Summary of Studies Supporting USDA Product Licensure

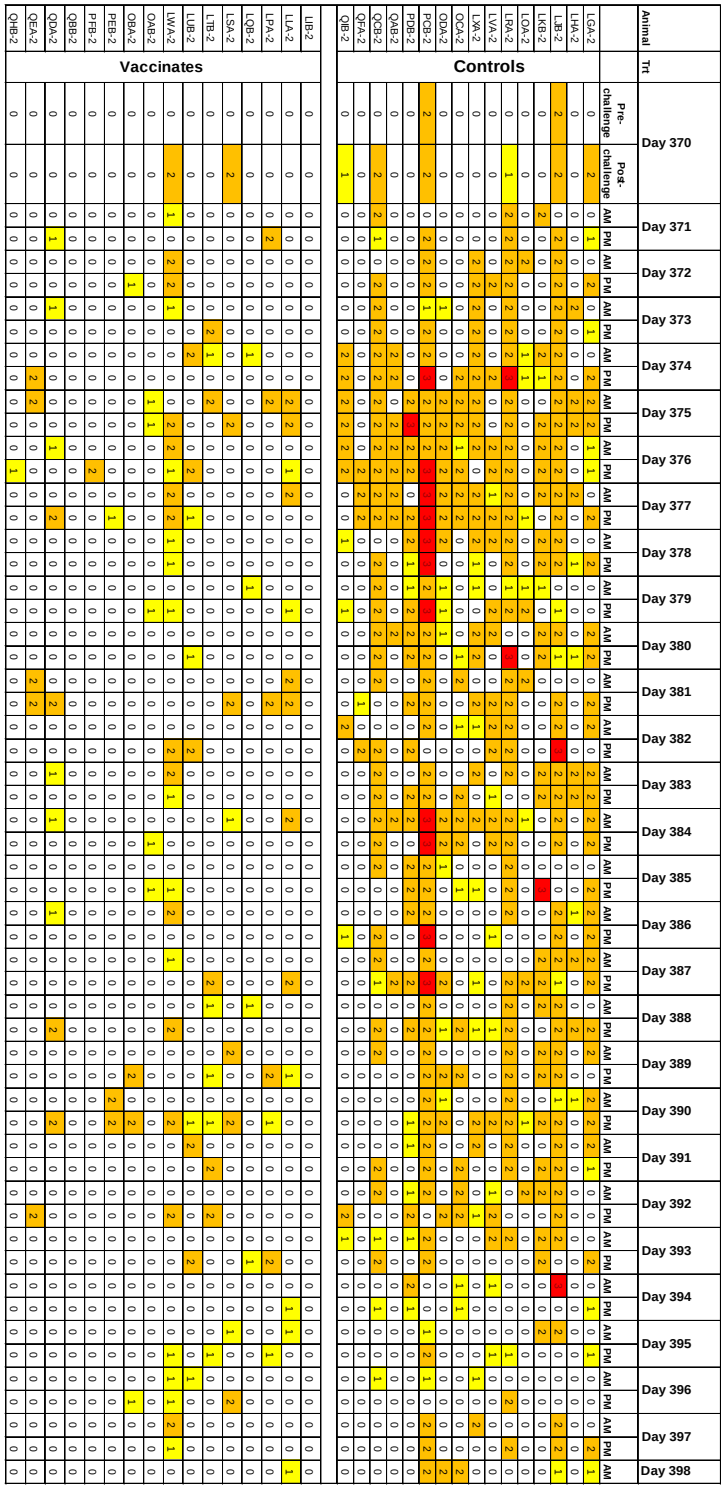
Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	14M1.20
True Name	Canine Parainfluenza-Bordetella Bronchiseptica Vaccine, Modified Live Virus, Avirulent Live Culture
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Vanguard Intranasal Rapid RESP 2 - No distributor specified Vanguard Intranasal Rapid RESP 2 SF - No distributor specified
Date of Compilation Summary	December 19, 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>Bordetella bronchiseptica (B. bronchiseptica)</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness against B. bronchiseptica infection one year after vaccination</td></tr>
<tr><td>Product Administration</td><td>One dose, administered intranasally</td></tr>
<tr><td>Study Animals</td><td>Study involved 16 vaccinated and 16 control puppies, 8 weeks of age</td></tr>
<tr><td>Challenge Description</td><td>Challenged with B. bronchiseptica, one year after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>After challenge, dogs were observed daily 28 days post-challenge.</td></tr>
<tr><td>Results</td><td>Number of days of coughing
Five number summary (Q=quartile)
<table>
<tr><th>Treatment</th><th colspan="5">Number of Days Animal Coughed</th></tr>
<tr><th></th><th>Min</th><th>Q1</th><th>Median</th><th>Q3</th><th>Max</th></tr>
<tr><td>Control</td><td>4.0</td><td>10.0</td><td>18.0</td><td>25.5</td><td>28.0</td></tr>
<tr><td>Vaccine</td><td>0.0</td><td>1.5</td><td>4.0</td><td>9.5</td><td>20.0</td></tr>
</table>
If coughing was observed at either of the two daily observation periods on a day, that day was positive for coughing.

