Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	1081.01
True Name	Bordetella Bronchiseptica Vaccine, Avirulent Live Culture
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Nobivac Feline Bb - Merck Animal Health Nobivac Feline Bb - No distributor specified
Date of Compilation Summary	April 09, 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	*Bordetella bronchiseptica*
Study Purpose	To demonstrate efficacy against *Bordetella bronchiseptica*
Product Administration	One dose administered by the intranasal route
Study Animals	4-week-old cats; 22 vaccinates and 11 controls
Challenge Description	Cats were challenged with *B. bronchiseptica* three weeks after vaccination.
Interval observed after challenge	Clinical signs were observed daily for 14 days post challenge.
\fResults	A difference in clinical signs was observed between the Controls (Group 1) and Vaccinates (Group 2) using a scoring system approved by APHIS. Raw data shown on attached pages.
USDA Approval Date	September 30, 2002

CLINICAL SIGN SCORING SYSTEM

Clinical Sign

Fever
103.0 - 103.9 (T3)
104.0 - 104.9 (T4)
105.0 - (T5)

Hypothermia (T6)

Ocular Discharge
Serous discharge (O1)
Mucopurulent discharge (O2)
Conjunctivitis (O3)

Nasal Discharge
Serous discharge (N1)
Mucopurulent discharge (N2)
Sneezing (N3)

Dyspnea
Audible rales (R1)
Induced coughing (R2)
Spontaneous coughing (R3)
Open mouth breathing (R4)

Depression
Inappetence (A)
Dehydration (H)
Dehydration (G1)

Death (X)

POST-CHALLENGE CLINICAL SCORES

GROUP 1

Days Post Challenge

Cat. No.	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
5045			T3	T3			N1				N3		N1				
1A0D	N1	N1		N1		N1	N1,R2	R2	R2	N1,R2,R3	N1,N3,R2	N2,N3	N2,R2	N1,N3	N1	N1	N1,R3
546A			T3		N1	N1,R2	N1	R2	N1,R2	N2,R3	N2	N3	N1,N3	N3	N3		N1,N3
0535						R2,R3		N1,R2,R3	N1,N3,R2	O1,N1,R3		N3,R2,R3	O1,N1			R2	
323F	N1					R3	N1		N1,R1,R3		N1	N1		N1	N1	N1	
5447			T3				T3,N1	N1,N3	N2,R3	R2,R3	N3	N1					N1
2567					N1,R2	R2	R3	R2,R3		O2,R2,R3	O1,N3,R2	N1,N3		N1	N1	N1,R2	N1
1519			T3			R1	R1,R3	O1,R3	N1,N3,R2,R3	N3,R2,R3	N1,N3,R3	R1,R2	N3	N3,R2	N3,R2,R3	N3,R2	R2
4C78			T3				N3	N1		N2,N3,R2,R3	N1	N1,N3	N1	N3,R2	R3	N1,R3	R3
4C08						R3		N3	R2,R3	N2,N3	N2,N3,R2	N3,R3			R3		
3E48					N1			N3,R3	N3	N3,R3	R2		R3	R2		R3	R2,R3

POST-CHALLENGE CLINICAL SCORES

GROUP 2

Days Post-Challenge

Cat. No.	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
4C00													N3	N1			
4875								T3									
1F6F																	
7334									N3			N3					
5259																	N3
2524													N3	N3	N1		N3
341E													N3				
0A23																	N1
3D15									N1	N1	N1	N1					
6F10								N3			N3					N3	N3
1338									N1								
3D77			T3					T3,N1	N1	N1							T6,N1,N3
690A							N3	N3								N1,N3	
4B49											N3						
2A37																	
0C49							N3	N1									
010A										N1,N3							N1
637D																N3	
331F																	
160A										N1							
2C64						N1	N1	N1	N1	N1				N1			
0022		N1						N1					N3				

Study Type	Efficacy
Pertaining to	*Bordetella bronchiseptica*
Study Purpose	To demonstrate efficacy (Onset of Immunity) against *Bordetella bronchiseptica*
Product Administration	One dose administered by the intranasal route
Study Animals	8-week-old cats; 22 vaccinates and 11 controls
Challenge Description	Cats were challenged with *B. bronchiseptica* 72 hours after vaccination.
Interval observed after challenge	Clinical signs were observed daily for 14 days post challenge.
Results	A difference in clinical signs was observed between the Controls and Vaccinates using a scoring system approved by APHIS. Raw data shown on attached pages.
USDA Approval Date	September 30, 2002

CLINICAL SIGN SCORING SYSTEM

Clinical Sign

Fever
103.0 - 103.9 (T3)
104.0 - 104.9 (T4)
105.0 - (T5)

Hypothermia (T6)

Ocular Discharge
Serous discharge (O1)
Mucopurulent discharge (O2)
Conjunctivitis (O3)

Nasal Discharge
Serous discharge (N1)
Mucopurulent discharge (N2)
Sneezing (N3)

