

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.

196 47E5.21 Page 1 of 33

Study Type	Efficacy					
Pertaining to	Borrelia burgdorferi					
Study Purpose	To demonstrate effectiveness against <i>Borrelia burgdorferi</i> in dogs.					
Product	Two doses were administered subcutaneously (SC) 3 weeks apart.					
Administration						
Study Animals	Study I: Eighteen (18) 8-14 week old puppies serologically negative for <i>B. burgdorferi</i> 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 <i>B. burgdorferi</i> were used in the final study analysis. Animals were					
	randomized into one group of 20 SC vaccinates and one group of 10 controls.					
Challenge	Study I: Four weeks after second vaccination all animals were					
Description	challenged with Borrelia burgdorferi.					
	Study II: Three weeks after second vaccination all animals were challenged with <i>Borrelia burgdorferi</i> .					
Interval observed	Study I: Dogs were observed daily for 90 days after challenge for					
after challenge	clinical signs associated with B. burgdorferi.					
	Study II: Dogs were observed daily for 126 days after challenge for clinical signs associated with <i>B. burgdorferi</i> .					
Results	Dogs were evaluated for clinical arthritis, and the detection of <i>B. burgdorferi</i> 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 <i>B. burgdorferi</i> isolation and/or detection. Data tables are appended to the end of this summary.					
USDA Approval Date	December 6, 1995					

196 47E5.21 Page 2 of 33

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

196 47E5.21 Page 3 of 33

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.

Blank - Negative for Borrelia Detection

196 47E5.21 Page 4 of 33

[&]quot;+" - Positive 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

Blank - Negative for Borrelia Detection

196 47E5.21 Page 5 of 33

[&]quot;+" - Positive 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

 $\label{lem:number-represents} \mbox{Number-represents the day post challenge the clinical sign was observed}$

Blank - No signs observed

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

196 47E5.21 Page 6 of 33

Study II: Detection of B Burgdorferi (Blood)

		Study II:							_		
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.

Blank - Negative for Borrelia Detection

196 47E5.21 Page 7 of 33

[&]quot;+" - Positive 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

196 47E5.21 Page 8 of 33

Study Type	Efficacy
Pertaining to	Borrelia burgdorferi
Study Purpose	To demonstrate effectiveness against <i>Borrelia burgdoferi</i> 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 <i>B</i> .
	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 <i>B</i> .
	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	Dogs were observed for 5 months after challenge.
challenge	
Results	Dogs were evaluated for <i>B. burgdorferi</i> disease. Clinical disease
	was evaluated by clinical arthritis, the isolation of <i>B. burgdorferi</i>
	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 <i>B. burgdorferi</i> disease
	2/12 (17%) - SC Vaccinates positive for <i>B. burgdorferi</i> 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 <i>B. burgdorferi</i> disease
	1/5 (20%) - SC Vaccinates positive for <i>B. burgdorferi</i> 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

196 47E5.21 Page 9 of 33

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	+	+	+	-

[&]quot;+" - Positive for Borrelia Detection

DPC is day post challenge

196 47E5.21 Page 10 of 33

[&]quot; - " - Negative for Borrelia Detection

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	-	1	-	-	-	-
11	SC Vaccinate	-	-	-	-	-	-
12	SC Vaccinate	-	ı	-	ı	ı	-
13	Control	-	-	-	-	-	-
14	Control	-	-	+	+	+	+
15	Control	-	-	+	+	+	+
16	Control	-	-	-	-	+	+
17	Control	-	-	-	+	+	+
18	Control	-	-	+	+	+	+
19	Control	-	ı	+	+	+	+
20	Control	-	-	+	+	+	+
21	Control	-	-	-	-	-	-
22	Control	-	-	+	+	+	+
23	Control	-	-	+	+	+	+
24	Control	-	-	+	+	+	+

