Summary of Studies Supporting USDA Product Licensure

Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	2126.R1
True Name	Borrelia Burgdorferi Bacterial Extract
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Vanguard CrLyme - No distributor specified
Date of Compilation Summary	December 26, 2017

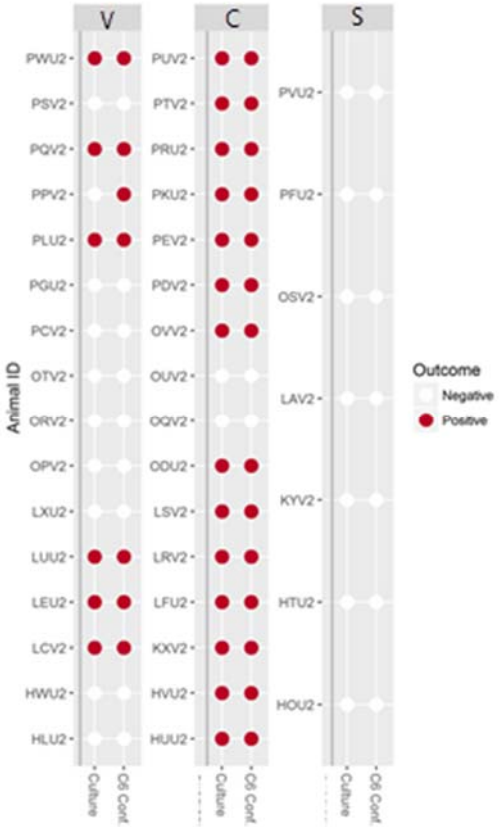
Disclaimer: Do not use the following studies to compare one product to another. Slight differences in study design and execution can render the comparisons meaningless.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Borrelia burgdorferi</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness against Borrelia burgdorferi</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered subcutaneously, 3 weeks apart.</td></tr>
<tr><td>Study Animals</td><td>Study involved 16 vaccinated, 16 placebo control, and 7 sentinel puppies, 8 weeks of age.</td></tr>
<tr><td>Challenge Description</td><td>Vaccinates and controls were challenged 480 days following administration of the second vaccination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Ninety days post-challenge skin, synovial joint tissues (left and right shoulder, left and right elbow, left and right carpus, left and right tarsus), and kidneys were collected, analyzed for histopathology, and cultured for B. burgdorferi. Lameness and anti-Borrelia C_6 antibody were also evaluated.</td></tr>
<tr><td>Results</td><td>
Table 1. Incidence of Disease in Non-vaccinated and Vaccinated Dogs
<table>
<tr><th rowspan="2">Treatment</th><th colspan="4">Disease?</th><th rowspan="2">Total</th></tr>
<tr><th colspan="2">No</th><th colspan="2">Yes</th></tr>
<tr><th></th><th>No. of Animals</th><th>%</th><th>No. of Animals</th><th>%</th><th>No. of Animals</th></tr>
<tr><td>NTX*</td><td>7</td><td>100.0</td><td>0</td><td>0.0</td><td>7</td></tr>
<tr><td>Unvaccinated Control Dogs</td><td>2</td><td>12.5</td><td>14</td><td>87.5</td><td>16</td></tr>
<tr><td>Vaccinated Dogs</td><td>9</td><td>56.3</td><td>7</td><td>43.7</td><td>16</td></tr>
</table>
*NTX – sentinel dogs. Unvaccinated/unchallenged.

An animal was designated diseased if it was either culture positive or C_6 positive, accompanied by histological changes in the tissues or lameness.

The raw data for the animals are shown on the attached page.
</td></tr>
<tr><td>USDA Approval Date</td><td>July 10, 2017</td></tr>
</table>

