Summary of Studies Supporting USDA Product Licensure

Establishment Name	Elanco US Inc.
USDA Vet Biologics Establishment Number	196
Product Code	47E5.21
True Name	Canine Coronavirus Vaccine, Killed Virus, Borrelia Burgdorferi Bacterin-Leptospira Canicola-Grippotyphosa-Icterohaemorrhagiae-Pomona Bacterial Extract
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	CvK + B. Burgdorferi - Elanco US Inc.
Date of Compilation Summary	December 20, 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	Borrelia burgdorferi
Study Purpose	To demonstrate effectiveness against *Borrelia burgdorferi* in dogs.
Product Administration	Two doses were administered subcutaneously (SC) 3 weeks apart.
Study Animals	Study I: Eighteen (18) 8-14 week old puppies serologically negative for *B. burgdorferi* were used in the final study analysis. Animals were randomized into one group of 8 SC vaccinates and one group of 10 controls. Study II: Thirty (30) 8 week old puppies serologically negative for *B. burgdorferi* were used in the final study analysis. Animals were randomized into one group of 20 SC vaccinates and one group of 10 controls.
Challenge Description	Study I: Four weeks after second vaccination all animals were challenged with *Borrelia burgdorferi*. Study II: Three weeks after second vaccination all animals were challenged with *Borrelia burgdorferi*.
Interval observed after challenge	Study I: Dogs were observed daily for 90 days after challenge for clinical signs associated with *B. burgdorferi*. Study II: Dogs were observed daily for 126 days after challenge for clinical signs associated with *B. burgdorferi*.
Results	Dogs were evaluated for clinical arthritis, and the detection of *B. burgdorferi* in blood, fluids, and tissues. Clinical arthritis was defined as the number of discontinuous occurrence of limp and/or lameness for a specific limb. Blood, synovial fluid, lymph nodes, skin and urine samples were collected for *B. burgdorferi* isolation and/or detection. Data tables are appended to the end of this summary.
USDA Approval Date	December 6, 1995

Study I: Arthritic Signs Observed

Dog	Treatment	Stiff	Lame	Limping
16	SC Vaccinate		87	
17	SC Vaccinate			
18	SC Vaccinate			
19	SC Vaccinate			
20	SC Vaccinate	78		
21	SC Vaccinate			
22	SC Vaccinate			
23	SC Vaccinate			

Dog	Treatment	Stiff	Lame	Limping
24	Control	59, 61, 87		86
25	Control	52, 62, 64, 65, 70, 71, 72, 73, 74, 75, 87	61, 77, 78	79, 80, 85
26	Control	74, 75	78, 79	80
27	Control	63, 64, 87		
28	Control	49		
29	Control	54, 58, 64, 76		
30	Control	59,78, 80		65, 69, 70, 71, 72, 73, 75, 76, 77, 79, 87
31	Control	41, 52, 57, 59, 60, 61		58, 75, 90
32	Control	50 , 55, 56, 58, 62, 70, 76	58, 59, 60, 61, 69, 73, 75, 77, 78, 85	52, 54, 56, 57, 58, 59, 60, 62, 65, 66, 68, 70, 71, 72, 74, 79, 80, 84, 86, 87, 90
33	Control	38, 41, 42,43, 45, 50, 63, 65, 66, 69, 71, 84	54, 58, 59, 60, 61, 62, 72, 73, 76, 77, 79	38,41,49,52,53, 55, 56, 57, 65, 66, 68, 69, 70, 74, 75, 78, 80, 86, 87, 90

Number - represents the day post challenge the clinical sign was observed

Blank - No signs observed

Clinical arthritis was defined as the number of discontinuous occurrence of limp and/or lameness for a specific limb

Study I: Detection of B Burgdorferi (Blood)

Dog	Treatment	9DPC	13DPC	20DPC	24DPC	31DPC	34DPC	35DPC	38DPC
16	SC Vaccinate								
17	SC Vaccinate								
18	SC Vaccinate								
19	SC Vaccinate								
20	SC Vaccinate								
21	SC Vaccinate								
22	SC Vaccinate								
23	SC Vaccinate								

Dog	Treatment	9DPC	13DPC	20DPC	24DPC	31DPC	34DPC	35DPC	38DPC
24	Control							+	
25	Control								
26	Control								
27	Control								
28	Control	+		+		+			+
29	Control					+			
30	Control								
31	Control				+		+		
32	Control		+						
33	Control						+		

*Samples were collected periodically from -1DPC through 90DPC, only dates with positive detection are listed. DPC is day post challenge.

