Summary of Studies Supporting USDA Product Licensure

Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	15K5.20
True Name	Canine Influenza Vaccine, H3N8, Killed Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Vanguard CIV - No distributor specified Vanguard CIV H3N8 - No distributor specified
Date of Compilation Summary	February 09, 2021

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), H3N8
Study Purpose	To demonstrate effectiveness against canine influenza virus, H3N8
Product Administration	Two doses, administered subcutaneously, 3 weeks apart.
Study Animals	Study involved 24 vaccinated and 24 placebo puppies, 7-8 weeks of age.
Challenge Description	Challenged with CIV H3N8 isolate A/Ca/CO/6723, 14 days following administration of the second vaccination.
Interval observed after challenge	After challenge, animals were observed daily for signs of clinical respiratory disease indicative of CIV, primarily cough. Lungs were evaluated in 4 randomly selected dogs per group 4 days after challenge. The remainder were evaluated 11 days after challenge.
Results	Efficacy was based on clinical observations, lung consolidation, and post-challenge viral isolation from nasal swabs.

Table 1: Summary of clinical observations, number and percentage of animals that ever had a positive observation for cough.

Treatment Group	Coughing	
	Number	%
Placebo	13	65
Vaccinates	2	10

The raw data are shown on the attached page.

Table 2: Five number summary of lung lesion scores by treatment group for diffuse and discrete lung consolidation. Percentage of lung mass abnormal (consolidated) was calculated for every animal (Q_1 = 25th percentile; Q_3 = 75th percentile).

Type of Consolidation	Treatment	N	Minimum	Q1	Median	Q3	Maximum
Diffuse	Placebo	24	0.00	37.05	80.13	91.57	100.00
	Vaccinates	24	0.00	0.00	17.13	93.24	100.00
Discrete	Placebo	24	0.00	0.44	1.72	5.86	32.05
	Vaccinates	24	0.00	0.07	0.28	0.49	5.00

In addition, 24/24 placebo dogs and 4/24 vaccinated dogs had histopathologic evidence of damage to the respiratory epithelium.
The raw data for the animals are shown on the attached page.

	Table 3: Five number summary for number of days with positive H3N8 nasal pharyngeal swab virus isolation post-challege (Q_1 = 25th percentile; Q_3 = 75th percentile). **Treatment** / **Minimum** / **Q1** / **Median** / **Q3** / **Maximum** **Placebo**: 4.00 / 4.00 / 5.00 / 6.00 / 7.00 **Vaccinates**: 0.00 / 0.00 / 0.00 / 1.00 / 2.00 The raw data for the animals are shown on the attached page.
USDA Approval Date	September 3, 2010

Table 4: Individual animal raw data for lung consolidation (% involvement)

			Type of Consolidation					Type of Consolidation	
Treatment	**Final Evaluation Day Post-Challenge**	**Animal**	**Diffuse**	**Discrete**	**Treatment**	**Final Evaluation Day Post-Challenge**	**Animal**	**Diffuse**	**Discrete**
Placebo	4	OZR-9	100.00	1.72	Vaccinates	4	PAR-9	42.30	0.50
		PKR-9	94.57	0.47			POQ-9	0.00	0.26
		QBQ-9	52.18	2.97			QCQ-9	1.41	0.47
		QER-9	84.08	1.05			QZQ-9	95.00	5.00
	11	OOR-9	0.80	8.13		11	OLR-9	98.28	0.07
		OPQ-9	92.41	0.00			OQR-9	1.19	0.00
		ORR-9	76.23	22.85			OSQ-9	82.49	0.20
		OTQ-9	90.29	1.17			OUQ-9	25.27	0.30
		PCQ-9	82.54	4.77			PBR-9	83.81	0.43
		PER-9	91.91	0.31			PDQ-9	0.00	0.20
		PHQ-9	77.73	0.09			PFQ-9	9.00	0.27
		PIQ-9	0.00	13.74			PGQ-9	0.00	0.00
		PLQ-9	91.22	2.07			PRR-9	0.00	0.00
		PPR-9	4.90	6.96			PSR-9	100.00	0.33
		PQQ-9	55.03	1.72			PTR-9	0.00	0.40
		PUR-9	0.00	0.30			PVR-9	0.00	0.07
		PWQ-9	44.62	1.68			PYR-9	1.19	0.15
		PXR-9	88.51	0.41			QDR-9	100.00	0.00
		PZR-9	17.47	3.75			QHR-9	0.00	0.00
		QFQ-9	75.74	8.78			QLQ-9	91.48	2.78
		QGR-9	89.83	3.42			QPR-9	95.23	0.50
		QKQ-9	95.46	0.00			QQR-9	88.15	0.50
		QTQ-9	98.31	1.08			QWR-9	0.00	0.40
		QXR-9	29.48	32.05			QYQ-9	97.62	2.56