Dyspnea
Audible rales (R1)
Induced coughing (R2)
Spontaneous coughing (R3)
Open mouth breathing (R4)

Depression
Inappetence (A)
Dehydration (H)
Dehydration (G1)

Death (X)

Controls

Days Post Challenge

Group 1	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
AWE1										R3	N1,R2,R3	N1,R2							N1,N3
AWJ4												R2,R3		R3	R2	N1,N3,R3	N3	N3	N3
AWK6						N1					N3		N1,R2	N1,N3					
AVV4									T3,O1			N2,R2	N2,R2	N2	N2	N2,N3	N2	N2	N1
AWC3													N2,N3	R2					
AVX3										R3	R2,R3	R2	N1,N3,R2,R3	N3,R2	N3,R2	N3	N1	N1,N3	
AWE2									O1,N3		N1,N3	N1	N1					R3	N1,R3
AWH3			T3								R2,R3	N2	N3	N3	N3				
AVZ1			T3									R3	N1					N1	
AWC1									R3	R2	N1,N3	N2,N3	N2	N2				N3	N1
AWG1														N2	N3				

Vaccinates (4.6)

Group 2	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
AVV2																			
AVV3													N3		N3	N1			
AVW1												R3	O2,R2	R2					
AVW4			O1							O1				R3	N3				
AVY2			N1	N1									N3			R2			
AVY3											R2,R3	N3			N3			N3	
AVY5										O1	R2	R3			R3				
AVZ2										N1		R3				N1,N3			
AWA3							N1	N1		R3	R2				R3				
AWB1									N1					N3		N3			N3
AWB3													N3				N3		N3
AWC4												N3	N3	N3		N3	N3		
AWD3										R3	R3					R3			
AWE3																			N3
AWE4																			
AWE6								N1						R2,R3		N1,R3			
AWF2											R2	N2,N3	N1,N3	N1	N1,N3	N3	N3		
AWF4										N3	N1,N3		N1,N3	N1,N3	N3	N3			
AWF5										T3	N3	R3			N1				
AWG2										R2	N3,R2,R3	N3	N3					N3	
AWG3												N3							
AWK7													N2,N3				N3		

<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 in pregnant animals</td></tr>
<tr><td>Product Administration</td><td>One dose administered by the intranasal route</td></tr>
<tr><td>Study Animals</td><td>110 queens enrolled with 78 queens producing kittens; 23 vaccinates and 3 controls in the 1st trimester, 21 vaccinates and 4 controls in the 2nd trimester, 23 vaccinates and 4 controls in the 3rd trimester. 209 kittens were 4 weeks of age at time of vaccination, 184 vaccinates and 25 controls.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>After vaccination, pregnant queens were observed daily for clinical signs until they gave birth. All kittens were observed for one week after birth for clinical signs. Kittens vaccinated at 4 weeks of age were observed for 21 days after vaccination for clinical signs.</td></tr>
<tr><td>Results</td><td><u>Pregnant Queen Results</u>
<table>
<tr><th></th><th colspan="2">1st Trimester</th><th colspan="2">2nd Trimester</th><th colspan="2">3rd Trimester</th></tr>
<tr><th></th><th>Cont.</th><th>Vacc.</th><th>Cont.</th><th>Vacc.</th><th>Cont.</th><th>Vacc.</th></tr>
<tr><td>Total Queens</td><td>5</td><td>38</td><td>5</td><td>31</td><td>4</td><td>27</td></tr>
<tr><td>No. of Litters</td><td>3</td><td>23</td><td>4</td><td>21</td><td>4</td><td>23</td></tr>
<tr><td>Did Not Conceive</td><td>2</td><td>15</td><td>1</td><td>10</td><td>0</td><td>4</td></tr>
<tr><td>Kittens Born</td><td>8</td><td>89</td><td>16</td><td>87</td><td>18</td><td>103</td></tr>
<tr><td>Kittens Stillborn</td><td>0</td><td>3</td><td>1</td><td>8</td><td>0</td><td>9</td></tr>
<tr><td>Kittens Died Later</td><td>0</td><td>2</td><td>1</td><td>7</td><td>1</td><td>6</td></tr>
<tr><td>Kittens Survived</td><td>8 (100%)</td><td>84 (94%)</td><td>14 (87%)</td><td>72 (83%)</td><td>17 (94%)</td><td>88 (85%)</td></tr>
</table>
No clinical signs were observed in any of the kittens during the 1-week observation period after birth.

Raw data shown on attached pages.