"+" - Positive for Borrelia Detection

Blank - Negative for Borrelia Detection

Study I: Detection of B Burgdorferi (Tissues and Fluid) at 90DPC

Dog	Treatment	Lymph Nodes	Synovial Fluid	Skin	Urine
16	SC Vaccinate				
17	SC Vaccinate		+		
18	SC Vaccinate				
19	SC Vaccinate		+		
20	SC Vaccinate	+			
21	SC Vaccinate	+			
22	SC Vaccinate				
23	SC Vaccinate				

Dog	Treatment	Lymph Nodes	Synovial Fluid	Skin	Urine
24	Control			+	
25	Control		+	+	
26	Control	+		+	no sample
27	Control		+		
28	Control		+		+
29	Control		+	+	
30	Control	+			+
31	Control		+	+	+
32	Control		+		
33	Control			+	

DPC is day post challenge

"+" - Positive for Borrelia Detection

Blank - Negative for Borrelia Detection

Study II: Arthritic Signs Observed

Dog	Treatment	Stiff	Lame	Limping
1	SC Vaccinate			
2	SC Vaccinate			
3	SC Vaccinate	54, 77, 95		
4	SC Vaccinate			
5	SC Vaccinate	41, 55, 56, 58, 112		
6	SC Vaccinate			
7	SC Vaccinate	104		
8	SC Vaccinate			
9	SC Vaccinate			
10	SC Vaccinate			
11	SC Vaccinate	95, 100		28, 98, 99
12	SC Vaccinate		41	
13	SC Vaccinate	98		
14	SC Vaccinate	90		
15	SC Vaccinate	80		84
16	SC Vaccinate	42		76
17	SC Vaccinate			
18	SC Vaccinate			
19	SC Vaccinate	120		
20	SC Vaccinate	44, 45, 57	41, 52, 54	77, 79, 91, 95, 104

Dog	Treatment	Stiff	Lame	Limping
21	Control	30, 50, 53, 56, 58, 63, 95		78
22	Control			
23	Control	63, 65, 93, 94, 106		43, 55, 100
24	Control	65, 82		
25	Control	38, 62, 63, 75, 98, 99, 100, 103, 106		104
26	Control	56, 71, 78, 93, 99,	59, 60, 61, 72, 73, 74, 75, 80, 81, 82, 83, 89, 90, 103, 104, 105, 106, 107, 108, 120, 121, 122, 125, 126	76, 77, 84, 85, 98, 109, 110, 115
27	Control	51, 79, 103		
28	Control	57, 105	105, 125	124
29	Control			
30	Control	104	76, 77, 126	75, 78, 82, 90, 101

Number - represents the day post challenge the clinical sign was observed

Blank - No signs observed

Clinical arthritis was defined as the number of discontinuous occurrence of limp and/or lameness for a specific limb

Study II: Detection of B Burgdorferi (Blood)

Dog	Treatment	30DPC	34DPC	35DPC	36DPC	37DPC	41DPC	43DPC	44DPC	76DPC	103DPC
1	SC Vaccinate										
2	SC Vaccinate										
3	SC Vaccinate										
4	SC Vaccinate										
5	SC Vaccinate										
6	SC Vaccinate										
7	SC Vaccinate										
8	SC Vaccinate					+					
9	SC Vaccinate										
10	SC Vaccinate										
11	SC Vaccinate										
12	SC Vaccinate										
13	SC Vaccinate										
14	SC Vaccinate										
15	SC Vaccinate										
16	SC Vaccinate										
17	SC Vaccinate										
18	SC Vaccinate										
19	SC Vaccinate										
20	SC Vaccinate										

Dog	Treatment	30DPC	34DPC	35DPC	36DPC	37DPC	41DPC	43DPC	44DPC	76DPC	103DPC
21	Control									+	
22	Control										
23	Control										
24	Control		+	+	+	+	+		+		
25	Control	+	+								
26	Control					+	+	+			+
27	Control										
28	Control										
29	Control										
30	Control										

*Samples were collected periodically from -1DPC through 126DPC, only dates with positive detection are listed. DPC is day post challenge.

"+" - Positive for Borrelia Detection

Blank - Negative for Borrelia Detection

Study II: Detection of B Burgdorferi (Tissues and Fluid) at 126DPC

Dog	Treatment	Lymph Nodes	Synovial Fluid	Skin	Urine
1	SC Vaccinate	+			
2	SC Vaccinate	+			
3	SC Vaccinate		+		+
4	SC Vaccinate	+			
5	SC Vaccinate	+			+
6	SC Vaccinate				
7	SC Vaccinate	+			
8	SC Vaccinate	+		+	
9	SC Vaccinate				
10	SC Vaccinate				
11	SC Vaccinate				+
12	SC Vaccinate		+		+
13	SC Vaccinate	+			
14	SC Vaccinate	+	+	+	
15	SC Vaccinate	+			+
16	SC Vaccinate		+		+
17	SC Vaccinate	+	+	+	
18	SC Vaccinate		+		
19	SC Vaccinate				
20	SC Vaccinate	+		+	

Dog	Treatment	Lymph Nodes	Synovial Fluid	Skin	Urine
21	Control	+	+		
22	Control	+	+	+	
23	Control		+		
24	Control		+	+	+
25	Control	+	+	+	+
26	Control	+	+	+	+
27	Control	+	+		
28	Control	+	+	+	+
29	Control	+	+	+	
30	Control	+			

DPC is day post challenge
"+" - Positive for Borrelia Detection
Blank - Negative for Borrelia Detection