196 47E5.21 Page 11 of 33

[&]quot;+" - 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	ı	-	1	1	-
8	Control	+	-	+	+	-
9	Control	+	-	+	+	+
10	Control	+	+	-	+	-
11	Control	-	-	+	-	-
12	Control	+	-	+	-	-
13	Control	+	+	-	+	-
14	Control	+	-	+	+	+
15	Control	-	-	+	+	-
16	Control	+	-	+	-	-

[&]quot;+" - Positive for Borrelia Detection

DPC is day post challenge

196 47E5.21 Page 12 of 33

[&]quot; - " - Negative for Borrelia Detection

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	-	-	-	ı	•	-
6	Control	-	-	+	+	+	+
7	Control	ı	ı	-	ı	ı	-
8	Control	ı	-	+	+	+	+
9	Control	=	=	-	+	+	+
10	Control	-	+	+	+	+	+
11	Control	ı	ı	+	+	+	+
12	Control	=	-	+	+	+	+
13	Control	-	=	+	+	+	+
14	Control	=	=	+	+	+	+
15	Control	=	=	-	+	+	+
16	Control	=	-	-	+	+	+

[&]quot;+" - Antibody positive for presence of B. burgdorferi infection

DPC is day post challenge

196 47E5.21 Page 13 of 33

[&]quot; - " -Antibody negative for presence of B. burgdorferi infection

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

196 47E5.21 Page 14 of 33

Study Type	Efficacy
Pertaining to	Leptospira canicola
Study Purpose	To demonstrate effectiveness against <i>Leptospira canicola</i> 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 <i>Leptospira canicola</i> organisms.
Interval observed after	Dogs were observed daily for 21 days after challenge for clinical
challenge	signs associated with <i>L. canicola</i> . 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 1
	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.
	of the basefine value.
	A dog was considered to have leukopenia if the platelet count
	dropped below 6 $k/\mu L$ and the count was less than 50% of the
	baseline value.
	buserine value.
	Data tables are appended to the end of this summary.
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USDA Approval Date	April 3, 1998

196 47E5.21 Page 15 of 33

		21DPC																		
		20DPC		9	8															
		10DPC 11DPC 12DPC 13DPC 14DPC 15DPC 16DPC 17DPC 18DPC 19DPC 21DPC			8									e e						
		18DPC				9								DPC = Day post-challenge						
		17DPC							AG					ost-ch						
		C 16DP(ŋ							Ξ	Dav p						
		C 15DP			A	AG			A					C = 1						
		C 14DP							A						Ш					
		C 13DF																		
a		PC 12D																		
allen		PC 11D																		
ost Ch						A														
erved F		9DPC									9								bserved	
Leptospira canicola Clinical Signs Observed Post Challenge	SC Vaccinates	8DPC												3.0-103.9°F)	4.0-104.9°F)	(3.0-105.9°F)			nical signs o	
ola Clinica	SC	7DPC									9			N1 - Fever (103.0-103.9°F)	N2 - Fever (104.0-104.9°F)	N3 - Fever (105.0-105.9°F)	N4 - <99.6°F	P - Death	Blank - no clinical signs observed	
ospira canic		6DPC				9						А								
Lepto		5DPC									9	9		G - Ocular Discharge Mucoid	H - Nasal Discharge Serous	I - Nasal Discharge Mucoid	J - Diarrhea Mild (loose stool)	K - Diarrhea Severe (bloody stool)	ē	
		4DPC						5	٧		5			G - Ocular Dis	H - Nasal Disc	I - Nasal Disch	J - Diarrhea M	K - Diarrhea S	L - Bloody Urine	M - Icterus
		3DPC						6				G								
		2DPC					9				9	AD				Bu	thargy	Mild/Mo	Severe	e Serous
		1DPC		А	A	0	0					A		tance	50	1 Breath	ssion/Le	nctivitis	nctivitis	Discharg
		ODPC				9			9		9	G		A-inappetance	B-Vomiting	C-Labored Breathing	D - Depression/Lethargy	E1 - Conjunctivitis Mild/Moderate	E2 - Conjunctivitis Severe	F- Ocular Discharge Serous
		Dog	12	13	14	15	16	17	18	19	20	21	22					_	_	

