



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	15Q5.20
True Name	Canine Influenza Vaccine, H3N2 & H3N8, Killed Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Nobivac Canine Flu Bivalent - No distributor specified
Date of Compilation Summary	April 12, 2019

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.

Study Type	Efficacy																					
Pertaining to	Canine Influenza Virus (CIV) Strain H3N8																					
Study Purpose	To demonstrate efficacy against CIV H3N8																					
Product Administration	Two doses administered subcutaneously, 3 weeks apart																					
Study Animals	6- to 7-week-old dogs; 21 vaccinates, 15 controls																					
Challenge Description	Dogs were challenged with a heterologous strain of CIV H3N8 at 13 days after the second vaccination.																					
Interval observed after challenge	Dogs were monitored daily for 10 days post-challenge for clinical signs of CIV as coughing and virus shedding. Lungs were evaluated 10 days following challenge.																					
Results	<p>Table 1. The percent of lung mass that was abnormal (consolidated) was determined, and a lung lesion score was calculated for every animal. The histopathology diagnosis is found in Table 4.</p> <table border="1"> <thead> <tr> <th>Group</th> <th>N</th> <th>Minimum</th> <th>Q1</th> <th>Median</th> <th>Q3</th> <th>Maximum</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>21</td> <td>0.00</td> <td>0.00</td> <td>0.00</td> <td>0.09</td> <td>2.88</td> </tr> <tr> <td>Controls</td> <td>15</td> <td>0.00</td> <td>0.26</td> <td>1.09</td> <td>9.84</td> <td>27.93</td> </tr> </tbody> </table> <p>*</p> <p>Table 2. Dogs observed with a moderate to severe cough on at least one day postchallenge were considered positive.</p> <p>Table 3. Nasal swabs were collected daily to evaluate duration of shedding of CIV.</p> <p>Raw data shown on attached pages.</p>	Group	N	Minimum	Q1	Median	Q3	Maximum	Vaccinates	21	0.00	0.00	0.00	0.09	2.88	Controls	15	0.00	0.26	1.09	9.84	27.93
Group	N	Minimum	Q1	Median	Q3	Maximum																
Vaccinates	21	0.00	0.00	0.00	0.09	2.88																
Controls	15	0.00	0.26	1.09	9.84	27.93																
USDA Approval Date	November 17, 2008																					