Table 5: Individual animal raw data for coughing

			Day of Study - Cough														
Treatment	Final Evaluation Day Post-Challenge	Animal	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46
Placebo	4	OZR-9	0	0	0	0	0	0	0	1							
		PKR-9	0	0	0	0	0	0	0	0							
		QBQ-9	0	0	0	0	0	0	0	0							
		QER-9	0	0	0	0	0	1	2	2							
	11	OOR-9	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		OPQ-9	0	0	0	0	0	0	2	0	0	0	0	2	0	0	0
		ORR-9	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
		OTQ-9	0	0	0	0	0	2	2	2	2	1	2	1	1	2	0
		PCQ-9	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0
		PER-9	0	0	0	0	0	1	2	2	2	2	0	0	1	0	0
		PHQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PIQ-9	0	0	0	0	0	1	2	2	1	1	1	1	1	0	1
		PLQ-9	0	0	0	0	0	2	2	1	0	2	2	1	0	0	0
		PPR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PQQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PUR-9	0	0	0	0	0	0	2	1	0	1	0	0	2	0	0
		PWQ-9	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0
		PXR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PZR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		QFQ-9	0	0	0	0	0	0	0	1	1	0	1	1	0	0	0
		QGR-9	0	0	0	0	0	0	2	0	1	0	2	1	0	0	1
		QKQ-9	0	0	0	0	0	1	1	2	2	1	1	0	0	2	1
		QTQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		QXR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vaccinates	4	PAR-9	0	0	0	0	0	0	0	0							
		POQ-9	0	0	0	0	0	0	0	0							
		QCQ-9	0	0	0	0	0	0	0	0							
		QZQ-9	0	0	0	0	0	0	0	0							
	11	OLR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		OQR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		OSQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		OUQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PBR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PDQ-9	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		PFQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PGQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PRR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PSR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PTR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PVR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		PYR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		QDR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		QHR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		QLQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		QPR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
		QQR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		QWR-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		QYQ-9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

0 = Absent
1 = Mild: Animal coughed once during clinical observation
2 = Moderate: Animal coughed 2x or more during clinical observation period
3 = Severe: Animal had persistent and prolonged cough

Table 6: Individual animal raw data for the number of days with positive H3N8 virus isolation post-challenge

Treatment	Final Observation Day Post-Challenge	Animal	Number of Days Positive	Treatment	Final Observation Day Post-Challenge	Animal	Number of Days Positive
Placebo	4	OZR-9	4	Vaccinates	4	PAR-9	1
		PKR-9	4			POQ-9	0
		QBQ-9	4			QCQ-9	0
		QER-9	4			QZQ-9	0
	11	OOR-9	6		11	OLR-9	0
		OPQ-9	6			OQR-9	0
		ORR-9	7			OSQ-9	0
		OTQ-9	6			OUQ-9	2
		PCQ-9	6			PBR-9	1
		PER-9	4			PDQ-9	0
		PHQ-9	4			PFQ-9	0
		PIQ-9	6			PGQ-9	0
		PLQ-9	6			PRR-9	1
		PPR-9	6			PSR-9	1
		PQQ-9	5			PTR-9	0
		PUR-9	5			PVR-9	1
		PWQ-9	5			PYR-9	0
		PXR-9	5			QDR-9	0
		PZR-9	4			QHR-9	1
		QFQ-9	6			QLQ-9	0
		QGR-9	5			QPR-9	0
		QKQ-9	6			QQR-9	0
		QTQ-9	5			QWR-9	1
		QXR-9	5			QYQ-9	0

Table 7. Individual animal raw data for histopathologic damage to respiratory epithelium

Treatment	Final Observation Day Post-Challenge	Animal	Histopathologic Damage to Respiratory Epithelium	Treatment	Final Observation Day Post-Challenge	Animal	Histopathologic Damage to Respiratory Epithelium
Placebo	4	OZR-9	+	Vaccinates	4	PAR-9	-
		PKR-9	+			POQ-9	-
		QBQ-9	+			QCQ-9	-
		QER-9	+			QZQ-9	-
		OOR-9	-			OLR-9	-
		OPQ-9	+			OQR-9	+
		ORR-9	+			OSQ-9	+
		OTQ-9	+			OUQ-9	-
		PCQ-9	+			PBR-9	-
		PER-9	+			PDQ-9	-
		PHQ-9	+			PFQ-9	-
		PIQ-9	+			PGQ-9	+
		PLQ-9	+			PRR-9	+
	11	PPR-9	+		11	PSR-9	-
		PQQ-9	+			PTR-9	-
		PUR-9	+			PVR-9	-
		PWQ-9	+			PYR-9	-
		PXR-9	+			QDR-9	-
		PZR-9	+			QHR-9	-
		QFQ-9	+			QLQ-9	-
		QGR-9	+			QPR-9	-
		QKQ-9	+			QQR-9	-
		QTQ-9	+			QWR-9	-
		QXR-9	+			QYQ-9	-

'+' denotes any degree of change to respiratory epithelium of the trachea, bronchi, and bronchioles.
'-' denotes no change to the respiratory epithelium of the trachea, bronchi, and bronchioles.