Study Type	Efficacy
Pertaining to	Borrelia burgdorferi
Study Purpose	To demonstrate effectiveness against *Borrelia burgdoferi* for one year duration of immunity.
Product Administration	Two doses were administered subcutaneously (SC) 3 to 4 weeks apart.
Study Animals	Study I: Twenty-four (24) dogs serologically negative for *B. burgdorferi* were used in the final study analysis. Animals were randomized into one group of 12 SC vaccinates and one group of 12 controls. Study II: Sixteen (16) dogs serologically negative for *B. burgdorferi* were used in the study. Animals were randomized into one group of 5 SC vaccinates, and one group of 11 controls.
Challenge Description	One year after second vaccination all animals were challenged with *Borrelia burgdorferi.*
Interval observed after challenge	Dogs were observed for 5 months after challenge.
Results	Dogs were evaluated for *B. burgdorferi* disease. Clinical disease was evaluated by clinical arthritis, the isolation of *B. burgdorferi* in skin, and detection of Borrelia infection by antibody profile. Clinical arthritis was defined as the number of discontinuous occurrence of limp and/or lameness for a specific limb. Results: Study I 10/12 (83%) - Controls positive for *B. burgdorferi* disease 2/12 (17%) - SC Vaccinates positive for *B. burgdorferi* disease Data tables are appended to the end of this summary. No animals (vaccinates or controls) were observed with clinical arthritis in this study. Study II 10/11 (91%) - Controls positive for *B. burgdorferi* disease 1/5 (20%) - SC Vaccinates positive for *B. burgdorferi* disease Data tables are appended to the end of this summary. Only one control animal was observed with clinical arthritis in this study. Dog #13 (control) was observed to be lame on 134DPC. All other animals were negative for clinical arthritis.
USDA Approval Date	January 2, 1997

Study I Isolation of *B. Burgdorferi* in Skin Samples

Animal	Treatment Group	28DPC*	63DPC	91DPC	118DPC
1	SC Vaccinate	-	+	-	+
2	SC Vaccinate	-	-	-	+
3	SC Vaccinate	-	-	-	-
4	SC Vaccinate	-	-	-	-
5	SC Vaccinate	-	-	-	-
6	SC Vaccinate	-	-	-	-
7	SC Vaccinate	-	-	-	-
8	SC Vaccinate	-	-	-	-
9	SC Vaccinate	-	-	-	-
10	SC Vaccinate	-	-	-	-
11	SC Vaccinate	-	-	-	-
12	SC Vaccinate	-	-	-	-
13	Control	-	-	-	-
14	Control	-	-	+	+
15	Control	-	+	-	+
16	Control	-	-	-	+
17	Control	-	+	+	-
18	Control	-	-	+	-
19	Control	-	+	+	+
20	Control	-	+	+	+
21	Control	-	-	-	-
22	Control	-	+	+	-
23	Control	-	+	+	+
24	Control	+	+	+	-

"+" - Positive for Borrelia Detection

" - " - Negative for Borrelia Detection

DPC is day post challenge

Study I Detection of Borrelia infection by serum antibody profile.

Animal	Treatment Group	-1DPC	28DPC	63DPC	89DPC	118DPC	146DPC
1	SC Vaccinate	-	-	-	+	+	+
2	SC Vaccinate	-	-	+	+	+	+
3	SC Vaccinate	-	-	-	-	-	-
4	SC Vaccinate	-	-	-	-	-	-
5	SC Vaccinate	-	-	-	-	-	-
6	SC Vaccinate	-	-	-	-	-	-
7	SC Vaccinate	-	-	-	-	-	-
8	SC Vaccinate	-	-	-	-	-	-
9	SC Vaccinate	-	-	-	-	-	-
10	SC Vaccinate	-	-	-	-	-	-
11	SC Vaccinate	-	-	-	-	-	-
12	SC Vaccinate	-	-	-	-	-	-
13	Control	-	-	-	-	-	-
14	Control	-	-	+	+	+	+
15	Control	-	-	+	+	+	+
16	Control	-	-	-	-	+	+
17	Control	-	-	-	+	+	+
18	Control	-	-	+	+	+	+
19	Control	-	-	+	+	+	+
20	Control	-	-	+	+	+	+
21	Control	-	-	-	-	-	-
22	Control	-	-	+	+	+	+
23	Control	-	-	+	+	+	+
24	Control	-	-	+	+	+	+

"+" - Antibody positive for presence of *B. burgdorferi* infection
" - " –Antibody negative for presence of *B. burgdorferi* infection
DPC is day post challenge

Study II Isolation of *B. burgdorferi* in Skin Samples

Animal	Treatment Group	36DPC	63DPC	91DPC	118DPC	152DPC
1	SC Vaccinate	-	-	-	-	-
2	SC Vaccinate	-	-	-	-	-
3	SC Vaccinate	-	-	-	-	-
4	SC Vaccinate	-	-	-	+	-
5	SC Vaccinate	-	-	-	-	-
6	Control	-	-	+	+	-
7	Control	-	-	-	-	-
8	Control	+	-	+	+	-
9	Control	+	-	+	+	+
10	Control	+	+	-	+	-
11	Control	-	-	+	-	-
12	Control	+	-	+	-	-
13	Control	+	+	-	+	-
14	Control	+	-	+	+	+
15	Control	-	-	+	+	-
16	Control	+	-	+	-	-

"+" - Positive for Borrelia Detection
" - " - Negative for Borrelia Detection

DPC is day post challenge

Study II Detection of Borrelia infection by serum antibody profile.