Table 1

Treatment Group	Animal ID	Raw Scores										Weighted Scores										Total Score			
		Rt. Cranial	Rt. Middle	Rt. Caudal	Rt. Access	Lt. Cranial	Lt. Cranial-Caudal	Lt. Caudal	Rt. Cranial	Rt. Middle	Rt. Caudal	Rt. Access	Lt. Cranial	Lt. Cranial-Caudal	Lt. Caudal	Rt. Cranial	Rt. Middle	Rt. Caudal	Rt. Access	Lt. Cranial	Lt. Cranial-Caudal		Lt. Caudal		
Controls	CYTAPA	0	0	0	0	5	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0.5	0.1	0.3	0.8
	CYTAPC	5	2	1	1	8	10	1	0.8	0.2	0.2	0.1	0.7	0.6	0.3	2.9									
	CYTAPF	50	60	0	5	5	0	10	7.6	6	0	0.5	0.5	0	2.6										
	CYTAPH	1	1	0	0	0	0	0	0.2	0.1	0	0	0	0	0.3										
	CYTAPW	0	0	0	0	0	0	1	0	0	0	0	0	0.3											
	CYTAPZ	0	0	0	0	0	0	0	0	0	0	0	0	0	0										
	CYTARB	1	0	2	2	0	0	1	0.2	0	0.5	0.2	0	0	0.3										
	CYTARK	0	1	1	0	0	1	2	0	0.1	0.2	0	0	0.1	0.5										
	CYTARZ	0	0	0	0	0	0	0	0	0	0	0	0	0	0										
	CYTASE	0	1	1	0	2	5	1	0	0.1	0.2	0	0.2	0.3	1.1										
	CYTASH	1	1	1	0	0	2	3	0.2	0.1	0.2	0	0	0.1	0.8										
	CYTASI	20	50	0	5	10	3	1	3	5	0	0.5	0.9	0.2	0.3										
	CYTATE	20	10	0	30	50	70	10	3	1	0	2.7	4.6	4.2	2.6										
	CYTATH	0	0	2	0	5	0	1	0	0	0.5	0	0.5	0	0.3										
CYTAUR	40	70	0	60	50	60	5	6.1	7	0	5.4	4.6	3.6	1.3											
CYTANX	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTANZ	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAPB	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAPD	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAPE	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAPG	0	0	0	0	1	0	0	0	0	0	0	0.1	0	0											
CYTAPI	0	2	0	0	0	0	0	0	0.2	0	0	0	0	0.2											
CYTARA	0	0	0	1	2	0	0	0	0	0	0.1	0.2	0	0.3											
CYTARC	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTARF	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTARH	0	1	0	0	0	1	0	0	0.1	0	0	0	0.1	0											
CYTARJ	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTARY	0	8	0	0	20	0	1	0	0.8	0	0	1.8	0	0.3											
CYTASF	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTASG	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTATD	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTATF	0	2	0	0	0	0	0	0	0.2	0	0	0	0	0.2											
CYTAFL	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAUC	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAVT	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAVJ	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
Vaccinates	CYTAPA	0	0	0	0	5	1	1	0	0	0	0	0	0	0										
	CYTAPC	5	2	1	1	8	10	1	0.8	0.2	0.2	0.1	0.7	0.6	0.3										
	CYTAPF	50	60	0	5	5	0	10	7.6	6	0	0.5	0.5	0	2.6										
	CYTAPH	1	1	0	0	0	0	0	0.2	0.1	0	0	0	0	0.3										
	CYTAPW	0	0	0	0	0	0	1	0	0	0	0	0	0.3											
	CYTAPZ	0	0	0	0	0	0	0	0	0	0	0	0	0	0										
	CYTARB	1	0	2	2	0	0	1	0.2	0	0.5	0.2	0	0	0.3										
	CYTARK	0	1	1	0	0	1	2	0	0.1	0.2	0	0	0.1	0.5										
	CYTARZ	0	0	0	0	0	0	0	0	0	0	0	0	0	0										
	CYTASE	0	1	1	0	2	5	1	0	0.1	0.2	0	0.2	0.3	1.1										
	CYTASH	1	1	1	0	0	2	3	0.2	0.1	0.2	0	0	0.1	0.8										
	CYTASI	20	50	0	5	10	3	1	3	5	0	0.5	0.9	0.2	0.3										
	CYTATE	20	10	0	30	50	70	10	3	1	0	2.7	4.6	4.2	2.6										
	CYTATH	0	0	2	0	5	0	1	0	0	0.5	0	0.5	0	0.3										
CYTAUR	40	70	0	60	50	60	5	6.1	7	0	5.4	4.6	3.6	1.3											
CYTANX	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTANZ	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAPB	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAPD	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAPE	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAPG	0	0	0	0	1	0	0	0	0	0	0	0.1	0	0.1											
CYTAPI	0	2	0	0	0	0	0	0	0.2	0	0	0	0	0.2											
CYTARA	0	0	0	1	2	0	0	0	0	0	0.1	0.2	0	0.3											
CYTARC	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTARF	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTARH	0	1	0	0	0	1	0	0	0.1	0	0	0	0.1	0											
CYTARJ	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTARY	0	8	0	0	20	0	1	0	0.8	0	0	1.8	0	0.3											
CYTASF	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTASG	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTATD	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTATF	0	2	0	0	0	0	0	0	0.2	0	0	0	0	0.2											
CYTAFL	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAUC	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAVT	0	0	0	0	0	0	0	0	0	0	0	0	0	0											
CYTAVJ	0	0	0	0	0	0	0	0	0	0	0	0	0	0											

