk of Lyme disease is on the rise

- Approximately 75% of unvaccinated dogs in endemic areas will eventually test positive for Lyme disease<sup>13</sup>
- Canine Lyme disease vaccine doses have decreased by 3% since 2010<sup>12</sup>
  - In 2013 only 3.4 million doses of Lyme vaccine were given, among a total of 49 million canine vaccinations<sup>12</sup>

### Get tough on canine Lyme with a 1-2 punch

OspC plays a pivotal role in Lyme disease transmission.

The unique dual action behind the 1-2 punch—why Nobivac Lyme is so effective

**1** Targets OspA in the tick's midgut<sup>14,15</sup>



When an unfed *Borrelia*-infected tick attaches to a dog, high levels of OspA are expressed by the *Borrelia* residing in the tick's midgut.

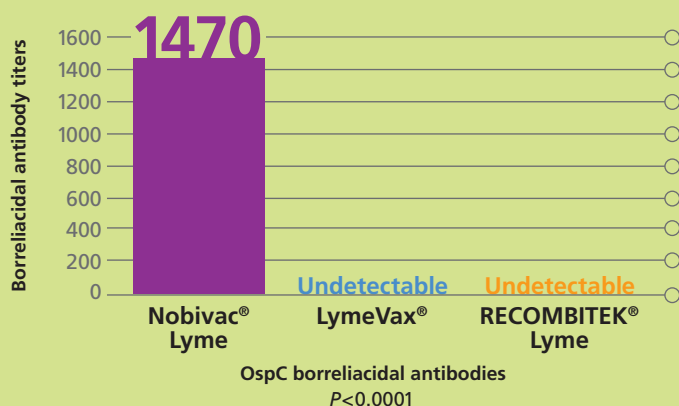
**2** Targets OspC in the tick's salivary glands and in the dog<sup>14,15</sup>



Soon after the tick begins its bloodmeal, OspA expression decreases and OspC expression increases, becoming the dominant Osp. Infection occurs when the *Borrelia*, which are now expressing only OspC, pass from the tick's midgut to its salivary glands and then into the dog.<sup>13</sup>

Nobivac Lyme is the vaccine with a traditional isolate targeted at OspA *and* a unique isolate proven to induce high levels of borreliacidal antibodies to OspC independent of the strain<sup>12</sup>

### Ability of vaccines to induce protective OspC borreliacidal antibodies



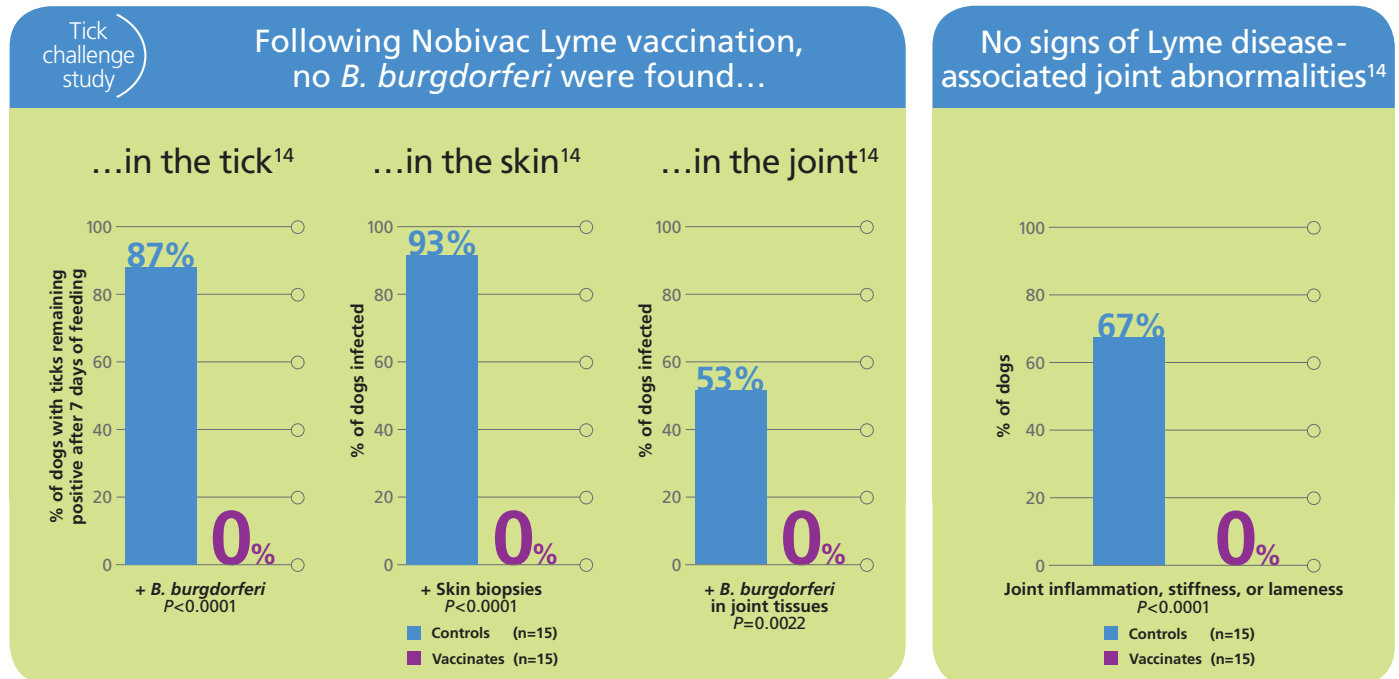
- All whole cell bacterins induce antibodies to OspA and OspC
- Nobivac Lyme induces **borreliacidal** antibodies that bind specifically to OspC, damaging the cell membrane and killing the *Borrelia*<sup>12,14</sup>

