



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	14M1.22
True Name	Canine Parainfluenza-Bordetella Bronchiseptica Vaccine, Modified Live Virus, Avirulent Live Culture
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Nobivac Intra-Trac KC - Merck Animal Health Nobivac Intra-Trac KC - No distributor specified
Date of Compilation Summary	February 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	<i>Bordetella bronchiseptica</i> (Bb)
Study Purpose	To demonstrate efficacy against Bb.
Product Administration	
Study Animals	
Challenge Description	
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	March 1, 1995

Study Type	Efficacy
Pertaining to	<i>Bordetella bronchiseptica</i> (Bb)
Study Purpose	To demonstration efficacy (Onset of Immunity) against Bb within 72 hours of vaccination.
Product Administration	
Study Animals	
Challenge Description	
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	March 12, 1996

Study Type	Efficacy																											
Pertaining to	Canine Parainfluenza (CPI)																											
Study Purpose	To demonstrate efficacy against CPI.																											
Product Administration	One dose administered by the intranasal route.																											
Study Animals	27, 2 to 3 week old, puppies: 20 vaccinates and 7 controls (non-vaccinates).																											
Challenge Description	All puppies were challenged with CPI virus, 3 weeks post-vaccination.																											
Interval observed after challenge	All puppies were observed daily for 14 days post-challenge for clinical signs and rectal temperatures were recorded. Nasal swabs were collected daily for 14 days post-challenge for viral isolation.																											
Results	<p><u>Neutralizing Antibodies to CPI after Vaccination</u></p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># with Positive Titer $\geq 1:4$</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>20</td> <td>20</td> </tr> <tr> <td>Controls</td> <td>7</td> <td>0</td> </tr> </tbody> </table> <p><u>Clinical Signs</u></p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># of Animals Affected*</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>20</td> <td>0</td> </tr> <tr> <td>Controls</td> <td>7</td> <td>4</td> </tr> </tbody> </table> <p>* An affected dog was defined as showing signs of respiratory distress, such as sporadic nasal discharge and/or spontaneous coughing.</p> <p>All dogs' temperatures remained within the normal range post-challenge.</p> <p><u>Virus Isolation</u></p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Positive for Virus Shedding</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>20</td> <td>0</td> </tr> <tr> <td>Controls</td> <td>7</td> <td>7</td> </tr> </tbody> </table> <p>Requirements per 9 CFR 113.316 were met.</p> <p>Raw data shown on attached pages.</p>	Group	# of Animals	# with Positive Titer $\geq 1:4$	Vaccinates	20	20	Controls	7	0	Group	# of Animals	# of Animals Affected*	Vaccinates	20	0	Controls	7	4	Group	# of Animals	# Positive for Virus Shedding	Vaccinates	20	0	Controls	7	7
Group	# of Animals	# with Positive Titer $\geq 1:4$																										
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USDA Approval Date	March 12, 1996																											

SERUM VN TITER VALUES OF VACCINATED STUDY GROUP

DOG NO.	PRE-VACC.	POST-VAC WEEK 3	POST-CHALL. WEEK 2
8 VAC	<2	16	512
9 VAC	<2	8	256
10 VAC	<2	64	512
11 VAC	<2	32	512
12 VAC	<2	64	256
13 VAC	<2	16	128
14 VAC	<2	32	128
15 VAC	<2	32	256
16 VAC	<2	128	1024
17 VAC	<2	64	512
18 VAC	<2	8	2048
19 VAC	<2	256	1024
20 VAC	<2	256	2048
21 VAC	<2	128	512
22 VAC	<2	128	256
23 VAC	<2	32	128
24 VAC	<2	32	128
25 VAC	<2	64	256
26 VAC	<2	32	256
27 VAC	<2	64	256

SERUM VN TITER VALUES OF NONVACCINATED STUDY GROUP

DOG NO.	PRE-VACC.	POST-VAC WEEK. 3	POST-CHALL. WEEK. 2
1 CON	< 2	< 2	2048
2 CON	< 2	< 2	2048
3 CON	< 2	< 2	2048
4 CON	< 2	< 2	2048
5 CON	< 2	< 2	2048
6 CON	< 2	< 2	1024
7 CON	< 2	< 2	1024