Table 2

Coughing Results following CIV Challenge

Treatment Group	Animal ID	Days Post-challenge												
		-2	-1	0	1	2	3	4	5	6	7	8	9	10
Controls	CYTAPA	-	-	-	-	C1	C1	C2	C0.5	-	C1	-	-	-
	CYTAPC	-	-	-	-	-	C1	-	-	-	-	C1	C1	-
	CYTAPF	-	-	-	-	-	-	-	C0.5	C1	C0.5	-	C1	-
	CYTAPH	-	-	-	-	-	-	-	-	-	C0.5	-	C0.5	-
	CYTAPW	-	-	-	-	-	C1	C1	C1	C1	-	-	-	-
	CYTAPZ	-	-	-	-	-	-	-	-	-	-	C0.5	-	-
	CYTARB	-	-	-	-	-	-	C2	C1	C1	-	-	-	C0.5
	CYTARK	-	-	-	-	-	C0.5	C1	C0.5	-	-	-	-	-
	CYTARZ	-	-	-	-	-	-	-	-	-	-	-	-	-
	CYTASE	-	-	-	-	-	C0.5	C2	C1	-	-	-	-	C0.5
	CYTASH	-	-	-	-	-	C1	C2	-	C2	C1	-	C1	C1
	CYTASI	-	-	-	-	-	C1	C1	-	C1	C1	C1	C1	-
	CYTATE	-	-	-	-	-	C1	-	-	-	C0.5	C2	C1	C0.5
	CYTATH	-	-	-	-	-	C1	C2	C0.5	-	C0.5	-	-	-
CYTAUR	-	-	-	-	-	-	C2	C0.5	-	C2	C1	C1	C0.5	
Vaccinates	CYTANX	-	-	-	-	-	C0.5	-	-	-	-	-	-	
	CYTANZ	-	-	-	-	-	-	-	-	-	-	-	-	
	CYTAPB	-	-	-	-	-	-	-	-	-	-	-	-	
	CYTAPD	-	-	-	-	-	-	-	-	-	-	-	-	
	CYTAPE	-	-	-	-	-	-	-	-	C1	-	-	-	
	CYTAPG	-	-	-	-	-	-	-	-	-	-	-	-	
	CYTAPI	-	-	-	-	-	-	-	-	-	-	-	-	
	CYTARA	-	-	-	-	-	-	-	-	-	-	-	-	C0.5
	CYTARC	-	-	-	-	-	-	-	-	-	-	-	-	-
	CYTARF	-	-	-	-	-	-	-	-	-	-	-	-	-
	CYTARH	-	-	-	-	-	-	-	-	C0.5	-	-	-	C1
	CYTARJ	-	-	-	-	-	-	-	-	-	-	-	-	-
	CYTARY	-	-	-	-	-	-	-	-	-	-	-	-	-
	CYTASF	-	-	-	-	-	-	-	-	-	-	-	-	-
	CYTASG	-	-	-	-	-	-	-	-	-	-	-	-	-
	CYTATD	-	-	-	-	-	-	-	-	-	-	-	-	C0.5
	CYTATF	-	-	-	-	-	-	-	C1	C0.5	C1	C0.5	C2	C1
CYTATL	-	-	-	-	-	-	-	-	-	-	-	-	-	
CYTAUC	-	-	-	-	-	-	-	-	C0.5	-	-	-	-	
CYTAVT	-	-	-	-	-	-	-	-	-	-	-	-	-	
CYTAVJ	-	-	-	-	-	-	-	-	-	-	-	-	-	

- = Absent

C0.5 = Mild: Only one brief cough is observed.

C1 = Moderate: Cough is persistent, occurring repeatedly in the observation period.

C2 = Severe: Cough is accompanied by choking or retching sounds.

Table 3

Post-challenge nasal CIV shedding

Treatment Group	Animal ID	Days Post-challenge										
		-1	1	2	3	4	5	6	7	8	9	10
Controls	CYTAPA	-	-	+	+	+	+	+	-	-	-	-
	CYTAPC	-	+	+	+	+	+	+	+	-	-	-
	CYTAPF	-	-	-	+	+	+	+	-	-	-	-
	CYTAPH	-	-	+	-	+	+	-	-	-	-	-
	CYTAPW	-	+	+	+	+	+	-	-	-	-	-
	CYTAPZ	-	-	+	+	+	+	-	-	-	-	-
	CYTARB	-	+	+	+	+	+	+	-	-	-	-
	CYTARK	-	-	-	+	+	-	-	-	-	-	-
	CYTARZ	-	+	+	+	+	-	+	-	-	-	-
	CYTASE	-	+	+	+	+	-	-	-	-	-	-
	CYTASH	-	+	+	+	+	+	-	-	-	-	-
	CYTASI	-	+	+	+	+	+	+	-	-	-	-
	CYTATE	-	+	+	+	+	+	+	-	-	-	-
	CYTATH	-	+	+	+	+	+	+	-	-	-	-
CYTAUR	-	+	+	+	+	+	+	-	-	-	-	
Vaccinates	CYTANX	-	-	+	-	-	-	-	-	-	-	-
	CYTANZ	-	+	+	-	+	+	+	-	-	-	-
	CYTAPB	-	-	+	-	-	-	-	-	-	-	-
	CYTAPD	-	-	-	-	-	-	-	-	-	-	-
	CYTAPE	-	+	-	-	+	-	-	-	-	-	-
	CYTAPG	-	-	-	-	-	-	-	-	-	-	-
	CYTAPI	-	-	-	-	-	-	-	-	-	-	-
	CYTARA	-	-	+	-	-	-	-	-	-	-	-
	CYTARC	-	-	+	-	+	+	+	-	-	-	-
	CYTARF	-	-	+	-	+	-	-	-	-	-	-
	CYTARH	-	-	+	-	+	+	-	-	-	-	-
	CYTARJ	-	-	+	-	-	-	-	-	-	-	-
	CYTARY	-	-	+	+	+	+	+	+	-	-	-
	CYTASF	-	+	+	-	-	+	-	-	-	-	-
	CYTASG	-	-	+	-	-	+	-	-	-	-	-
	CYTATD	-	+	+	-	-	+	-	-	-	-	-
	CYTATF	-	+	+	-	-	+	-	-	-	-	-
	CYTATL	-	-	+	-	-	-	-	-	-	-	-
CYTAUC	-	+	+	-	-	-	-	-	-	-	-	
CYTAVT	-	-	+	-	-	-	-	-	-	-	-	
CYTAVJ	-	-	-	-	-	-	-	-	-	-	-	