The raw data is shown on the attached page</td></tr>
<tr><td>USDA Approval Date</td><td>June 20, 2014</td></tr>
</table>

Table 3: Individual Animal Data for Coughing Post-challenge



Key

Trt = treatment 1 = mild cough

2 = moderate cough 3 = severe cough

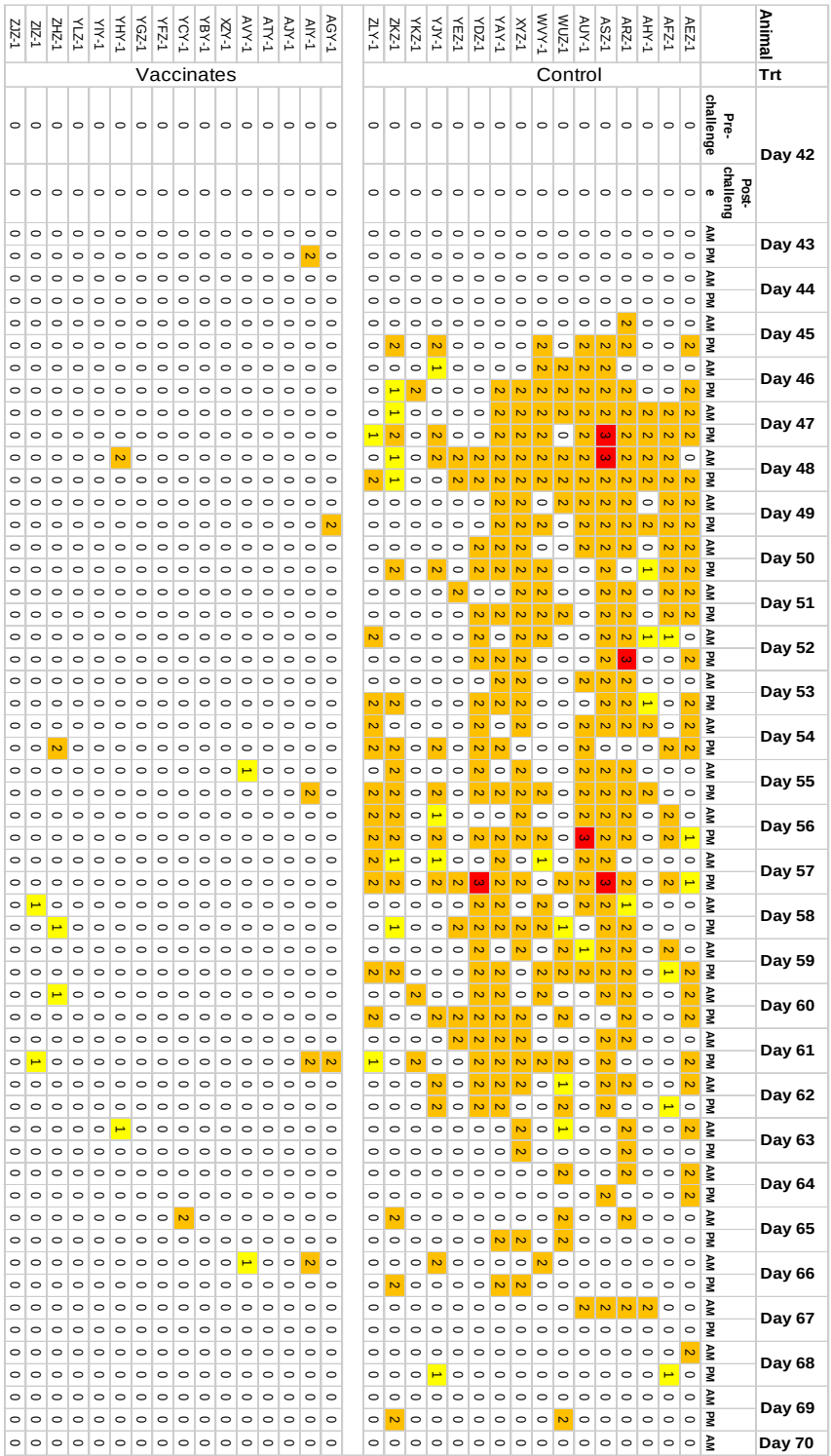
<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bordetella bronchiseptica (B. bronchiseptica)</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate efficacy against B. bronchiseptica infection</td></tr>
<tr><td>Product Administration</td><td>One dose, administered intranasally</td></tr>
<tr><td>Study Animals</td><td>Study involved 16 vaccinated and 16 control puppies, 8 weeks of age</td></tr>
<tr><td>Challenge Description</td><td>Challenged with B. bronchiseptica, 42 days after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>After challenge, dogs were observed daily for coughing for 28 days</td></tr>
<tr><td>Results</td><td>A dog was considered affected if coughing was observed at least once on 2 or more consecutive days.

