Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	15P5.20
True Name	Canine Influenza Vaccine, H3N2, Killed Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Nobivac Canine Flu H3N2 - No distributor specified
Date of Compilation Summary	April 11, 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.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Canine Influenza Virus (CIV) H3N2</td></tr>
<tr><td>Study Purpose</td><td>Efficacy against CIV H3N2 in cats</td></tr>
<tr><td>Product Administration</td><td>Two doses administered subcutaneously, 21 days apart</td></tr>
<tr><td>Study Animals</td><td>10- to 12-week-old cats, seronegative to CIV H3N2; 10 vaccinates and 10 controls</td></tr>
<tr><td>Challenge Description</td><td>All cats were challenged with CIV H3N2, 2 weeks after the second vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Lung were evaluated 8 days following challenge.</td></tr>
<tr><td>Results</td><td>The percent of the lung mass that was abnormal (consolidated) was calculated for every animal.

5-number summary for lung consolidation (%)
<table>
<tr><th>Group</th><th>Minimum</th><th>Lower Quartile</th><th>Median</th><th>Upper Quartile</th><th>Maximum</th></tr>
<tr><td>Vacc</td><td>0.00</td><td>0.00</td><td>0.10</td><td>0.70</td><td>10.90</td></tr>
<tr><td>Control</td><td>0.00</td><td>6.50</td><td>11.90</td><td>18.70</td><td>94.00</td></tr>
</table>
Lung consolidation scores (%), ranked by group
<table>
<tr><th>Vacc</th><th>Control</th></tr>
<tr><td>0</td><td>0</td></tr>
<tr><td>0</td><td>4.8</td></tr>
<tr><td>0</td><td>6.5</td></tr>
<tr><td>0</td><td>9.1</td></tr>
<tr><td>0</td><td>10.7</td></tr>
<tr><td>0.2</td><td>13.1</td></tr>
<tr><td>0.7</td><td>14.7</td></tr>
<tr><td>0.7</td><td>18.7</td></tr>
<tr><td>5</td><td>38.2</td></tr>
<tr><td>10.9</td><td>94</td></tr>
</table>
Raw data shown on attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>April 18, 2017</td></tr>
</table>

Table 1. Vaccinates Post-CIV H3N2 Challenge Lung Lesion Scores

Treatment Group	Cat ID	Raw Scores							Weighted Scores							Total Score
		R. Cranial	R. Middle	R. Caudal	Access	L.Cr-Cr	L. Cr-Cau	L. Caudal	R. Cranial	R. Middle	R. Caudal	Access	L. Cr-Cr	L.Cr-Cau	L. Caudal	
H3N2 CIV Vaccinates (Minimum Dose)	CDS2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0.0**
	CDS5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0.0**
	CDT4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0.0**
	CDW1	20	20	0	0	0	0	0	3.04	2.00	0	0	0	0	0	**5.0**
	CDW2	1	5	0	0	0	0	0	0.15	0.50	0	0	0	0	0	**0.7**
	CEB1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0.0**
	CEF2	0	0	3	0	0	0	0	0	0	0.74	0	0	0	0	**0.7**
	CEF5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0.0**
	CEL3	0	30	30	5	0	0	0	0	3.00	7.44	0.45	0	0	0	**10.9**
	CEN4	1	0	0	0	0	0	0	0.15	0	0	0	0	0	0	**0.2**

Table 2. Controls Post-CIV H3N2 Challenge Lung Lesion Scores

Treatment Group	Cat ID	Raw Scores							Weighted Scores							Total Score
		R. Cranial	R. Middle	R. Caudal	Access	L.Cr-Cr	L. Cr-Cau	L. Caudal	R. Cranial	R. Middle	R. Caudal	Access	L. Cr-Cr	L.Cr-Cau	L. Caudal	
C Placebo Vaccinates	CDS1	20	15	0	2	20	0	0	3.04	1.50	0	0.18	1.82	0	0	**6.5**
	CDS6	5	8	0	8	2	8	7	0.76	0.80	0	0.72	0.18	0.48	1.81	**4.8**
	CDT1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0.0**
	CDW3	15	25	2	5	15	20	3	2.28	2.50	0.50	0.45	1.37	1.20	0.78	**9.1**
	CEB2	8	40	2	8	35	5	3	1.22	4.00	0.50	0.72	3.19	0.30	0.78	**10.7**
	CEB4	20	20	10	45	50	8	8	3.04	2.00	2.48	4.05	4.55	0.48	2.07	**18.7**
	CEF1	35	90	30	50	45	45	20	5.32	9.00	7.44	4.50	4.10	2.70	5.18	**38.2**
	CEF6	10	40	20	35	0	0	4	1.52	4.00	4.96	3.15	0	0	1.04	**14.7**
	CEL1	75	95	100	100	95	100	95	11.40	9.50	24.80	9.00	8.65	6.00	24.61	**94.0**
	CEN2	20	25	10	30	0	10	7	3.04	2.50	2.48	2.70	0	0.60	1.81	**13.1**