+ = Positive; - = Negative

Table 4

Histopathology results

Treatment Group	Animal ID	Histopathological Lesions
Controls	CYTANY	Severe suppurative bronchointerstitial pneumonia with proliferative bronchiolitis (no tracheal tissue)
	CYTARG	Mild focally extensive interstitial pneumonia. Lymph node: Mild hyperplasia
	CYTARI	Mild focally extensive interstitial pneumonia
	CYTAVL	Mild interstitial pneumonia with mild pulmonary hemorrhage and edema (no tracheal tissue)
	CYTAPA	Mild Focally extensive interstitial pneumonia. Trachea: No significant Lesion (NSL)
	CYTAPC	Moderate suppurative bronchointerstitial pneumonia with proliferative bronchiolitis & mild tracheitis
	CYTAPF	Severe suppurative bronchointerstitial pneumonia with proliferative bronchiolitis & mild tracheitis
	CYTAPH	Mild to moderate focally extensive interstitial pneumonia with mild acute tracheitis
	CYTAPW	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTAPZ	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTARB	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTARK	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTARZ	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTASE	Mild to moderate suppurative bronchointerstitial pneumonia with proliferative bronchiolitis. Trachea: NSL
	CYTASH	Mild bronchointerstitial pneumonia. Trachea: NSL
	CYTASI	Mild to moderate suppurative bronchointerstitial pneumonia with proliferative bronchiolitis and mild tracheitis. Lymph node: Moderate hyperplasia
	CYTATE	Severe suppurative bronchointerstitial pneumonia with proliferative bronchiolitis (no tracheal tissue)
	CYTATH	Mild bronchointerstitial pneumonia. Trachea: NSL
CYTAUR	Severe suppurative bronchointerstitial pneumonia with proliferative bronchiolitis. Trachea: NSL	
Vaccinates	CYTANX	Mild to moderate focally interstitial pneumonia. Trachea: NSL
	CYTANZ	Mild to moderate focally extensive interstitial pneumonia with mild acute tracheitis
	CYTAPB	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTAPD	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTAPE	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTAPG	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTAPI	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTARA	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTARC	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTARF	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTARH	Mild bronchointerstitial pneumonia. Trachea: NSL
	CYTARJ	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTARY	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTASF	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTASG	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTATD	Mild focally extensive interstitial pneumonia. Trachea: NSL
	CYTATF	Mild bronchointerstitial pneumonia. Trachea: NSL
	CYTATL	Mild Focally extensive interstitial pneumonia. Trachea: NSL
CYTAUC	Mild to moderate focally interstitial pneumonia. Trachea: NSL	
CYTAVT	Mild to moderate focally extensive interstitial pneumonia with mild acute tracheitis	
CYTAVJ	Mild focally extensive interstitial pneumonia. Trachea: NSL	

Dog was considered affected if classified with moderate or severe pneumonia.