Animal	Treatment Group	0DPC	34DPC	62DPC	90DPC	117DPC	152DPC
1	SC Vaccinate	-	-	-	-	-	-
2	SC Vaccinate	-	-	-	-	-	-
3	SC Vaccinate	-	-	-	-	-	-
4	SC Vaccinate	-	-	+	+	+	+
5	SC Vaccinate	-	-	-	-	-	-
6	Control	-	-	+	+	+	+
7	Control	-	-	-	-	-	-
8	Control	-	-	+	+	+	+
9	Control	-	-	-	+	+	+
10	Control	-	+	+	+	+	+
11	Control	-	-	+	+	+	+
12	Control	-	-	+	+	+	+
13	Control	-	-	+	+	+	+
14	Control	-	-	+	+	+	+
15	Control	-	-	-	+	+	+
16	Control	-	-	-	+	+	+

"+" - Antibody positive for presence of *B. burgdorferi* infection

" - " –Antibody negative for presence of *B. burgdorferi* infection

DPC is day post challenge

Study Type	Efficacy
Pertaining to	Canine coronavirus
Study Purpose	To demonstrate effectiveness against intestinal disease due to canine coronavirus
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. Study data, however, are no longer available.
USDA Approval Date	December 3, 1984

Study Type	Efficacy
Pertaining to	Leptospira canicola
Study Purpose	To demonstrate effectiveness against *Leptospira canicola* in 6 week old dogs.
Product Administration	Two doses were administered subcutaneously (SC) 3 weeks apart.
Study Animals	Twenty-three (23) 6 week old puppies serologically negative for Leptospira were randomized into one group of 11 SC vaccinates and one group of 12 controls.
Challenge Description	Twenty-one (21) days after second vaccination all animals were challenged with *Leptospira canicola* organisms.
Interval observed after challenge	Dogs were observed daily for 21 days after challenge for clinical signs associated with *L. canicola*. Blood samples were collected through 14 days after challenge.
Results	Efficacy was determined by comparing vaccinates versus controls in clinical signs, thrombocytopenia, and leukopenia. A dog was considered to have thrombocytopenia if the platelet count dropped below 200 k/µL and the count was less than 50% of the baseline value. A dog was considered to have leukopenia if the platelet count dropped below 6 k/µL and the count was less than 50% of the baseline value. Data tables are appended to the end of this summary.
USDA Approval Date	April 3, 1998

Leptospira canicola Clinical Signs Observed Post Challenge

SC Vaccinates																					
Dog	0DPC	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC	15DPC	16DPC	17DPC	18DPC	19DPC	20DPC	21DPC
12																						
13		A																			G	
14		A														A				B	BJ	
15	G	D					G				A					AG	G		G			
16		D	G																			
17				G	G																	
18	G				A										A	A		AG				
19																						
20	G		G		G	G		G		G												
21	G	A	AD	G		G	A															
22																	H					

A-inappetance	G - Ocular Discharge Mucoid	N1 - Fever (103.0-103.9°F)	DPC = Day post-challenge
B-Vomiting	H - Nasal Discharge Serous	N2 - Fever (104.0-104.9°F)	
C-Labored Breathing	I - Nasal Discharge Mucoid	N3 - Fever (105.0-105.9°F)	
D - Depression/Lethargy	J - Diarrhea Mild (loose stool)	N4 - <99.6°F	
E1 - Conjunctivitis Mild/Moderate	K - Diarrhea Severe (bloody stool)	P - Death	
E2 - Conjunctivitis Severe	L - Bloody Urine	Blank - no clinical signs observed	
F- Ocular Discharge Serous	M - Icterus		

Leptospira canicola Clinical Signs Observed Post Challenge

Controls																					
Dog	0DPC	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC	15DPC	16DPC	17DPC	18DPC	19DPC	20DPC	21DPC
23					A,D,K,M,N4	P																
24			D,G,N3		A,D,G,J	A,D,G	A,D,K	C,D,G,L,N4	P													
25			N2	B	G		A,K	A,G	A	D		A,D,N1	D		G							
26		A,G	D,G,N1	D,G,N1	G	D	A,D,J	A,G,K	A,D,K	A,D		G	D,G								B	
27			N1	A	A	A,N1	A,K	A,D,G								A		A,G				
28		A	GN2	A	A,G,L	A,D,G,K,L,M,N4	A,D,E2,M,N4	P														
29			D,N2	J,K	A,B,D,G,L	D,G,K,L,N4	A,D,E1,K,L,M,N4	P														
30		G	N2			G,K	A,D,G,K	G	G,K				G			G	G					
31	H		N2	G,K	B,D,K,L	D,G,K,L,N4	P															
32			N1	G	G,L	D,K,L	A,D,G,K,L,M,N4	P														
33	G	G	G,N2	A,G,N1	A,G	A,B,J	A,D,G,K,L	A,D,G,K,L	A,D,G,K,L	A,D,G,K,L	A,K	G	G			G,L		A,G	G			
34			A,N1	A,G,N2		G	A,D,G,K,L	A,D,K,L,N1	A,D,G,L,N1	A,D,G,K,L	A,K	G,K	G,K									