<table>
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<tr><td>Pertaining to</td><td>Canine Influenza Virus (CIV) H3N2</td></tr>
<tr><td>Study Purpose</td><td>Efficacy against CIV H3N2 in dogs</td></tr>
<tr><td>Product Administration</td><td>Two doses administered subcutaneously, 21 days apart</td></tr>
<tr><td>Study Animals</td><td>7- to 8-week-old dogs; seronegative to CIV H3N2; 11 vaccinates and 19 controls</td></tr>
<tr><td>Challenge Description</td><td>All dogs were challenged with CIV H3N2, 2 weeks after the second vaccination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Dogs were observed for 10 days after challenge. Lungs were evaluated at death or 10 days following challenge.</td></tr>
<tr><td>Results</td><td>The percent of the lung mass that was abnormal (consolidated) was calculated for every animal.

Table 1. Five number summary for lung consolidation

<table>
<tr><th>Group</th><th>Minimum</th><th>Lower Quartile</th><th>Median</th><th>Upper Quartile</th><th>Maximum</th></tr>
<tr><td>Vaccinates</td><td>0.0</td><td>0.0</td><td>0.0</td><td>1.8</td><td>21.9</td></tr>
<tr><td>Controls</td><td>0.0</td><td>0.4</td><td>7.4</td><td>27.5</td><td>46.5</td></tr>
</table>

Table 3. Summary of mortality

<table>
<tr><th>Group</th><th>Mortality</th></tr>
<tr><td>Vaccinates</td><td>0/11 (0%)</td></tr>
<tr><td>Controls</td><td>8/19 (42%)</td></tr>
</table>

Raw data shown on attached pages.</td></tr>
<tr><td>USDA Approval Date</td><td>November 16, 2015</td></tr>
</table>

Table 1. Post-CIV H3N2 Challenge Lung Lesion Scores by lung lobe for Percent Consolidation - Raw Scores

Treatment Group	Dog ID	Raw Scores						
		R. Cranial	R. Middle	R. Caudal	Access	L. Cr-Cr	L. Cr-Cau	L. Caudal
Vaccinates	CGZ	0	0	0	0	0	0	0
	CHJ	0	0	0	0	0	0	0
	CHK	0	0	0	0	0	0	0
	CHX	0	5	0	0	0	0	0
	CHY	20	20	0	0	30	20	50
	CIK	0	20	0	5	0	0	0
	CJA	0	0	0	0	0	0	0
	CKE	0	10	0	0	0	0	0
	CKN	0	0	0	0	0	0	0
	CLM	0	0	0	0	0	0	0
	CNH	0	5	0	0	50	15	0
Controls	CGJ	0	0	0	0	0	0	0
	CGN	5	40	0	0	50	70	1
	CGR	0	50	0	0	0	0	0
	CHD	40	100	2	5	60	90	5
	CHI	0	0	0	0	0	0	0
	CHL	5	5	0	10	15	0	0
	CHU	0	0	0	0	0	0	0
	CHV	0	0	0	0	0	0	0
	CID	0	0	0	0	0	0	0
	CIN	50	100	30	100	70	80	5
	CIX	2	10	0	0	50	80	0
	CIY	5	10	0	0	10	5	1
	CJI	0	0	0	5	0	5	0
	CKF	0	70	0	60	40	40	0
	CKM	20	100	10	5	40	70	8
	CKT	0	0	0	0	15	100	0
	CLI	30	100	0	30	70	80	5
	CNE	15	100	20	100	50	80	20
	CNG	40	100	5	10	70	40	20

R. is Right side
L. is Left side

Table 2. Post-CIV H3N2 Challenge Lung Lesion Scores by lung lobe for Percent Consolidation - Weighted Scores