Study Type	Efficacy																		
Pertaining to	Canine Influenza Virus (CIV) Strain H3N2																		
Study Purpose	To demonstrate efficacy against CIV H3N2																		
Product Administration	Two doses administered subcutaneously, 3 weeks apart																		
Study Animals	7- to 8-week old dogs; 18 vaccinates and 19 controls																		
Challenge Description	All dogs were challenged with a heterologous strain of CIV H3N2 at 13 days after the 2 nd vaccination.																		
Interval observed after challenge	Dogs were observed for 10 days after challenge. Lungs were evaluated at death or 10 days following challenge.																		
Results	<p>Table 1. The percent of the lung mass that was abnormal (consolidated) was determined, and a lung lesion score was calculated for every animal.</p> <table border="1"> <thead> <tr> <th>Group</th> <th>Minimum</th> <th>Q1</th> <th>Median</th> <th>Q3</th> <th>Maximum</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>0.0</td> <td>11.3</td> </tr> <tr> <td>Controls</td> <td>0.0</td> <td>1.4</td> <td>4.5</td> <td>16.9</td> <td>31.1</td> </tr> </tbody> </table> <p>Raw data shown on attached pages.</p>	Group	Minimum	Q1	Median	Q3	Maximum	Vaccinates	0.0	0.0	0.0	0.0	11.3	Controls	0.0	1.4	4.5	16.9	31.1
Group	Minimum	Q1	Median	Q3	Maximum														
Vaccinates	0.0	0.0	0.0	0.0	11.3														
Controls	0.0	1.4	4.5	16.9	31.1														
USDA Approval Date	July 15, 2016																		

CIV Post-Challenge Lung Lesion Scores

Treatment Group	Dog ID	Raw Scores										Weighted Scores										Total Score		
		R. Cranial	R. Middle	R. Caudal	R. Access	L.Cr- Cr	L. Cr- Cau	L. Caudal	R. Cranial	R. Middle	R. Caudal	R. Access	L. Cr- Cr	L. Cr- Cau	L. Caudal									
	CEN	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CER	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CEU	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CEX	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CFI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CFJ	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CGG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
A	CHD	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CHW	0	0	0	0	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0.9
Bivalent CIV	CIL	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.2
Vaccinates	CIM	0	60	0	0	0	60	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11.4
	CIT	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CIV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CIX	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CJC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CJF	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	CJG	0	5	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0	0	0	0	0	0	1.3
	CKP	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0

CIV Post-Challenge Lung Lesion Scores - continued

Treatment Group	Dog ID	Raw Scores								Weighted Scores								Total Score	
		R. Cranial	R. Middle	R. Caudal	R. Access	L.Cr- Cr	L. Cr- Cau	L. Caudal	L. L.	R. Cranial	R. Middle	R. Caudal	R. Access	L. Cr- Cr	L. Cr- Cau	L. Caudal	L. L.		
B Placebo- Vaccinated Controls	CEK	5	2	0	0	0	0	0	0	0	0	0	0.76	0.20	0.00	0.00	0.00	0.00	1.0
	CEL	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
	CEP	20	50	0	5	90	80	10	0	0	0	0	3.04	5.00	0.45	8.19	4.80	2.59	24.1
	CET	0	5	5	0	0	0	0	0	0	0	0	0.00	0.50	1.24	0.00	0.00	0.00	1.7
	CEV	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
	CFH	0	0	5	5	0	0	7	0	0	0	0	0.00	0.00	1.24	0.45	0.00	1.81	3.5
	CFK	5	20	10	0	20	30	2	0	0	0	0	0.76	2.00	2.48	0.00	1.82	0.52	9.4
	CGJ	40	0	0	0	0	0	2	0	0	0	0	6.08	0.00	0.00	0.00	0.00	0.52	6.6
	CHC	40	30	0	5	40	80	15	0	0	0	0	6.08	3.00	0.00	0.45	3.64	3.89	21.9
	CHX	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
	CHY	10	70	30	10	40	90	20	0	0	0	0	1.52	7.00	7.44	0.90	3.64	5.18	31.1
	CIS	20	40	20	30	20	70	5	0	0	0	0	3.04	4.00	4.96	2.70	1.82	1.30	22.0
	CIU	10	0	0	0	0	10	0	0	0	0	0	1.52	0.00	0.00	0.00	0.00	0.00	2.1
	CIW	10	60	0	10	50	20	2	0	0	0	0	1.52	6.00	0.00	0.90	4.55	1.20	14.7
	CIZ	5	5	0	0	10	5	0	0	0	0	0	0.76	0.50	0.00	0.00	0.91	0.30	2.5
	CJA	60	0	0	0	0	0	0	0	0	0	0	9.12	0.00	0.00	0.00	0.00	0.00	9.1
	CJH	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
CJI	60	90	0	10	0	0	0	0	0	0	0	9.12	9.00	0.00	0.90	0.00	0.00	19.0	
CKK	0	40	2	0	0	0	0	0	0	0	0	0.00	4.00	0.50	0.00	0.00	0.00	4.5	