A-inappetance	G - Ocular Discharge Mucoid	N1 - Fever (103.0-103.9°F)
B-Vomiting	H - Nasal Discharge Serous	N2 - Fever (104.0-104.9°F)
C-Labored Breathing	I - Nasal Discharge Mucoid	N3 - Fever (105.0-105.9°F)
D - Depression/Lethargy	J - Diarrhea Mild (loose stool)	N4 - <99.6°F
E1 - Conjunctivitis Mild/Moderate	K - Diarrhea Severe (bloody stool)	P - Death
E2 - Conjunctivitis Severe	L - Bloody Urine	Blank - no clinical signs observed
F- Ocular Discharge Serous	M - Icterus	

DPC = Day post-challenge

Leptospira canicola White Blood Cell Count Post Challenge

SC Vaccinates															
Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
12	22.1	25.8	15.1	17	20.3	19.3	20	20.7	16.5	19.4	19.3	10.7	17.2	19.6	16.6
13	12.3	12.4	9.3	9.6	10.5	9	8	12.5	11.8	10.4	8.8	12.7	10.2	9.7	9.1
14	21.7	19.8	12.3	12.9	14	15.5	13.6	17.4	19.2	19.3	16.9	15.3	14	23.2	15.7
15	13.3	8.8	9.6	12.7	8.2	11.5	12.2	13.1	11.8	8.5	8.5	13.1	9.2	10.2	9.4
16	14	13.2	9.5	7.6	8.4	10.1	10.2	9.4	11.4	9.7	11.3	9.3	10.1	10.8	10.5
17	14.3	16.1	12.8	11.8	12.2	10.7	13.2	12.5	9.8	7.3	8.8	9.5	10.3	9.9	12.3
18	11	11.4	10.6	10.1	10.2	9.4	11.7	9.7	9.3	9.3	9.1	11.6	11.7	17.2	17.6
19	8.9	8.4	8	9.1	8.4	6.6	7.2	7.5	6.4	8.2	7	8.8	7.3	12.3	13.4
20	11.2	15.8	10.7	9.1	7.6	8	9	9.2	10.5	11.4	7	13	9.3	7.6	12.7
21	11	10.5	9.5	15.1	14.6	14.1	13.9	13.4	20.7	14.9	11.7	16.5	13.2	14.7	21.7
22	10.2	15.6	9.4	12.1	9.5	12.7	11	7.3	8.3	11.7	7.7	10.2	9.2	11	11.5

DPC = Day post-challenge. Values reported as k/µL.

Leptospira canicola White Blood Cell Count Post Challenge															
Controls															
Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
23	18.3	21.7	14.2	7.4	21.7	.	.								
24	16.1	20	16.7	6.1	11.5	15.6	14.6	20.5							
25	17.1	11.3	13	8.3	10	12.6	13.6	17	26	28.1	36.6	36.7	26.2	29.4	21.9
26	9	7.9	9.6	5.6	5.7	6.7	8		11.7	13.8	16.6	9.6	11.5	12.7	13.9
27	10.4	8.9	5.5	4.1	5.2	8.6	19.4	21	16.2	7.9	11.3	13.9	15	11.5	13.3
28	9.6	18.4	6.4	3.9	7	19.4	13.2								
29	12.2	19.4	7.8	4.2	5	5.3	17.5								
30	9.5	11.9	9.5	3.2	6.1	7.9	10.6	11.1	10.4	8.7	11.4	9.2	12.69	16.7	12.2
31	8.9	10.6	6.4	4	6	10.3									
32	11.9	12.2	11.5	5.3	6	6.6	15.8								
33	11.8	17.5	6.1	2.6	5.3	4.4	8.7	13	22.8	22.8	20.5	31.5	26.3	17.4	16.9
34	7	9.6	10.1	3.4	5.6	3.8	6	12	12.6	17.3	15.3	10.9	15.7	15.9	20.2

DPC = Day post-challenge. Values reported as k/µL.

Leptospira canicola Platelet Counts Post Challenge

SC Vaccinates

Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
12	444.3	538	480	452	473	512	531	582	478	631	512	381	483	511	470
13	551.3	679	559	573	576	539	467	636	565	470	501	616	550	510	467
14	473.3	571	452	505	444	536	497	604	693	695	567	568	508	802	640
15	459.7	407	381	543	421	503	612	633	576	497	482	560	438	463	461
16	477.3	377	409	452	456	492	555	558	655	512	519	302	428	399	390
17	318	243	247	311	324	329	389	351	314	288	270	261	232	257	278
18	425.7	331	356	381	398	453	542	247	463	483	405	480	406	554	572
19	348.7	330	353	324	403	375	376	375	379	476	381	414	418	516	524
20	555.3	494	497	530	483	523	538	706	704	662	493	601	462	464	469
21	378.3	332	354	476	447	469	441	514	650	581	501	521	429	474	583
22	469.3	413	455	581	478	576	517	469	473	597	492	500	497	495	593

DPC = Day post-challenge. Values reported as k/µL.