Table 1: Clinical Respiratory Sign (Coughing)

<table>
<tr><th rowspan="2">Treatment</th><th rowspan="2">Total</th><th colspan="2">At least 1 day</th><th colspan="2">At least one occurrence of 2 consecutive days</th><th colspan="3">Duration</th></tr>
<tr><th>Positive</th><th>Negative</th><th>Positive</th><th>Negative</th><th>Q1</th><th>Median</th><th>Q3</th></tr>
<tr><td>Control</td><td>16</td><td>16/16 (100%)</td><td>0/16 (0%)</td><td>15/16 (94%)</td><td>1/16 (6%)</td><td>18.5</td><td>22.0</td><td>23.5</td></tr>
<tr><td>Vaccinated</td><td>16</td><td>7/16 (44%)</td><td>9/16 (56%)</td><td>0/16 (0%)</td><td>16/16 (100%)</td><td>0</td><td>0</td><td>9.5</td></tr>
</table>

Please see attached page for individual raw data.</td></tr>
<tr><td>USDA Approval Date</td><td>April 18, 2013</td></tr>
</table>

Table 2: Individual Animal Data of Coughing



Key

Trt = treatment group 1 = mild cough

2 = moderate cough 3 = severe cough

Study Type	Efficacy
Pertaining to	Canine Parainfluenza Virus (CPIV)
Study Purpose	To demonstrate effectiveness against Canine Parainfluenza Virus respiratory disease one year after vaccination.
Product Administration	One dose, administered intranasally.
Study Animals	Study involved 20 vaccinated and 10 control puppies seronegative to CPIV, 7-8 weeks of age.
Challenge Description	Challenged with CPIV strain, one year after vaccination.
Interval observed after challenge	After challenge dogs were observed for 14 days and sampled for nasal secretions to measure challenge virus shedding.

Results	An animal was considered affected if the nasal virus isolation titer was > 0.5 $\log_{10}$ $TCID_{50}$/mL at any point post-challenge. **Table 1:** Frequency distribution of ever having CPIV detected post-challenge in nasal swabs

	Ever Detected?				
	No		Yes		Total
	No. of Animals	%	No. of Animals	%	No. of Animals
Treatment					
Controls	2	20.00	8	80.00	10
Vaccinates	16	80.00	4	20.00	20

The raw data is shown on the attached page.