CIV Post-Challenge Lung Tissue Histopathology Results

Treatment Group	Dog ID	block/tube	% distribution	severity	broncho	interstitial	nature	bronchioles	vessels	cuffs	atelectasis	atel severity	lesion group
A Bivalent CIV Vaccinates	CEN	15	0	0	0	0	0	0	C	1	100	2	B
	CER	17	0	0	0	0	0	0	C	1	90	1	B
	CEU	2	0	0	0	0	0	0	O	0	100	2	A
	CEX	4	0	0	0	0	0	0	C	2	100	2	B
	CFI	8	0	0	0	0	0	0	C	1	100	2	B
	CFJ	9	0	0	0	0	0	0	O	0	100	2	A
	CGG	11	0	0	0	0	0	0	O	0	100	2	A
	CHD	19	0	0	0	0	0	0	O	0	100	1	A
	CHW	20	0	0	0	0	0	0	C	2	100	1	B
	CIL	23	30	1	0	30	S	S	C	3	80	1	C
	CIM	24	90	3	75	15	S	S	O	0	80	1	E
	CIT	26	0	0	0	0	0	0	O	0	90	1	A
	CIV	28	0	0	0	0	0	0	O	0	100	1	A
	CIX	30	0	0	0	0	0	0	O	0	100	1	A
	CJC	33	0	0	0	0	0	0	C	1	100	1	A
	CJF	34	0	0	0	0	0	0	O	0	100	1	A
	CJG	35	0	0	0	0	0	0	O	0	100	1	A
	CKP	38	0	0	0	0	0	0	O	0	100	2	A

• Percent distribution refers to the amount of section affected. 100 percent being diffuse and less is regional or multifocal.

• Severity score is 1 –mild, 2- moderate, 3-severe.

• Broncho and interstitial scores are percent consolidated area in the section.

• Nature is S for suppurative.

• Bronchiolar codes are: H- for hyperplasia, S - suppurative bronchitis, B- for increased basophilia likely bronchiolar epithelial hypertrophy, N for necrosis and M for metaplasia.

• Vessels C- indicated perivascular cuffing and cuff

• Cuffs: 3 was common cuffs with 3-5 layers of lymphocytes and plasma cells, 2 were occasional cuffs, and 1 scattered cuffs of 1-3 layers.

• The percent of lung atelectic and the score simply notes some common collection artifact.

• Lesion groups: A – normal, B- rare perivascular lymphoid cuffs, C- Larger cuffs and mild suppurative interstitial pneumonia, D- Suppurative pneumonia less than 50% of section consolidated, and E- Suppurative bronchopneumonia with more than 50% of lung consolidated.

CIV Post-Challenge Lung Tissue Histopathology Results - continued

Treatment Group	Dog ID	block/tube	% distribution	severity	broncho	interstitial	nature	bronchioles	vessels	cuffs	atelectasis	atel severity	lesion group
B Placebo-Vaccinated Controls	CEK	13	0	0	0	0	0	0	C	3	100	2	B
	CEL	14	0	0	0	0	0	0	C	1	100	2	B
	CEP	16	95	3	85	10	S	MS	C	3	100	1	E
	CET	1	0	0	0	0	0	0	O	0	100	2	A
	CEV	3	0	0	0	0	0	0	O	0	100	2	A
	CFH	7	0	0	0	0	0	0	C	1	100	2	B
	CFK	10	100	3	90	5	S	HMS	C	3	100	2	E
	CGJ	12	100	3	90	10	S	MS	C	2	100	1	E
	CHC	18	100	3	100	0	S	MS	C	3	90	1	E
	CHX	21	0	0	0	0	0	0	O	0	80	1	A
	CHY	22	100	3	100	0	0	HS	C	3	100	1	E
	CIS	25	95	3	90	5	S	MS	C	2	90	1	E
	CIU	27	60	3	40	20	S	MS	C	3	90	1	D
	CIW	29	95	3	95	0	S	MS	C	3	100	1	E
	CIZ	31	25	2	10	15	S	HS	C	1	0	0	D
	CJA	32	100	3	100	0	S	HS	C	3	0	0	E
	CJH	36	0	0	0	0	0	0	C	1	100	1	B
	CJI	37	100	3	100	0	S	MHS	C	3	0	0	E
	CKK	39	10	1	5	5	S	MS	C	3	90	2	C

• Percent distribution refers to the amount of section affected. 100 percent being diffuse and less is regional or multifocal.