CLINICAL OBSERVATION RECORD OF VACCINATE (V) AND CONTROL (C) DOGS DURING 14 DAY POST-CHALLENGE PERIOD

DOG	Day Post-Challenge													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
ID#														
V 08	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 09	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 10	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 11	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 12	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 13	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 14	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 15	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 16	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 17	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- - CPI Clinical Signs Attributed Not Observed
 N1 - Nose, Clear Discharge
 N2 - Nose, Mucopurulent Discharge
 C1 - Palpation of Trachea/Larynx: Slight Coughing
 C2 - Palpation of Trachea/Larynx: Severe Coughing
 R1 - Respiration: Spontaneous Coughing With Exercise
 R2 - Respiration: Spontaneous Coughing With At Rest
 A1 - Auscultation: Congestion (Nasal)
 A2 - Auscultation: Dry Rales
 A3 - Auscultation: Moist Rales
 A4 - Auscultation: Solid Area (No Sound)

CLINICAL OBSERVATION RECORD OF VACCINATE (V) AND CONTROL (C) DOGS DURING 14 DAY POST-CHALLENGE PERIOD

DOG	Day Post-Challenge													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
V 18	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 19	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 20	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 21	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 22	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 23	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 24	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 25	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 26	-	-	-	-	-	-	-	-	-	-	-	-	-	N1
V 27	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- - CPI Clinical Signs Attributed Not Observed
 N1 - Nose, Clear Discharge
 N2 - Nose, Mucopurulent Discharge
 C1 - Palpation of Trachea/Larynx: Slight Coughing
 C2 - Palpation of Trachea/Larynx: Severe Coughing
 R1 - Respiration: Spontaneous Coughing With Exercise
 R2 - Respiration: Spontaneous Coughing With At Rest
 A1 - Auscultation: Congestion (Nasal)
 A2 - Auscultation: Dry Rales
 A3 - Auscultation: Moist Rales
 A4 - Auscultation: Solid Area (No Sound)

CLINICAL OBSERVATION RECORD OF VACCINATE (V) AND CONTROL (C) DOGS DURING 14 DAY POST-CHALLENGE PERIOD

DOG	Day Post-Challenge													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
C 01	-	-	-	-	-	-	-	-	-	-	R1	-	-	-
C 02	-	-	-	-	-	-	-	-	-	-	-	-	-	-
C 03	-	-	-	-	-	-	-	-	-	-	-	-	-	-
C 04	-	-	-	-	N2	-	-	-	-	R2	-	-	-	-
C 05	-	-	-	N1	N1	-	-	-	-	-	-	N1	E1	-
C 06	-	-	-	-	N1	N1	-	-	R2	-	-	N1	N1	N1
C 07	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- = CPI Clinical Signs Attributed Not Observed
 N1 = Nose, Clear Discharge
 N2 = Nose, Mucopurulent Discharge
 C1 = Palpation of Trachea/Larynx: Slight Coughing
 C2 = Palpation of Trachea/Larynx: Severe Coughing
 R1 = Respiration: Spontaneous Coughing With Exercise
 R2 = Respiration: Spontaneous Coughing With At Rest
 A1 = Auscultation: Congestion (Nasal)
 A2 = Auscultation: Dry Rales
 A3 = Auscultation: Moist Rales
 A4 = Auscultation: Solid Area (No Sound)