<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 evaluate safety under typical field conditions.</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered subcutaneously 3 weeks apart</td></tr>
<tr><td>Study Animals</td><td>691 dogs were enrolled over 25 study sites representing 3 different geographical regions:
186 animals at minimum age (8-10 weeks)
505 animals at ≥11 weeks of age

A total of 1,359 vaccinations were given.</td></tr>
<tr><td>Challenge Description</td><td>N/A</td></tr>
<tr><td>Interval observed after challenge</td><td>Animals were observed immediately after each vaccination, and then daily until 10 days post second vaccination.</td></tr>
<tr><td>Results</td><td>In total, 668 dogs completed this study. The 23 animals that did not complete the study were due to owner noncompliance, animal movement to different owners, and 1 death (not attributed to the product).

Table 1: Frequency Distribution of Abnormal Health Events by Animal Age Group Across All Injections (n=Number of Injections per Age Group)*

<table>
<tr><th>Age</th><th>Adverse Event</th><th>Number of events (percentage of injections)</th></tr>
<tr><td rowspan="12">Minimum Age (8-10 weeks, n=355)</td><td>Vomiting</td><td>9 (2.54%)</td></tr>
<tr><td>Diarrhea</td><td>6 (1.69%)</td></tr>
<tr><td>Depression</td><td>3 (0.85%)</td></tr>
<tr><td>Anorexia</td><td>2 (0.56%)</td></tr>
<tr><td>Crying</td><td>1 (0.28%)</td></tr>
<tr><td>Decreased appetite</td><td>1 (0.28%)</td></tr>
<tr><td>Enteritis</td><td>1 (0.28%)</td></tr>
<tr><td>Eyelid edema</td><td>1 (0.28%)</td></tr>
<tr><td>Facial swelling</td><td>1 (0.28%)</td></tr>
<tr><td>General pain</td><td>1 (0.28%)</td></tr>
<tr><td>Muscle tremor</td><td>1 (0.28%)</td></tr>
<tr><td>Not drinking</td><td>1 (0.28%)</td></tr>
<tr><td>Pyoderma</td><td>1 (0.28%)</td></tr>
<tr><td rowspan="6">Older (≥11 weeks, n=1004)</td><td>Vomiting</td><td>12 (1.2%)</td></tr>
<tr><td>Diarrhea</td><td>5 (0.5%)</td></tr>
<tr><td>Depression</td><td>6 (0.6%)</td></tr>
<tr><td>Anorexia</td><td>2 (0.2%)</td></tr>
<tr><td>Decreased appetite</td><td>3 (0.3%)</td></tr>
<tr><td>Bradycardia</td><td>1 (0.1%)</td></tr>
</table>
</td></tr>
</table>

Nail disorder	1 (0.1%)
Cough	2 (0.2%)
Discus prolapse	1 (0.1%)
Injection site pain	3 (0.3%)
Injection site swelling**	3 (0.3%)
Labored breathing	2 (0.2%)
Lameness	1 (0.1%)
Nasal discharge	2 (0.2%)
Panting	1 (0.1%)
Pruritus	1 (0.1%)
Pulmonary congestion	1 (0.1%)
Pustules	1 (0.1%)
Skin Tumor NOS	1 (0.1%)
Sneezing	1 (0.1%)
Trauma NOS	1 (0.1%)
Weakness	3 (0.3%)

* Includes adverse events that were documented by the investigator as either related or not related associated with vaccination
**Injection site swelling size ranged from 0.5 cm to 2 cm

Table 2: Adverse Events Deemed by Investigator as Not Related or Related to Vaccination

Adverse Event	**Total Number of Events (related or not related to vaccination)**	**Number of Events Not Attributed to Vaccination**	**Number of Events Attributed to Vaccination**
Vomiting	21	14	7
Diarrhea	11	9	2
Depression	9	5	4
Anorexia	4	2	2
Decreased appetite	4	2	2
Injection site pain	3	2	1
Injection site swelling	3	0	3
Weakness	3	3	0
Cough	2	2	0
Labored breathing	2	2	0

	Nasal Discharge	2	1	1
	Bradycardia	1	1	0
	Claw/nail disorder	1	1	0
	Crying	1	0	1
	Discus prolapse	1	1	0
	General pain	1	0	1
	Enteritis	1	1	0
	Eyelid oedema	1	1	0
	Facial swelling	1	1	0
	Panting	1	1	0
	Pustules	1	1	0
	Pyoderma	1	1	0
	Skin Tumor	1	1	0
	Trauma	1	1	0
	Lameness	1	0	1
	Muscle tremor	1	0	1
	Not drinking	1	0	1
	Pruritus	1	0	1
	Pulmonary congestion	1	0	1
	Sneezing	1	0	1
USDA Approval Date	September 2, 2009			