• Severity score is 1 -mild, 2- moderate, 3-severe.

• Broncho and interstitial scores are percent consolidated area in the section.

• Nature is S for suppurative.

• Bronchiolar codes are: H- for hyperplasia, S - suppurative bronchitis, B- for increased basophilia likely bronchiolar epithelial hypertrophy, N for necrosis and M for metaplasia.

• Vessels C- indicated perivascular cuffing and cuff

• Cuffs: 3 was common cuffs with 3-5 layers of lymphocytes and plasma cells, 2 were occasional cuffs, and 1 scattered cuffs of 1-3 layers.

• The percent of lung atelectic and the score simply notes some common collection artifact

• Lesion groups: A - normal, B- rare perivascular lymphoid cuffs, C- Larger cuffs and mild suppurative interstitial pneumonia, D- Suppurative pneumonia less than 50% of section consolidated, and E- Suppurative bronchopneumonia with more than 50% of lung consolidated.

Post-Challenge Clinical Observations

Treatment Group	Dog ID	Study Day											
		33	34*	35	36	37	38	39	40	41	42	43	44
A Bivalent CIV Vaccinates	CEN	-	-	-	-	-	-	C ₁	C ₃	C ₂	C ₃	C ₃	C ₂
	CER	-	-	-	-	-	-	-	-	-	-	C ₂	C ₃
	CEU	-	-	-	-	-	-	-	-	-	-	-	-
	CEX	-	-	-	-	-	-	-	-	-	-	-	-
	CFI	-	-	-	-	-	-	C ₁	-	C ₃	C ₁	-	-
	CFJ	-	-	-	-	-	-	-	-	-	C ₁	-	-
	CGG	-	-	-	-	-	-	-	-	-	-	-	-
	CHD	-	-	-	-	-	-	-	-	-	-	-	-
	CHW	-	-	-	-	C ₁	-	-	-	-	C ₂ , N ₁	C ₃ , S	C ₂ , N ₁
	CIL	-	-	-	-	-	-	-	-	-	-	-	-
	CIM	-	-	-	-	-	-	-	-	C ₂	C ₂	C ₂	C ₂ , N ₂
	CIT	-	-	-	-	-	-	-	-	-	-	-	-
	CIV	-	-	-	-	-	-	-	-	C ₁	-	-	C ₃
	CIX	-	-	-	-	-	-	-	-	-	-	-	-
	CJC	-	-	-	-	-	-	-	-	-	-	-	-
	CJF	-	-	-	-	-	-	-	-	-	-	-	-
CJG	-	-	-	-	-	-	-	-	-	-	-	C ₂	
CKP	-	-	-	-	-	-	-	-	-	-	-	-	
B Placebo- Vaccinated Controls	CEK	-	-	-	-	-	-	-	-	C ₂	C ₂	C ₂ , N ₁	C ₃ , S
	CEL	-	-	-	-	-	-	-	-	-	-	-	-
	CEP	-	-	-	-	-	C ₃ , S	C ₃	C ₃	Grey blocking			
	CET	-	-	-	-	-	-	-	-	-	-	-	-
	CEV	-	-	-	-	-	-	-	-	-	-	-	-
	CFH	-	-	-	-	-	-	-	-	-	S	-	C ₃
	CFK	-	-	-	-	-	-	C ₃	D, C ₂	N ₂	D, C ₂ , N ₂	C ₂	C ₂
	CGJ	-	-	-	-	-	-	-	-	C ₃	C ₂ , D, N ₃	Grey blocking	
	CHC	-	-	-	-	-	-	-	-	C ₂	C ₂	D, B	Grey blocking
	CHX	-	-	-	-	-	S	C ₁	-	C ₃ , S	C ₃	C ₃	C ₂ , N ₂
	CHY	-	-	-	-	-	-	C ₃	C ₃	C ₂	C ₃	C ₃	C ₃
	CIS	-	-	-	-	-	C ₂	C ₂	C ₃ , D, B	Grey blocking			
	CIU	-	-	-	-	-	-	-	-	-	C ₃	C ₃	N ₃
	CIW	-	-	-	-	-	-	C ₁	-	C ₃	-	C ₃	C ₃ , N ₁
	CIZ	-	-	-	-	-	-	-	-	C ₃	C ₃	C ₂	C ₃
	CJA	-	-	-	-	-	-	-	-	C ₁	-	S	N ₁
CJH	-	-	-	-	-	-	-	-	C ₂	-	-	C ₃	
CJI	-	-	-	-	-	-	-	-	S	-	C ₂	C ₃	
CKK	-	-	-	-	-	-	C ₁	C ₃	C ₃	C ₃	C ₃	C ₃	