The level of OspC borreliacidal antibodies was identified by a flow cytometric procedure that detects the response by monitoring increased fluorescence intensity. The change in mean fluorescence intensity in serum from vaccinated dogs was measured and compared with control serum from a healthy, nonvaccinated dog to determine OspC antibody response.





The borreliacidal antibodies in Nobivac Lyme were shown to be highly effective in killing *B. burgdorferi* and preventing infection<sup>14</sup>



The tick challenge study was a placebo-controlled trial involving thirty 8-week-old puppies. Dogs were challenged 44 days following first vaccination.

Nobivac Lyme is proven to aid in the prevention of subclinical arthritis in addition to clinical disease<sup>14</sup>

The presence of nonviable organisms was also confirmed by darkfield microscopy.

**Nobivac<sup>®</sup> Lyme induces high levels of borreliacidal antibodies against OspC independent of the strain<sup>14</sup>**

**Nobivac<sup>®</sup> Lyme**

*A powerful weapon against Lyme disease*

# Nobivac<sup>®</sup> Lyme—Protection<sup>SHARED</sup>

## Powerful comparative benefits and proven safety<sup>12</sup>

	Nobivac <sup>®</sup> Lyme	LymeVax <sup>®</sup>	RECOMBITEK <sup>®</sup> Lyme	Duramune <sup>®</sup> Lyme	Vanguard <sup>®</sup> crLyme
Induces <b>OspA</b> borreliacidal antibodies	✓	✓	✓	✓	✓
Induces <b>OspC</b> borreliacidal antibodies	✓				?
Aids in the <b>prevention of clinical disease</b> caused by <i>Borrelia burgdorferi</i>	✓	✓	✓	✓	✓
Aids in the <b>prevention of subclinical arthritis</b> associated with <i>B. burgdorferi</i>	✓				✓
Subcutaneous administration	✓	✓	✓	✓	✓
Initial vaccination	8 weeks	9 weeks	9 weeks	9 weeks	8 weeks
Second dose	2-4 weeks	2-3 weeks	2-3 weeks	2-3 weeks	3 weeks
Annual vaccination recommended	1 year	1 year	1 year	1 year	1 year

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## An exceptional safety profile you can rely on<sup>12</sup>

- Proven safe and well tolerated in a field safety trial of more than 600 dogs
  - 99.3% reaction-free
- Since 2009, Nobivac Lyme has been safely administered to over 4 million dogs

## Additional steps for the pet owner<sup>13,16</sup>

- Check pets daily for ticks, especially after time spent outdoors
- Remove ticks right away with appropriate methods
- Make a 'tick check' part of every veterinary visit
- Discuss geographic incidence of tickborne diseases with the veterinarian
- Reduce the tick habitat on your property
- In case of heavy outdoor tick infestation, treat the yard with acaricides licensed for outdoor use; this may also be best left to pest control professionals
- In case of indoor tick infestation, get help from pest control professionals
- Prevent tick infestations by regularly treating dogs all year long with effective acaricides



**Nobivac<sup>®</sup> Lyme**

*A powerful weapon against Lyme disease*

# Nobivac<sup>®</sup>—Protection<sup>SHARED</sup>

Advanced vaccines to protect extraordinary bonds...