<u>4 week-old Kitten Results</u>
<table>
<tr><th>Adverse Event</th><th>Number</th></tr>
<tr><td>Nasal discharge</td><td>1</td></tr>
<tr><td>Kittens with no reaction</td><td>208</td></tr>
</table></td></tr>
<tr><td>USDA Approval Date</td><td>June 15, 1999</td></tr>
</table>

Group	Queen	Litter Number	Total Kittens	Stillborn	Died Later	Survived
1st Trimester Controls	95AJE3	5	2	0	0	2
	Q3	1	3	0	0	3
	95APH5	6	3	0	0	3
1st Trimester Vaccinates	Z21	1	4	0	0	4
	02Z	1	4	0	1	3
	96QNP2	2	2	0	0	2
	96QPH5	2	5	0	0	5
	Z56	2	5	0	0	5
	Z13	1	2	0	0	2
	77C	1	3	2	0	1
	96QPC3	2	5	0	0	5
	77N	2	4	0	0	4
	96QPQ3	2	4	0	0	4
	95APH2	8	2	0	0	2
	73I	4	5	0	0	5
	95APE4	4	2	0	0	2
	95APH3	5	4	0	0	4
	Y96	3	6	0	0	6
	96QPT3	5	4	0	0	4
	932472	6	4	0	0	4
	96QPX5	3	5	0	0	5
	932388	8	3	0	1	2
	95AQL3	6	5	0	0	5
	156	4	6	0	0	6
	932396	7	3	0	0	3
	95ASF4	6	2	1	0	1

Group	Queen	Litter Number	Total Kittens	Stillborn	Died Later	Survived	
2nd Trimester Controls	X46	3	5	0	0	5	
	93CAH3	1	3	1	0	2	
	93APJ5	NA	5	0	0	5	
	41275	NA	3	0	1	2	
2nd Trimester Vaccinates	02U	1	4	0	0	4	
	935	2	3	0	0	3	
	971	1	5	3	2	0	
	96	1	7	0	0	7	
	96QPX2	2	5	2	0	3	
	X70	2	6	0	0	6	
	Z18	1	2	0	0	2	
	70A	3	5	0	0	5	
	125	2	5	0	0	5	
	95AIZ3	5	3	1	0	2	
	96QPZ2	1	3	2	1	0	
	96QPI5	2	4	0	2	2	
	95AHH3	6	4	0	1	3	
	932300	NA	6	0	0	6	
	93AYP4	NA	1	0	1	0	
	94BEF4	NA	5	0	0	5	
	Q10	1	4	0	0	4	
	942937	5	5	0	0	5	
	Q7	NA	4	0	0	4	
	Q2	NA	3	0	0	3	
	95AJV5	NA	3	0	0	3	1 deformed kitten

Group	Queen	Litter Number	Total Kittens	Stillborn	Died Later	Survived
3rd Trimester Controls	96QOA4	2	6	0	1	5
	95MFQ3	6	1	0	0	1
	93AVM4	1	4	0	0	4
	96QNJ4	3	7	0	0	7
3rd Trimester Vaccinates	76D	1	4	2	0	2
	96QOO4	2	3	1	2	0
	01E	2	5	0	1	4
	072	2	5	0	1	4
	74S	3	6	0	0	6
	942813	6	2	0	0	2
	96QNH5	2	8	0	0	8
	01I	2	6	1	1	4
	96QMV1	1	7	2	0	5
	93BLH5	2	3	0	0	3
	96QNG5	2	6	0	0	6
	01D	2	7	0	0	7
	93CEC4	1	4	0	0	4
	96QNQ4	1	3	0	0	3
	155	2	4	1	0	3
	95AQW2	5	4	0	0	4
	932269	4	4	0	0	4
	113	1	5	2	0	3
	96QNC3	2	4	0	0	4
	X98	NA	2	0	1	1
	Q4	1	3	0	0	3
	Q13	NA	4	0	0	4
	Q20	1	4	0	0	4

NA = Not Available

<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 field conditions</td></tr>
<tr><td>Product Administration</td><td>One dose administered by the intranasal route</td></tr>
<tr><td>Study Animals</td><td>Study 1: 619 cats from 8 states between 6 weeks and 18 years of age. Study 2: 587 cats from 11 states between 4 weeks and 16 years of age.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>Clinical signs observed by owner for 14 days post-vaccination</td></tr>
<tr><td>Results</td><td>Study 1:
<table>
<tr><th>Adverse Event</th><th>Number of Cats</th></tr>
<tr><td>Coughing</td><td>3</td></tr>
<tr><td>Sneezing</td><td>5</td></tr>
<tr><td>Sneezing, coughing</td><td>3</td></tr>
<tr><td>Serous nasal discharge</td><td>4</td></tr>
<tr><td>Cats with no reaction</td><td>604</td></tr>
</table>
Study 2:
<table>
<tr><th>Adverse Event</th><th>Number of Cats</th></tr>
<tr><td>Coughing</td><td>1</td></tr>
<tr><td>Sneezing, coughing</td><td>2</td></tr>
<tr><td>Sneezing, coughing, serous nasal discharge</td><td>2</td></tr>
<tr><td>Coughing, inappetence</td><td>1</td></tr>
<tr><td>Cats with no reaction</td><td>581</td></tr>
</table></td></tr>
<tr><td>USDA Approval Date</td><td>May 11, 1998 & April 8, 1999</td></tr>
</table>