Table 2. Individual Animal Data for Disease



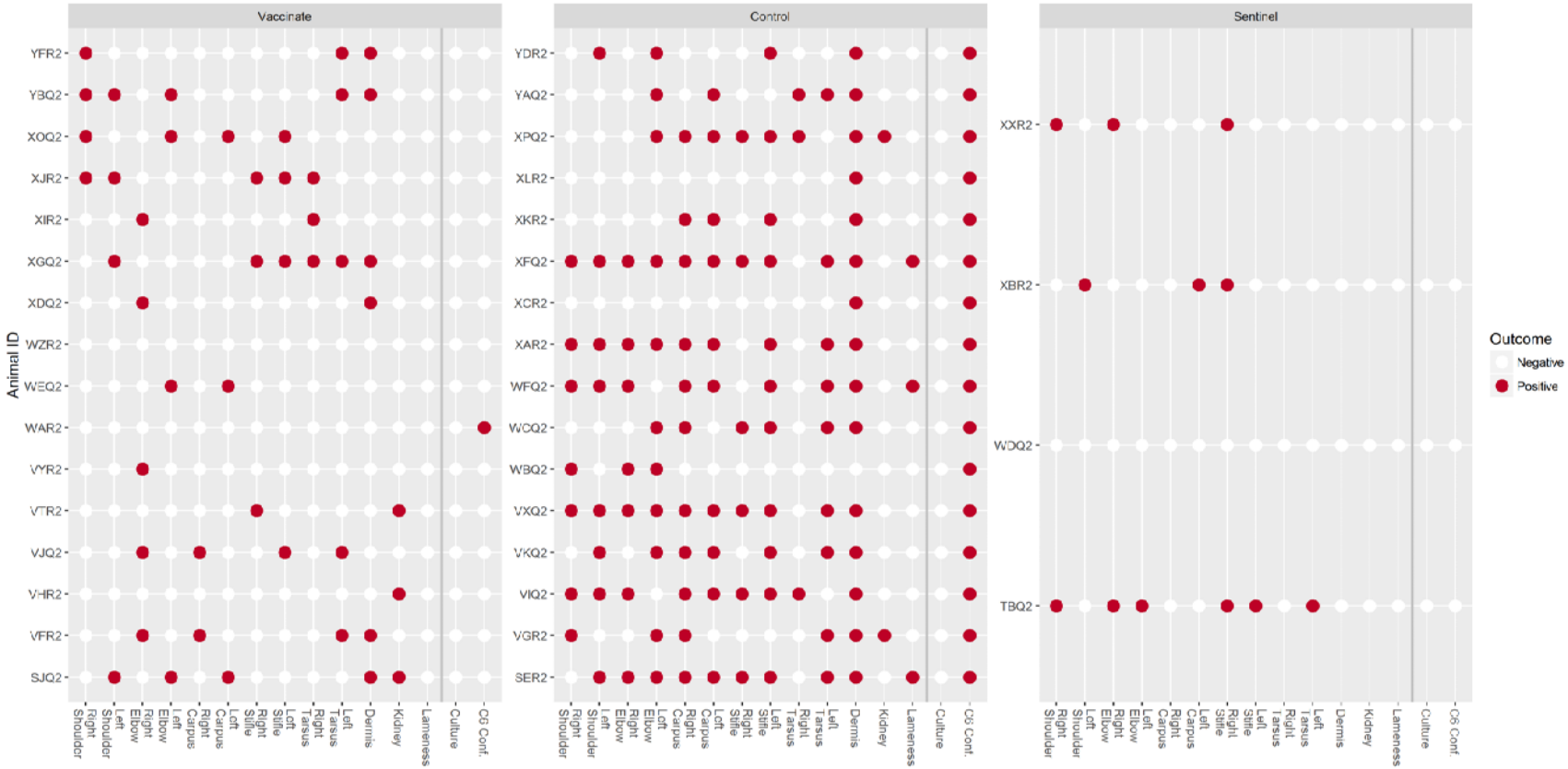
V=vaccinate, C=control, S=sentinel

All challenged animals had at least mild histological changes in the tissues.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Borrelia burgdorferi</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness against Borrelia burgdorferi</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered subcutaneously, 3 weeks apart.</td></tr>
<tr><td>Study Animals</td><td>Study involved 16 vaccinated and 16 placebo puppies, and 4 sentinels, 8 weeks of age.</td></tr>
<tr><td>Challenge Description</td><td>Vaccinates and controls were challenged 21 days following administration of the second vaccination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Ninety days post-challenge, bone (femur and humerus), skin, synovial joint tissues (left and right shoulder, left and right elbow, left and right carpus, left and right tarsus), and kidneys were collected and were analyzed for histopathology. Lameness and anti-Borrelia C6 antibody were evaluated.</td></tr>
<tr><td>Results</td><td>An animal was designated diseased if it was either culture positive or C6 positive, accompanied by histological changes in the tissues or lameness.