## That's Protection<sup>SHARED</sup>

### Nobivac<sup>®</sup>:Lepto<sub>4</sub> and Nobivac<sup>®</sup> Canine 1-DAPPv+L<sub>4</sub>

*Because life is precious*

- The canine leptospirosis vaccines with **2** critical indications
  - Prevents or aids in the prevention of urinary shedding
  - Aids in the prevention of mortality
- Proven safe and well tolerated in many breeds including small breeds
- Featuring an even higher level of quality due to VacciPure™ filtration

### Nobivac<sup>®</sup>:Lyme

*A powerful weapon against Lyme disease*

- The vaccine that induces **2** borreliacidal antibodies against
  - OspA in the tick's midgut
  - OspC in the tick's salivary glands and in the dog independent of the borrelia strain
- Nobivac Lyme is proven to aid in the prevention of subclinical arthritis and other signs of Lyme disease
  - No joint inflammation, stiffness, or lameness was observed

*Ask about the Merck Animal Health line  
of flea and tick products!*



To learn more, contact your  
Merck Animal Health sales  
representative, or give us a call:

#### Customer Service

**1-800-521-5767**

(Monday – Friday, 9:00 AM – 6:00 PM EST)

#### Technical Services

**1-800-224-5318**

(Monday – Friday, 8:30 AM – 5:00 PM EST)

#### Vaccine Protocol Help Line

**1-866-437-7955**

(Monday – Friday, 8:00 AM – 5:00 PM EST)

**References:** **1.** American Humane Association. US pet (dog and cat) population fact sheet: pet demographic data. <http://www.americanhumane.org/assets/pdfs/pets-fact-sheet.pdf>. Accessed November 19, 2013. **2.** Pets and Parasites: the pet owner's parasite resource. CAPC 2012 forecast for Lyme disease. [http://www.petsandparasites.org/expert\\_insights/capc-2012-forecast-for-lyme-disease](http://www.petsandparasites.org/expert_insights/capc-2012-forecast-for-lyme-disease). Accessed November 18, 2013. **3.** American Humane Association. Keeping pets (dogs and cats) in homes: a three-phase retention study. 2012. <http://www.americanhumane.org/aha-petsmart-retention-study-phase-1.pdf>. Accessed November 19, 2013. **4.** Centers for Disease Control and Prevention. CDC provides estimate of Americans diagnosed with Lyme disease each year. <http://www.cdc.gov/media/releases/2013/p0819-lyme-disease.html>. Accessed November 18, 2013. **5.** Centers for Disease Control and Prevention. Reported cases of Lyme disease by state or locality, 2003-2012. [http://www.cdc.gov/lyme/stats/chartstables/reportedcases\\_statelocality.html](http://www.cdc.gov/lyme/stats/chartstables/reportedcases_statelocality.html). Accessed November 18, 2013. **6.** Centers for Disease Control and Prevention. Reported cases of Lyme disease by year, United States, 2003-2012. <http://www.cdc.gov/lyme/stats/chartstables/casebyyear.html>. Accessed November 18, 2013. **7.** IDEXX Reference Laboratories. Diagnosing and managing canine leptospirosis. [http://www.idexx.com/pubwebresources/pdf/en\\_us/smallanimal/reference-laboratories/diagnostic-updates/realpcr-canine-leptospirosis.pdf](http://www.idexx.com/pubwebresources/pdf/en_us/smallanimal/reference-laboratories/diagnostic-updates/realpcr-canine-leptospirosis.pdf). Accessed December 5, 2013. **8.** Greene CE, Sykes JE, Brown CA, Hartmann K. Leptospirosis. In: Greene CE, ed. *Infectious Diseases of the Dog and Cat*. 3rd ed. St. Louis, MO: Saunders/Elsevier; 2006:402-417. **9.** Parasite prevalence maps. <http://www.cpcvet.org/parasite-prevalence-maps/>. Accessed December 3, 2013. **10.** Harvard School of Public Health. Biodiversity and Infectious Diseases - The Center for Health and the Global Environment. <http://chge.med.harvard.edu/topic/biodiversity-and-infectious-diseases>. Accessed December 4, 2013. **11.** Kahn CM, Line S, eds. Leptospirosis. In: *The Merck Veterinary Manual*. 9th ed. Whitehouse Station, NJ: Merck & Co., Inc.; 2005:525-529. **12.** Data on file, Merck Animal Health. **13.** Stafford KC III. Tick Management Handbook: an integrated guide for homeowners, pest control operations, and public health officials for the prevention of tick-associated disease. Bulletin no. 1010. New Haven: The Connecticut Agricultural Experiment Station; 2007. **14.** LaFleur RL, Dant JC, Wasmoen TL, et al. Bacterin that induces anti-OspA and anti-OspC borrelial antibodies provides a high level of protection against canine Lyme disease. *Clin Vaccine Immunol*. 2009;16(2):253-259. **15.** Schwan TG, Piesman J. Vector interactions and molecular adaptations of Lyme disease and relapsing fever spirochetes associated with transmission by ticks. *Emerg Infect Dis*. 2002;8(2):115-121. **16.** Centers for Disease Control and Prevention. Preventing ticks on your pets. [http://www.cdc.gov/lyme/prev/on\\_pets.html](http://www.cdc.gov/lyme/prev/on_pets.html). Accessed December 5, 2013.