DAILY TEMPERATURE (F) READINGS OF THE VACCINATED GROUP

DAY POST-CHALLENGE	DOG TATOO NUMBER									
	8	9	10	11	12	13	14	15	16	17
-2	101	100.1	100.1	100.8	101	100.1	100.8	100.7	100.9	100.3
-1	101.1	101.1	101	101.1	101.2	100.3	100.7	100.4	100.6	100.7
0	101.1	100.6	100.5	100.9	101.1	101.1	101.2	100.9	101.5	100.9
1	101.2	100.9	101.1	101	101.5	100.3	101	101	101.3	101.2
2	100.8	100.8	101	101	101	99.9	100.9	100.5	100.9	100.8
3	100.9	100.5	100.7	100.9	100.9	100.4	101	100.7	100.9	100.9
4	101.1	100.9	100.9	100.7	101.1	100.7	100.7	100.7	100.9	100.1
5	100.1	101.2	101	101	101.3	100.3	100.7	100.2	100.6	100.6
6	100.8	100.5	100.6	100.6	100.5	101	101.5	101.6	100.8	101.4
7	101.4	100.8	101.4	101.1	101.3	101.3	101.4	101.4	101.7	101.4
8	102	101	101.2	100.6	101	101.1	101.1	101.3	101	101.4
9	101	100.9	100.9	100.8	100.9	101	101	101	101.1	101
10	101.6	101	100.9	101.2	101.6	101.3	101.2	101.4	101.6	101.5
11	101.7	101.2	101.8	101.6	101.1	101	101.7	101.6	101.6	101.2
12	101	101.2	100.4	101.1	101.3	100.4	100.5	101.1	101.1	100.3
13	100.9	100.9	101.1	101	101.4	100.8	100.9	101	101.5	101
14	101	101.3	101.2	101.3	101.4	200.9	101.3	101.5	101.9	101.7

DAILY TEMPERATURE (F) READINGS OF THE VACCINATE GROUP

DAY POST-CHALLENGE	DOG TATOO NUMBER									
	18	19	20	21	22	23	24	25	26	27
-2	101.5	100.4	100.1	100.5	100.4	100.7	101	100.5	100.5	100.8
-1	101.4	100.8	100.2	100.8	100.3	100.8	100.4	100.6	100.4	100.1
0	101.6	100.9	100.4	100.9	100.3	100.9	100.6	100.5	101	100.9
1	100.4	100.9	100.7	100.7	100.4	100.8	100.4	100.9	100.6	100.4
2	100.6	100.7	100.8	100.6	100.2	101.4	100.5	101.1	100.7	101
3	100.7	100.4	100.7	100.7	100.4	100.5	100.8	100.9	100.8	100.4
4	100.9	101	100.3	100.8	100.5	100.6	100.4	100.7	100.6	100.7
5	101.3	100.9	100.6	101.1	100.7	101.3	100.7	100.7	100.3	100.9
6	101.4	101	101.4	101.1	101.1	101.9	100.8	101	100.7	101
7	101.4	100.9	101.4	100.8	100.8	101.8	100.5	100.9	100.9	100.7
8	101.4	100.8	101	101.1	101.3	101.6	100.9	101.2	100.6	100.8
9	101.3	101.2	100.8	101.1	101	101.9	101.1	100.7	100.7	100.9
10	101.6	101.1	101.5	101.6	101.7	101.6	101.2	101.5	101	101.2
11	101.1	101.4	100.9	101	100.9	100.8	100.6	100.7	101.1	100.9
12	101.6	101	100.9	101.4	101.6	101.9	101	101.2	101.3	100.9
13	101.6	101.4	101	101.4	101.2	102	100.8	101.2	101.1	100.7
14	101.2	101	101	100.9	100.7	101.5	100.4	101.1	100.4	100.1

DAILY TEMPERATURE (F) READINGS OF THE NON-VACCINATE CONTROL GROUP

DAYS POST-CHALLENGE	DOG TATOO NUMBER						
	1	2	3	4	5	6	7
-1	101.1	100.7	101.2	100.7	99.5	100.5	100.5
-2	100.9	100.7	100.5	100.7	101	100.9	100.8
0	100.8	100.9	100.8	100.6	101.3	100.9	101
1	100.8	100.4	100.8	100.5	101.1	100.9	100.6
2	101	100.3	100.9	100.9	100.9	100.8	100.4
3	101.2	100.8	100.7	101	100.9	100.8	101.2
4	101.3	100.7	100.8	101.1	101.5	100.9	101.2
5	101.3	101.1	101.1	100.7	101.1	100.8	100.9
6	101.6	101	100.9	101.1	101.3	100.4	100.8
7	101.2	101.1	101.3	101.1	101.2	101.3	101.5
8	101.4	101.1	101.5	101.2	101.2	100.6	101.2
9	102	101.5	102.2	101.6	101.2	101.4	101.5
10	101.4	101.1	101.2	101	101.6	101.4	101.5
11	101.8	102.1	101.8	101.7	101.5	101	101.7
12	101	101.3	101.6	101	101.3	101.6	1001.1
13	100.9	100.7	101.3	100.7	101.6	101	101.4
14	102	101	101.3	101.2	101.5	101	101.7