Treatment Group	Dog ID	Weighted Scores							Total Score
		R. Cranial	R. Middle	R. Caudal	Access	L. Cr-Cr	L. Cr-Cau	L. Caudal	
Vaccinates	CGZ	0	0	0	0	0	0	0	**0.0**
	CHJ	0	0	0	0	0	0	0	**0.0**
	CHK	0	0	0	0	0	0	0	**0.0**
	CHX	0	0.50	0	0	0	0	0	**0.5**
	CHY	3.04	2.00	0	0	2.73	1.20	12.95	**21.9**
	CIK	0	2.00	0	0.45	0	0	0	**2.5**
	CJA	0	0	0	0	0	0	0	**0.0**
	CKE	0	1.00	0	0	0	0	0	**1.0**
	CKN	0	0	0	0	0	0	0	**0.0**
	CLM	0	0	0	0	0	0	0	**0.0**
	CNH	0	0.50	0	0	4.55	0.90	0	**6.0**
Controls	CGJ	0	0	0	0	0	0	0	**0.0**
	CGN	0.76	4.00	0	0	4.55	4.20	0.26	**13.8**
	CGR	0	5.00	0	0	0	0	0	**5.0**
	CHD	6.08	10.00	0.50	0.45	5.46	5.40	1.30	**29.2**
	CHI	0	0	0	0	0	0	0	**0.0**
	CHL	0.76	0.50	0	0.90	1.37	0	0	**3.5**
	CHU	0	0	0	0	0	0	0	**0.0**
	CHV	0	0	0	0	0	0	0	**0.0**
	CID	0	0	0	0	0	0	0	**0.0**
	CIN	7.60	10.00	7.44	9.00	6.37	4.80	1.30	**46.5**
	CIX	0.30	1.00	0	0	4.55	4.80	0	**10.7**
	CIY	0.76	1.00	0	0	0.91	0.30	0.26	**3.2**
	CJI	0	0	0	0.45	0	0.30	0	**0.8**
	CKF	0	7.00	0	5.40	3.64	2.40	0	**18.4**
	CKM	3.04	10.00	2.48	0.45	3.64	4.20	2.07	**25.9**
	CKT	0	0	0	0	1.37	6.00	0	**7.4**
	CLI	4.56	10.00	0	2.70	6.37	4.80	1.30	**29.7**
	CNE	2.28	10.00	4.96	9.00	4.55	4.80	5.18	**40.8**
	CNG	6.08	10.00	1.24	0.90	6.37	2.40	5.18	**32.2**

R. is Right side
L. is Left side

Table 3. Mortality due to Severe Clinical Disease during observation after challenge

Treatment Group	Dog ID	Mortality
Vaccinates	CGZ	No
	CHJ	No
	CHK	No
	CHX	No
	CHY	No
	CIK	No
	CJA	No
	CKE	No
	CKN	No
	CLM	No
	CNH	No
Controls	CGJ	No
	CGN	No
	CGR	No
	CHD	Yes
	CHI	No
	CHL	Yes
	CHU	No
	CHV	No
	CID	No
	CIN	Yes
	CIX	No
	CIY	No
	CJI	No
	CKF	Yes
	CKM	Yes
	CKT	No
	CLI	Yes
	CNE	Yes
	CNG	Yes

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>Bivalent Canine Influenza Virus H3N2/H3N8 Vaccine</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate safety of the product under typical field conditions</td></tr>
<tr><td>Product Administration</td><td>2 doses administered subcutaneously 3 weeks apart</td></tr>
<tr><td>Study Animals</td><td>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</td></tr>
<tr><td>Challenge Description</td><td>NA</td></tr>
<tr><td>Interval observed after vaccination</td><td>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.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><th>Type of Adverse Events</th><th>Minimum Age (7 weeks)</th><th>Others (8 weeks or older)</th><th>Total</th></tr>
<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>
</table>
*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.
** Includes adverse events that were documented by the investigator as either related or unknown whether the adverse event was related or not.
***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
</td></tr>
</table>

USDA Approval Date	August 1, 2016

<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 of the product under typical field conditions</td></tr>
<tr><td>Product Administration</td><td>2 doses administered subcutaneously 3 weeks apart</td></tr>
<tr><td>Study Animals</td><td>350 cats representing four different geographic locations; 111 cats were 10 weeks of age, 1 cat was 8 weeks of age, and 238 cats were 11 weeks of age or older.</td></tr>
<tr><td>Challenge Description</td><td>NA</td></tr>
<tr><td>Interval observed after vaccination</td><td>Cats were observed immediately after vaccination for adverse events. Client-owned cats were monitored daily, the owners were contacted 14 days following each vaccination to confirm health status, and a physical examination was performed on Day 22. Purpose-bred cats were observed daily for adverse events for 14 days following each vaccination including monitoring for injection site reactions.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><th>Type of Adverse Events</th><th>No. of Cats at 10 weeks of age</th><th>No. of Cats 11 weeks or older</th><th>Total No. of AEs</th></tr>
<tr><td>Injection Site Oedema (Transient, <1.0 cm)*</td><td>0</td><td>19</td><td>19</td></tr>
<tr><td>Other Immune System Disorder NOS</td><td>0</td><td>1</td><td>1</td></tr>
<tr><td>Other**</td><td>3***</td><td>24</td><td>33</td></tr>
<tr><td>No Adverse Events</td><td>109</td><td>196</td><td></td></tr>
</table>
*Swellings were identified 0-1 day after vaccination, but all of them resolved within 32 days.
**These adverse events were affirmed by the investigator as not related to vaccination and included diarrhea, external ear disorder, tooth disorder, murmur, arthritis, sinusitis, alopecia, systemic disorder NOS, dermatitis and eczema, other immune system disorder NOS, hypersensitivity reaction, lameness, eye disorder, musculoskeletal disorder NOS, respiratory tract infection NOS, urine abnormalities, emesis, skin lesion NOS, skin and tissue infection NOS, and digestive tract disorder NOS.
***One of the cats was 8 weeks of age.
</td></tr>
<tr><td>USDA Approval Date</td><td>February 20, 2018</td></tr>
</table>