Leptospira canicola Platelet Counts Post Challenge															
Controls															
Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
23	300	238	148	11	7.7	D	D	D	D	D	D	D	D	D	D
24	342	204	161	64.1	40.5	45.3	123	207	D	D	D	D	D	D	D
25	519.7	267	213	187	134	117	160	285	497	710	714	823	738	810	717
26	404.7	278	279	196	150	172	194	ND	302	441	721	648	599	590	588
27	482.7	281	225	119	55	49.9	100	157	405	455	492	552	528	428	435
28	242.3	209	60.4	45.9	3.9	11.1	11.3	D	D	D	D	D	D	D	D
29	529.7	521	305	195	37.6	15.8	42.2	D	D	D	D	D	D	D	D
30	329.3	292	167	107	61.7	81.6	122	242	412	518	697	504	632	596	551
31	432.7	327	150	80.2	38	14	D	D	D	D	D	D	D	D	D
32	395.7	329	195	103	33.3	14.2	44.1	D	D	D	D	D	D	D	D
33	563.7	409	182	115	67.1	8.5	2.4	11.4	87.1	235	417	744	701	726	714
34	232.7	174	150	64.5	41.6	8.3	6.8	82.8	142	273	310	383	479	475	564
ND= No Data															
D = dead															

DPC = Day post-challenge. Values reported as k/µL.

Study Type	Efficacy
Pertaining to	Leptospira grippotyphosa
Study Purpose	To demonstrate effectiveness against *Leptospira grippotyphosa* in 6-week-old dogs.
Product Administration	Two doses were administered subcutaneously (SC) 3 weeks apart.
Study Animals	Twenty (20) 6-week-old puppies were randomized into one group of 10 SC vaccinates and one group of 10 controls.
Challenge Description	Fifteen (15) days after second vaccination all animals were challenged with *Leptospira grippotyphosa* organisms.
Interval observed after challenge	Dogs were observed daily for 21 days after challenge
Results	Efficacy was based on the reduction in spirochetemia in vaccinates when compared to controls. A data table is appended to the end of this summary.
USDA Approval Date	January 12, 1999

Isolation of Leptospira from Blood Collected from Dogs Post Challenge

Control Animals													
Dog	0DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
1						+							
2					+		+	+					
3				+	+								
4					+	+							
5				+	+	+							
6						+	+	+	+	+	NA	NA	NA
7				+	+	+	+	+	+	NA	NA	NA	NA
8					+	+	+	+	+	+	NA	NA	NA
9				+	+	+	+	+	+	+	NA	NA	NA
10					+	+	+	+	+	+	NA	NA	NA

NA - Animal Dead or euthanized / no sample taken

+ - Positive for Leptospira

*Leptospira was not isolated in any of the SC vaccinates

Study Type	Efficacy
Pertaining to	Leptospira icterohaemorrhagiae
Study Purpose	To demonstrate effectiveness against *Leptospira icterohaemorrhagiae* in 6 week old dogs.
Product Administration	Two doses were administered subcutaneously (SC) 3 weeks apart.
Study Animals	Twenty-two (22) 6 week old puppies serologically negative for *Leptospira icterohaemorrhagiae* were randomized into one group of 10 SC vaccinates and one group of 12 controls.
Challenge Description	Twenty-one (21) days after second vaccination all animals were challenged with *Leptospira icterohaemorrhagiae* organisms.
Interval observed after challenge	Dogs were observed daily for 21 days after challenge for clinical signs associated with *L. icterohaemorrhagiae*. Blood samples were collected through 14 days after challenge.
Results	Efficacy was determined by comparing vaccinates versus controls in clinical signs, thrombocytopenia, and leukopenia. A dog was considered to have thrombocytopenia if the platelet count dropped below 200 k/µL and the count was less than 50% of the baseline value. A dog was considered to have leukopenia if the platelet count dropped below 6 k/µL and the count was less than 50% of the baseline value. Data tables are appended to the end of this summary.
USDA Approval Date	March 31, 1998

Leptospira Ictero Clinical Signs Observed Post Challenge

SC Vaccinates

Dog	0DPC	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC	15DPC	16DPC	17DPC	18DPC	19DPC	20DPC	21DPC
11							A															
12																						
13				E		D								E				E	D		E	
14				E			E		F										D	E		
15		A,E							E				D								E	
16																				A		
17																						
18																			D			
19							E															
20			D	D		D	D					D		E			E					