REISOLATION OF CHALLENGE VIRUS ISOLATE DO08 FROM VACCINATE (V)
AND CONTROL (C) DOGS DURING 14 DAY POST-CHALLENGE PERIOD

DOG	Day Post-Challenge														
ID#	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
V 08	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 09	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 11	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 12	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 13	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 14	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 15	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 16	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 17	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 18	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 19	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 21	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 22	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 23	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 24	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 25	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 26	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
V 27	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

DOG	Day Post-Challenge														
ID#	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
C 01	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
C 02	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
C 03	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
C 04	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
C 05	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
C 06	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
C 07	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-

Study Type	Safety																																										
Pertaining to	ALL																																										
Study Purpose	To demonstrate safety under field conditions including pregnant animals.																																										
Product Administration	One dose administered by the intranasal route.																																										
Study Animals	<p><u>Study 1</u>: 653 dogs of various ages, breeds, and sex; 223 dogs were 2 weeks of age, and 37 dogs were pregnant (4 in 1st trimester, 3 in 2nd trimester, and 30 in 3rd trimester).</p> <p><u>Study 2</u>: 505 dogs of various ages, breeds, and sex; 135 dogs were 2 weeks of age, and 38 dogs were pregnant (13 in 1st trimester, 6 in 2nd trimester, and 19 in 3rd trimester).</p>																																										
Challenge Description	Not applicable																																										
Interval observed after challenge	Dogs were observed daily for 14 days post-vaccination.																																										
Results	<p style="text-align: center;"><u>Summary of Adverse Events (from both studies)</u></p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th>Group</th> <th># of Dogs</th> <th># of Adverse Events (AE)</th> <th>% with AE</th> </tr> </thead> <tbody> <tr> <td>2-week-old puppies</td> <td>358</td> <td>1</td> <td>0.3</td> </tr> <tr> <td>> 2 week-old dogs</td> <td>725</td> <td>3</td> <td>0.4</td> </tr> <tr> <td>Pregnant Dogs*</td> <td>75</td> <td>0</td> <td>0</td> </tr> <tr> <td> 1st Trimester</td> <td>17</td> <td>0</td> <td>0</td> </tr> <tr> <td> 2nd Trimester</td> <td>9</td> <td>0</td> <td>0</td> </tr> <tr> <td> 3rd Trimester</td> <td>49</td> <td>0</td> <td>0</td> </tr> <tr> <td>Total</td> <td>1158</td> <td>4</td> <td>0.3</td> </tr> </tbody> </table> <p>*Licensee affirms pregnant dogs whelped with no adverse reaction to the pregnancy or puppies born attributed to the product.</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th>Adverse Event</th> <th># of Dogs*</th> </tr> </thead> <tbody> <tr> <td>Mucopurulent nasal discharge 10 days post-vaccination</td> <td>1</td> </tr> <tr> <td>Tracheobronchitis 2 days post-vaccination</td> <td>1</td> </tr> <tr> <td>Skin on muzzle, nose, lips swollen/edematous</td> <td>1</td> </tr> <tr> <td>Vomited, loose stool, wheezing, red/raised bumps</td> <td>1</td> </tr> </tbody> </table> <p>*All dogs recovered with treatment. Licensee affirms no adverse event was attributed to the product.</p>	Group	# of Dogs	# of Adverse Events (AE)	% with AE	2-week-old puppies	358	1	0.3	> 2 week-old dogs	725	3	0.4	Pregnant Dogs*	75	0	0	1 st Trimester	17	0	0	2 nd Trimester	9	0	0	3 rd Trimester	49	0	0	Total	1158	4	0.3	Adverse Event	# of Dogs*	Mucopurulent nasal discharge 10 days post-vaccination	1	Tracheobronchitis 2 days post-vaccination	1	Skin on muzzle, nose, lips swollen/edematous	1	Vomited, loose stool, wheezing, red/raised bumps	1
Group	# of Dogs	# of Adverse Events (AE)	% with AE																																								
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