USDA Approval Date	October 3, 2017

Table 2: Individual animal data of ever having CPIV detected post-challenge and duration in days of virus detection.

Treatment Number	Animal	Ever Detected	Duration in Days
Un-vaccinated/ Control Animals	6531989	**Yes**	**4**
	6532195	**Yes**	**1**
	6531814	No	0
	6532004	**Yes**	**1**
	6531849	No	0
	6532420	**Yes**	**4**
	6531997	**Yes**	**5**
	6531857	**Yes**	**4**
	6532128	**Yes**	**6**
	6532080	**Yes**	**1**
Vaccinated Animals	6531881	No	0
	6531962	No	0
	6532136	No	0
	6532446	**Yes**	**1**
	6531792	No	0
	6531890	No	0
	6532047	**Yes**	**1**
	6532055	No	0
	6531822	No	0
	6531831	No	0
	6532411	No	0
	6532438	No	0
	6532063	No	0
	6532071	No	0
	6531806	No	0
	6531865	**Yes**	**1**
	6532098	No	0
	6532110	No	0
	6532101	No	0
	6532144	**Yes**	**3**

Table 3. Nasal swab virus isolation titer data post-challenge for each animal by treatment group

Animal	Trt	SD 367	SD 368	SD 369	SD 370	SD 371	SD 372	SD 373	SD 374	SD 375	SD 376	SD 377	SD 378	SD 379	SD 380
6531814	Control Animals	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531849		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531857		<= 0.5	<= 0.5	1.8	1.8	<= 0.5	1	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531989		<= 0.5	1	2	2.3	1.3	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531997		<= 0.5	1	2	1.5	0.8	0.8	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532004		<= 0.5	<= 0.5	<= 0.5	0.8	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532080		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	1	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532128		<= 0.5	1	1	1.5	1	1.5	0.8	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532195		<= 0.5	1	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532420		<= 0.5	<= 0.5	1.8	2.3	1.8	0.8	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531792	Vaccinated Animals	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531806		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531822		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531831		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531865		<= 0.5	<= 0.5	0.8	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531881		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531890		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6531962		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532047		<= 0.5	<= 0.5	<= 0.5	1.3	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532055		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532063		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532071		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532098		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532101		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532110		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532136		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532144		<= 0.5	1.8	1	2.8	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532411		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532438		<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5
6532446		<= 0.5	1	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5	<= 0.5

TRT – Treatment Group
SD – Study Day
<=0.5 is considered negative

Study Type	Efficacy
Pertaining to	Canine Parainfluenza (CPIV)
Study Purpose	To demonstrate effectiveness against CPIV infection
Product Administration	One dose, administered intranasally
Study Animals	Study involved 20 vaccinated and 10 control puppies, 7-9 weeks of age
Challenge Description	Challenged with CPIV, 3 weeks after vaccination
Interval observed after challenge	After challenge, dogs were observed daily for 2 weeks and nasal swab samples were collected daily for 12 days.
Results	CPIV was detected in nasal swabs of 9/10 controls and 6/20 vaccinates during the observation period. Number of days of nasal shedding Five-number summary (*Q*=quartile) *Group* | *Min* | *Q1* | *Median* | *Q3* | *Max* *Vaccinates* | 0 | 0 | 0 | 1 | 5 *Controls* | 0 | 2 | 3.5 | 6 | 6 Please see attached page for individual raw data.
USDA Approval Date	March 14, 2013

Table 2: Individual animal data for CPIV Quantitative Virus Isolation from Nasal Swabs Post-Challenge