**Nobivac**<sup>®</sup>  
Essential protection for essential bonds



# Protection for any dog

Nobivac<sup>®</sup> offers a range of core vaccine options, as well as unique non-core vaccine options, so you can build the right protocols for your patients

## CANINE VACCINES

	Distemper Virus*	Adenovirus Type 2	Parainfluenza	Parvovirus	Leptospira	Coronavirus	Lyme	Canine Influenza Virus†	Bordetella‡	Rabies	Non-adjuvanted
<b>1-year vaccines</b>											
● Nobivac <sup>®</sup> Canine 1-DAPPv	●	●	●	●							●
● Nobivac <sup>®</sup> Canine 1-DAPPv+Cv	●	●	●	●		●					●
● Nobivac <sup>®</sup> Canine 1-DAPPvL <sub>2</sub>	●	●	●	●	●						●
● Nobivac <sup>®</sup> Canine 1-DAPPvL <sub>2</sub> +Cv	●	●	●	●	●	●					●
● Nobivac <sup>®</sup> Lepto <sub>4</sub>					●						
● Nobivac <sup>®</sup> Canine 1-DAPPv+L <sub>4</sub>	●	●	●	●	●						
● Nobivac <sup>®</sup> Canine 1-Cv						●					
● Nobivac <sup>®</sup> Canine 1-Pv				●							●
● Nobivac <sup>®</sup> Puppy-DPv	●			●							●
● Nobivac <sup>®</sup> Lyme						●					
● Nobivac <sup>®</sup> Canine Flu H3N8							●				
● Canine Influenza Vaccine H3N2 <sup>†</sup>							●				
● Nobivac <sup>®</sup> 1-Rabies									●		
<b>3-year vaccines</b>											
● Nobivac <sup>®</sup> Canine 3-DAPv	●	●		●							●
● Nobivac <sup>®</sup> 3-Rabies									●		●
● Nobivac <sup>®</sup> 3-Rabies CA									●		●
<b>Intranasal vaccines</b>											
● Nobivac <sup>®</sup> Intra-Trac <sup>®</sup> KC			●					●			●
● Nobivac <sup>®</sup> Intra-Trac <sup>®</sup> <sub>3</sub>		●	●					●			●
● Nobivac <sup>®</sup> Intra-Trac <sup>®</sup> <sub>3</sub> ADT		●	●					●			●

Colored dot(s) next to product names indicate cap color(s).  
\* Modified live virus. † Avirulent live.

<sup>†</sup> Canine Influenza Vaccine H3N2 is conditionally licensed and has a reasonable expectation of efficacy and safety.

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