A-inappetance	F - Nasal Discharge Serous	K - Bloody Urine
B-Vomiting	G - Nasal Discharge Mucoid	L - Fever >103.0°F
C - Depression/Lethargy	H- Diarrhea Mild (loose stool)	M - Death
D- Ocular Discharge Serous	I- Diarrhea Moderate (Watery stool)	Blank - no clinical Sign observed
E - Ocular Discharge Mucoid	J - Diarrhea Severe (bloody stool)	

DPC = Day post-challenge

Leptospira Ictero Clinical Signs Observed Post Challenge

Controls

Dog	0DPC	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC	15DPC	16DPC	17DPC	18DPC	19DPC	20DPC	21DPC
21					F		A															
22					F					B										E		
23			L	L									E				E	E	E	E		
24			L	L																		
25																						
26																						
27			L	D	D	E		J	A				E			D						
28			L,E	K	A,C,D,J	M																
29			L			D													D			
30				L,D	A,E	M																
31			L	E			A					E					E		D			
32							E												B			

A-inappetance	F - Nasal Discharge Serous	K - Bloody Urine
B-Vomiting	G - Nasal Discharge Mucoid	L - Fever >103.0°F
C - Depression/Lethargy	H- Diarrhea Mild (loose stool)	M - Death
D- Ocular Discharge Serous	I- Diarrhea Moderate (Watery stool)	Blank - no clinical Sign observed
E - Ocular Discharge Mucoid	J - Diarrhea Severe (bloody stool)	

DPC = Day post-challenge

Leptospira ictero White Blood Cell Count Post Challenge

SC Vaccinates

Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
11	7.2	7.3	12.4	7.9	6.8	10.1	6.4	6.4	6.4	8.5	8.9	9.7	9.6	7.2	6.4
12	10	13.9	10.4	8.9	9.1	12.4	15.2	8.2	11.1	8.6	7.7	10.2	9	9.1	12.3
13	7.6	15.4	9.6	13.2	9.1	14.2	8.8	9.2	9.6	8.3	10.6	6.7	7.8	7.8	8.4
14	13.4	7.6	12.6	8.2	12.6	11.3	9.3	7.3	11.8	8	13.2	9.8	10	12.8	9.1
15	9.8	11.4	9.8	9	8	8.3	11.2	10.2	8	7.5	10.4	7.7	11.1	7.5	10.9
16	9.1	8.8	9.5	6.8	8.1	9.1	9.4	8.4	10.1	7.7	8.7	9.5	10	8.3	8.3
17	9.1	7.1	7.8	8.1	7.5	7.2	10.5	9.4	11.4	7.6	11.7	7.1	10.2	7.5	7.3
18	7.2	7.7	10.5	9.1	6.6	7.3	7.1	8.4	7.4	8	9	8.1	6.5	7.8	6.4
19	9.5	13.8.	8.4	11.7	11.7	8.7	6.7	10.5	7.5	8.2	7.7	7.8	7	8.8	6.7
20	13.1	9.9	5.3	9.1	11.9	14.8	14.4	6.4	9.1	8.7	12.5	12.6	7.6	8.1	8.9

DPC = Day post-challenge. Values reported as k/µL.

Leptospira ictero White Blood Cell Count Post Challenge															
Controls															
Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
21	7.4	6.6	9.6	6.7	8.2	6.2	8.6	6.7	6.5	8.1	10.4	6.4	8.5	6.5	6.2
22	7.4	8.5	9.3	8.2	6.5	7.3	13.4	9.4	7.2	8.2	13.4	10.1	7.7	7.6	9.4
23	9.3	12.2	9.4	11.6	7.1	9	10	7	6.5	7.1	11.9	7	9.6	11	11.8
24	13.7	19.6	10.6	7.8	11.8	15.3	16.7	19.8	16	13.7	19.2	24.9	13.3	24.4	12.3
25	10	13.9	8.5	6.9	9.1	7	10.9	12.8	9.6	10	13.9	9.4	8.3	9	7.1
26	8.4	8.6	9	3.9	11.8	12.2	15.4	11.3	11.8	9	10.2	13.3	8.6	8.9	10.5
27	7.8	7.5	9.4	15.8	14.6	10.7	9.8	7.5	8.6	12.1	8.6	8.3	11.4	7.4	9.5
28	7.8	8.8	6.7	4.5	7.3	7.3	8.8	14.7	10	11.6	11.7	14	8.3	7.8	7.7
29	7.8	6.7	5.8	4.1	26.4	D									
30	8.8	7.6	5	7.2	7.8	7.5	7.8	6.2	9.9	8	10.3	10.1	9.9	9.4	9.6
31	11	8.1	8.3	4.2	19	D									
32	8.3	9.3	6.2	5	10.7	12.6	10.6	13.5	14.5	9.6	14.1	9.9	10	10.1	9.3
D = dead															

DPC = Day post-challenge. Values reported as k/µL.