Animal	Trt	Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28	Day 29	Day 30	Day 31	Day 32	Day 33
1220604	Control	0.5	2.5	2	0.5	0.8	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220701		0.5	0.5	0.5	0.5	0.5	0.5	2.3	0.5	0.5	0.5	0.5	0.5
1220705		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220706		0.5	2.3	2.8	3	2.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221003		0.5	2.5	0.5	0.5	0.8	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221201		0.5	3	2.5	3.5	1.3	1.8	1	0.5	0.5	0.5	0.5	0.5
1221302		0.5	2.8	3	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221401		0.8	3	2.8	1.5	1.8	0.8	0.5	0.5	0.5	0.5	0.5	0.5
1221404		1.8	1.5	2.3	0.8	0.8	1.5	0.5	0.5	0.5	0.5	0.5	0.5
1221406		0.5	2.8	3.5	2.8	0.8	1	0.5	0.5	0.5	0.5	0.5	0.5
1220601	Vaccinated	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220602		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220603		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220702		0.5	0.8	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220703		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220704		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220901		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1220902		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221001		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221002		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221101		0.5	0.5	0.5	0.8	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221102		0.5	1.3	2.8	3	0.8	1.5	0.5	0.5	0.5	0.5	0.5	0.5
1221202		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221203		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	1	0.5	0.5
1221301		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221303		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221402		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221403		0.5	0.5	0.8	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221405		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
1221407		0.5	0.5	0.5	2.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

Trt = treatment
Green shading denotes positive virus isolation

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>ALL</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate safety under conditions of normal use</td></tr>
<tr><td>Product Administration</td><td>One dose, administered intranasally</td></tr>
<tr><td>Study Animals</td><td>Study involved 674 dogs total, with 239 dogs approximately 7-9 weeks of age and 435 dogs 10 weeks of age or older. Dogs were assigned to one of two lots of vaccine (T01- 309 animals; T02- 305 animals) or to a non-treated control group (T03- 60 animals).</td></tr>
<tr><td>Challenge Description</td><td>N/A</td></tr>
<tr><td>Interval observed after challenge</td><td>Immediate abnormal health events were assessed for approximately 10-15 minutes post-vaccination and late abnormal health events were assessed for 14 days post-vaccination.</td></tr>
<tr><td>Results</td><td>There were no immediate post-vaccination reactions observed in any of the vaccinated groups (T01, T02). There were no abnormal health events associated with the control group (T03).

<u>Frequency Distribution of Late Abnormal Health Events with dogs administered the product (T01 and T02)</u>
<table>
<tr><th>Clinical Signs Associated with Abnormal Health Event †</th><th>Number/Total Number of Animals (%)</th></tr>
<tr><td>Anorexia</td><td>3/614 (0.49%)</td></tr>
<tr><td>Ataxia</td><td>1/614 (0.16%)</td></tr>
<tr><td>Cough*</td><td>7/614 (1.14%)</td></tr>
<tr><td>Cystitis</td><td>2/614 (0.33%)</td></tr>
<tr><td>Dermatitis</td><td>1/614 (0.16%)</td></tr>
<tr><td>Diarrhea</td><td>4/614 (0.65%)</td></tr>
<tr><td>Emesis*</td><td>3/614 (0.49%)</td></tr>
<tr><td>Emesis</td><td>5/614 (0.80%)</td></tr>
<tr><td>Internal ear disorder (head tilt)</td><td>1/614 (0.16%)</td></tr>
<tr><td>Lethargy</td><td>5/614 (0.81%)</td></tr>
<tr><td>Nystagmus</td><td>1/614 (0.16%)</td></tr>
<tr><td>Otitis externa</td><td>2/614 (0.33%)</td></tr>
<tr><td>Pruritis</td><td>1/614 (0.16%)</td></tr>
<tr><td>Pyrexia</td><td>2/614 (0.33%)</td></tr>
<tr><td>Rhinitis</td><td>2/614 (0.33%)</td></tr>
<tr><td>Sneezing*</td><td>8/614 (1.30%)</td></tr>
<tr><td>Urticaria**</td><td>1/614 (0.16%)</td></tr>
</table>
†One dog accounted for the abnormal health events of anorexia, ataxia, head tilt, nystagmus, lethargy, and otitis externa which was affirmed by licensee to not be related to vaccination.
*Mild, transient, and associated with the normal response to vaccination by licensee.</td></tr>
</table>

	**Urticaria occurred six days after administration of the vaccination.
USDA Approval Date	July 09, 2015