



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	15K5.20
True Name	Canine Influenza Vaccine, H3N8, Killed Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Nobivac Canine Flu H3N8 - Merck Animal Health Nobivac Canine Flu H3N8 - No distributor specified Nobivac Flu H3N8 - 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. Caudal	Rt. Cranial	Rt. Middle	Rt. Caudal	Rt. Access	Lt. Cranial	Lt. Caudal			
Controls	CYTAPA	0	0	0	0	5	1	0	0	0	0	0.5	0.1	0	0.3	0.8
	CYTAPC	5	2	1	1	8	10	0.8	0.2	0.2	0.1	0.7	0.6	0	0.3	2.9
	CYTAPF	50	60	0	5	5	0	7.6	6	0	0.5	0.5	0	0	2.6	17.1
	CYTAPH	1	1	0	0	0	0	0.2	0.1	0	0	0	0	0	0	0.3
	CYTAPW	0	0	0	0	0	1	0	0	0	0	0	0	0	0.3	0.3
	CYTAPZ	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	CYTARB	1	0	2	2	0	0	0.2	0	0	0.5	0.2	0	0	0.3	1.1
	CYTARK	0	1	1	0	0	1	0	0.1	0.1	0.2	0	0	0.1	0.5	0.9
	CYTARZ	0	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	0.3	1.1
	CYTASH	1	1	1	0	0	2	3	0.2	0.1	0.2	0	0	0.1	0.8	1.4
	CYTASI	20	50	0	5	10	3	1	3	5	0	0.5	0.9	0.2	0.3	9.8
	CYTATE	20	10	0	30	50	70	10	3	1	0	2.7	4.6	4.2	2.6	18.1
	CYTATH	0	0	2	0	5	0	1	0	0	0.5	0	0.5	0	0.3	1.2
CYTAUR	40	70	0	60	50	60	5	6.1	7	0	5.4	4.6	3.6	1.3	27.9	
Vaccinates	CYTANX	0	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	0
	CYTAPB	0	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	0
	CYTAPE	0	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	0.1	0	0	0	0.1
	CYTAPI	0	2	0	0	0	0	0	0.2	0	0	0	0	0	0	0.2
	CYTARA	0	0	0	1	2	0	0	0	0	0.1	0.2	0	0	0	0.3
	CYTARC	0	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	0
	CYTARH	0	1	0	0	0	1	0	0	0.1	0	0	0	0.1	0	0.2
	CYTARJ	0	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	1.8	0	0	0.3	2.9
	CYTASF	0	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	0	
CYTATD	0	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	0.2	
CYTATL	0	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	0	
CYTAVT	0	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	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	Safety						
Pertaining to	ALL						
Study Purpose	To demonstrate safety under field conditions						
Product Administration	Two doses administered subcutaneously, 13-23 days apart.						
Study Animals	746 dogs of various breed, age, and sex representing 4 different geographical regions; 249 dogs of minimum age (6 - 8 weeks of age) were enrolled						
Challenge Description	Not applicable						
Interval observed after challenge	All dogs were observed immediately after vaccination and then daily for 14 days post-vaccination for signs of local or systemic reactions. Additionally, purpose-bred dogs were observed during the 2 - 6 hour post-vaccination time frame.						
Results	<p><u>Adverse Event (AE) Summary</u></p> <table border="1"> <tr> <td># of Dogs with No Adverse Event</td> <td>681 (91%)</td> </tr> <tr> <td># of Dogs with AEs Observed*</td> <td>65</td> </tr> <tr> <td># of AEs Attributed to the Vaccine</td> <td>0</td> </tr> </table> <p>*Licensee affirms the AEs observed in the dogs were not related to the vaccine. The AEs included conjunctivitis, cherry eye, and respiratory disease.</p>	# of Dogs with No Adverse Event	681 (91%)	# of Dogs with AEs Observed*	65	# of AEs Attributed to the Vaccine	0
# of Dogs with No Adverse Event	681 (91%)						
# of Dogs with AEs Observed*	65						
# of AEs Attributed to the Vaccine	0						
USDA Approval Date	April 3, 2009						