Leptospira ictero Platelet Counts Post Challenge

SC Vaccinates															
Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
11	449.7	432	619	476	440	667	457	447	488	442	591	586	536	471	359
12	518.3	475	456	447	428	526	645	435	480	505	487	453	473	461	517
13	489.3	595	425	560	424	580	445	517	416	508	522	415	347	337	349
14	451.7	258	413	349	457	374	344	335	376	331	431	330	263	351	281
15	357.7	380	297	286	275	282	435	400	314	285	388	288	401	290	369
16	369	264	298	217	264	278	308	268	281	253	316	258	286	284	294
17	473.7	407	400	386	332	214	542	457	513	436	529	417	498	373	381
18	506	482	569	392	397	351	393	419	327	424	406	388	283	391	287
19	477	467	386	552	529	417	459	500	378	489	356	383	331	406	352
20	502.3	412	506	483	525	515	555	352	392	358	488	501	325	340	378

DPC = Day post-challenge. Values reported as k/µL.

Leptospira ictero Platelet Counts Post Challenge

Controls

Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
21	534.3	291	315	207	301	341	545	506	529	537	575	434	399	414	410
22	428.7	238	250	168	126	184	261	288	340	412	520	421	369	386	367
23	411.3	374	307	265	289	362	393	361	369	447	546	444	422	583	535
24	344.7	251	130	99.5	116	189	312	497	440	480	618	635	461	658	451
25	566	401	220	146	189	288	483	611	458	466	660	519	427	432	409
26	392	302	213	94.9	84.5	210	361	381	421	444	467	578	513	452	388
27	475.7	399	423	483	413	335	386	437	465	575	469	461	540	372	474
28	411.7	214	93.5	60.5	128	213	307	332	467	612	622	618	495	467	383
29	332	136	101	6.7	11.2	D									
30	421.9	204	80.9	53.9	119	231	379	512	549	516	642	494	411	421	427
31	319.3	163	94.4	36.7	11.9	D									
32	267	184	55	7.7	88.8	196	257	347	525	430	529	360	337	287	301

D = Dead

DPC = Day post-challenge. Values reported as k/µL.

Study Type	Efficacy
Pertaining to	Leptospira pomona
Study Purpose	To demonstrate effectiveness against *Leptospira pomona* in 6 week old dogs.
Product Administration	Two doses were administered subcutaneously (SC) 3 weeks apart.
Study Animals	Twenty (20) 6 week old puppies serologically negative for *Leptospira* were randomized into one group of 10 SC vaccinates and one group of 10 controls.
Challenge Description	Twenty-five (25) days after second vaccination all animals were challenged with *Leptospira pomona* organisms.
Interval observed after challenge	Dogs were observed daily for 21 days after challenge. Blood samples were collected through 14 days after challenge.
Results	Efficacy was based on the reduction in spirochetemia in vaccinates when compared to controls. A Data table is appended to the end of this summary.
USDA Approval Date	January 12, 1999

Isolation of Leptospira from Blood Collected from Dogs Post Challenge

Control Animals														
Dog	0DPC	1DPC	2DPC	3DPC	4DPC	5DPC	6DPC	7DPC	8DPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
1			+	+	+	+									
2															
3			+	+	+										
4				+	+										
5			+	+	+	+									
6			+	+											
7		+	+	+											
8			+	+	+										
9		+	+	+	+										
10		+		+	+										

DPC= Day post challenge

*Leptospira was not isolated from blood in any of the SC vaccinates

Study Type	Safety
Pertaining to	All
Study Purpose	Demonstrate safety of product under typical use conditions
Product Administration	Either one or two doses of vaccine 2-4 weeks apart by the subcutaneous route. A total of 1231 doses were administered.
Study Animals	A total of 621 dogs, 358 under 6 weeks of age and 263 greater than 6 weeks of age, privately owned and from commercial kennels were enrolled in the study.
Challenge Description	NA
Interval observed after challenge	No challenge. Observed for 30 minutes after vaccination and then daily for 2 weeks after each vaccination.
Results	Frequency of events is appended to the end of this summary.
USDA Approval Date	November 15, 2002

Summary of Reactions:

	Puppies up to 6 weeks of age				Dogs > 6 Weeks of Age					
Reaction Type	**<24hr**	**>24hrs**	**Total Reactions by dose**	**%**	**<24hr**	**>24hrs**	**Total Reactions by dose**	**%**	**Sum of Doses**	**Reaction Rate**
None	NA	NA	696	97.21%	NA	NA	506	98.25%	1202	97.64%
Salivation	0	0	0	0.00%	1	0	1	0.19%	1	0.08%
Lethargy	3	6	9	1.26%	0	0	0	0.00%	9	0.73%
Anorexia	3	10	13	1.82%	0	0	0	0.00%	13	1.06%
Injection Site Swelling	0	4	4	0.56%	0	1	1	0.19%	5	0.41%
Injection Site Pain	3	0	3	0.42%	5	0	5	0.97%	8	0.65%
Facial Swelling	0	0	0	0.00%	1	0	1	0.19%	1	0.08%
Vomiting or Diarrhea	3	0	3	0.42%	1	0	1	0.19%	4	0.32%
Mortality*	0	0	0	0.00%	2	0	2	0.39%	2	0.16%
Total Doses			**716**				**515**		**1231**	

*Confirmed by cooperator to be due to causes other than vaccination

Some dogs had more than one adverse event, so total events do not agree with doses administered.