Table 1. Incidence of Disease in Non-vaccinated and Vaccinated Dogs
<table>
<tr><th rowspan="3">Treatment</th><th colspan="4">Disease?</th><th rowspan="2">Total</th></tr>
<tr><th colspan="2">No</th><th colspan="2">Yes</th></tr>
<tr><th>No. of Animals</th><th>%</th><th>No. of Animals</th><th>%</th><th>No. of Animals</th></tr>
<tr><td>NTX*</td><td>4</td><td>100.0</td><td>0</td><td>0.0</td><td>4</td></tr>
<tr><td>Unvaccinated Control Dogs</td><td>0</td><td>0.0</td><td>16</td><td>100.0</td><td>16</td></tr>
<tr><td>Vaccinated Dogs</td><td>16</td><td>100.0</td><td>0</td><td>0.0</td><td>16</td></tr>
</table>
*NTX – sentinel dogs. Unvaccinated/unchallenged.

The raw data for the animals are shown on the attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>August 22, 2017</td></tr>
</table>



Histopathology results for tissue (joint, skin, kidney), lameness, tissue culture, and C_6 confirmation results for each dog by treatment group. Abnormal histopathology tissue results were positive if the score was ≥ 1or results = 'Yes'. Skin was the only tissue cultured and it was negative for all dogs. A dog was considered lame if it ever experienced lameness during the study.

Study Type	Safety
Pertaining to	ALL
Study Purpose	To demonstrate safety under conditions of normal use
Product Administration	Two doses, administered subcutaneously 3-4 weeks apart.
Study Animals	Study involved 620 dogs total, with 203 dogs $\leq$ 8 weeks of age and 417 dogs $\geq$ 9 weeks of age from three different geographical locations.
Challenge Description	N/A
Interval observed after challenge	Immediate abnormal health events were assessed by the Examining Veterinarian or by a trained specialist for approximately 10-20 minutes post (each) vaccination. Dogs were observed for late abnormal health events primarily by their owners, or by Veterinarians or trained specialists. The observations were performed for 10 days post (each) vaccination.
Results	A total of 9 cases did not complete the study: 5 cases were related to non-compliance due to reasons other than abnormal health event, 2 cases were due to abnormal health events unrelated to the IVP and 2 cases were due to owner's decision to withdraw the animal from the study. See following page for data.
USDA Approval Date	July 08, 2015

Results

Table 1: Frequency Distribution of Immediate Abnormal Health events. (IVP-Investigational Veterinary Product)

		Number of Dogs	
Abnormal Health Events	**Number of Vaccinations[a]**	**Overall N (%)**	**Related to IVP N (%)**
Emesis	1231	1 (0.08%)	0 (0%)
Injection Site Self-Trauma[b]	1231	1 (0.08%)	1 (0.08%)
Injection Site Paraesthesia	1231	5 (0.41%)	3 (0.24%)
Vocalization at Administration	1231	15 (1.22%)	9 (0.73%)

[a]A total of 1232 vaccinations were performed but 1231 are being reported since immediate abnormal health events were not recorded for one dog

[b]Scratching, biting, or rubbing at injection site

Table 2: Frequency Distributions of Other Immediate Abnormal Health Events. (IVP-Investigational Veterinary Product)

		Number of Dogs	
Abnormal Health Events	**Number of Vaccinations[a]**	**Overall N (%)**	**Related to IVP N (%)**
Injection Site Oedema	1231	1 (0.08%)	1 (0.08%)
Injection Site Reaction	1231	1 (0.08%)	0 (0%)
Lethargy	1231	1 (0.08%)	1 (0.08%)

[a]A total of 1232 vaccinations were performed but 1231 are being reported since immediate abnormal health events were not recorded for one dog

Table 3: Frequency Distributions of Late Abnormal Health Events. (IVP-Investigational Veterinary Product)

		Number of Dogs	
Abnormal Health Event	**Number of Vaccinations**	**Overall N (%)**	**Related to IVP N (%)**
Anorexia	1232	4 (0.32%)	1 (0.08%)
Diarrhea	1232	12 (0.97%)	2 (0.16%)
Emesis	1232	8 (0.65%)	0 (0%)
Hyperthermia	1232	1 (0.08%)	1 (0.08%)
Injection Site Oedema	1232	40 (3.25%)	40 (3.25%)
Injection Site Pain	1232	4 (0.32%)	4 (0.32%)
Lameness	1232	1 (0.08%)	0 (0%)
Lethargy	1232	6 (0.49%)	3 (0.24%)
Muscle Tremor	1232	1 (0.08%)	1 (0.08%)