*Day of Challenge; C1 = Cough, Once; C2 = Cough, Persistent; C3 = Cough w/Retching; S = Sneezing;
N1 = Serous Nasal Discharge; N2 = Mild Mucopurulent Nasal Discharge; N3 = Severe Mucopurulent Nasal Discharge;
D = Depression; B = Dyspnea

Grey blocking: humane endpoints of clinical signs were reached

Study Type	Safety																																		
Pertaining to	Bivalent Canine Influenza Virus H3N2/H3N8 Vaccine																																		
Study Purpose	To demonstrate safety of the product under typical field conditions																																		
Product Administration	2 doses administered subcutaneously 3 weeks apart																																		
Study Animals	347 dogs; 110 dogs were 7 weeks of age, which is the recommended minimum age, and 237 dogs were 8 weeks of age or older representing five different geographic locations																																		
Challenge Description	NA																																		
Interval observed after vaccination	Dogs were observed immediately after vaccination for adverse events. Client-owned dogs were monitored daily and the owners were contacted 14 days following each vaccination to confirm health status, and a physical examination was performed on Day 21. Purpose-bred dogs were observed 2-6 hours post vaccination then daily for adverse events for 14 days following each vaccination including monitoring for injection site reactions.																																		
Results	<table border="1"> <thead> <tr> <th>Type of Adverse Events</th> <th>Minimum Age (7 weeks)</th> <th>Others (8 weeks or older)</th> <th>Total</th> </tr> </thead> <tbody> <tr> <td>Injection Site Swelling (Transient, <1.0 inch diameter)*</td> <td>0</td> <td>4</td> <td>4</td> </tr> <tr> <td>Coughing**</td> <td>0</td> <td>1</td> <td>1</td> </tr> <tr> <td>Diarrhea**</td> <td>0</td> <td>2</td> <td>2</td> </tr> <tr> <td>Emesis**</td> <td>0</td> <td>4</td> <td>4</td> </tr> <tr> <td>Lethargy**</td> <td>0</td> <td>2</td> <td>2</td> </tr> <tr> <td>Other***</td> <td>0</td> <td>13</td> <td>13</td> </tr> <tr> <td>No Adverse Events</td> <td>110</td> <td>214</td> <td>324</td> </tr> </tbody> </table> <p>*Swellings were identified 6-7 days after vaccination. Swelling for 3 dogs resolved within 7 days. In one dog, swelling was still present at 14 days post-injection.</p> <p>** Includes adverse events that were documented by the investigator as either related or unknown whether the adverse event was related or not.</p> <p>***These were affirmed by investigator as not related to vaccination which included a non-serious soft-tissue injury, ocular irritation/infection, soreness in leg, pruritis, urinary tract infection, hit-by-car, gi upset/emesis, diarrhea</p>			Type of Adverse Events	Minimum Age (7 weeks)	Others (8 weeks or older)	Total	Injection Site Swelling (Transient, <1.0 inch diameter)*	0	4	4	Coughing**	0	1	1	Diarrhea**	0	2	2	Emesis**	0	4	4	Lethargy**	0	2	2	Other***	0	13	13	No Adverse Events	110	214	324
Type of Adverse Events	Minimum Age (7 weeks)	Others (8 weeks or older)	Total																																
Injection Site Swelling (Transient, <1.0 inch diameter)*	0	4	4																																
Coughing**	0	1	1																																
Diarrhea**	0	2	2																																
Emesis**	0	4	4																																
Lethargy**	0	2	2																																
Other***	0	13	13																																
No Adverse Events	110	214	324																																

USDA Approval Date	August 1, 2016
---------------------------	----------------