196 47E5.21 Page 16 of 33

Leptospira canicola Clinical Signs Observed Post Challenge	Controls	6PPC 7DPC 8DPC 10DPC 11DPC 11DPC 13DPC 14DPC 15DPC 15DPC 15DPC 15DPC 15DPC 18DPC 19DPC 20DPC 21DPC	d	A,D,K C,D,G,L,N4 P	A,K A,G A D A,D,N1 D G G	A,D,J A,G,K A,D,K A,D G D,G B B B	A,K A,D,G A	,E2,M,N4	1,K,L,M,N4	9 9 9 9 9 X5YO	р	j,X,L,M,N4	D,G,K,L A,D,G,K,L A,D,G,K,L A,D,G,K,L A,K G G G G G,L G,L A,C G,L	D,G,K,L A,D,K,L,N1 A,D,G,K,L A,K G,K G,K G,K	N1 - Fever (103.0-103.9 ⁴ F) DPC = Day post-challenge	N2 - Fever (104.0-104.9 ⁻ F)	N3 - Fever (105.0-105.9 ⁻ F)	N4 - <99.6³F	P - Death	Blank - no clinical signs observed	
tospira canico		OPC 6DPC		A,D,K	A,K	A,D,J	A,K	A,D,E2,M,N4	A,D,E1,K,L,M,N4	A,D,G,K		A,D,G,K,L,M,N4	A,D,G,K,L	A,D,G,K,L A	N	N2	N	N/		8	
Lept		SDPC		A,D,G		0	A,N1	A,D,G,K,L,M,N4	D,G,K,L,N4	G,K	D,G,K,L,N4	D'K,L	A,B,J	9	G - Ocular Discharge Mucoid	harge Serous	narge Mucoid	J - Diarrhea Mild (loose stool)	evere (bloody stool)	ē	
		3dQ4	A,D,K,M,N4	L,D,G,J	9	5	٧	A,G,L	A,B,D,G,L		1'X'0'8	1′9	A,G		G - Ocular Dis	H - Nasal Discharge Serous	I - Nasal Discharge Mucoid	J - Diarrhea M	K - Diarrhea Severe (bl	L - Bloody Urine	M - Icterus
		3DPC			8	D,G,N1	А	A	J,K		g'K	9	A,G,N1	A,G,N2					oderate		S
		2DPC		D,G,N3	N2	D,G,N1	N1	GN2	D,N2	N2	N2	N1	G,N2	A,N1			hing	D - Depression/Lethargy	E1 - Conjunctivitis Mild/Moderate	E2 - Conjunctivitis Severe	F- Ocular Discharge Serous
		1DPC				A,G		A		9			9		A-inappetance	ting	C-Labored Breathing	ression/	junctivit	junctivit	ar Dische
		0DPC									Ŧ		9		A-inapp	B-Vomiting	C-Labor	D - Dep	E1 - Con	E2 - Con	F- Oculi
		Dog	23	24	25	26	27	28	29	30	31	32	33	34							

196 47E5.21 Page 17 of 33

14DPC 16.6 10.5 12.3 17.6 11.5 13.4 21.7 15.7 9.4 12.7 9.1 13DPC 19.6 23.2 10.2 10.8 17.2 12.3 9.9 9.7 14.7 9.7 11 12DPC 17.2 11.7 13.2 10.2 10.3 10.1 9.3 14 9.2 7.3 9.2 11DPC 11.6 15.3 16.5 10.2 10.7 12.7 13.1 9.3 9.5 8.8 13 10DPC 19.3 11.3 11.7 16.9 8.8 8.5 89 7.7 9.1 Leptospira canicola White Blood Cell Count Post Challenge 10.4 14.9 9DPC 19.4 19.3 11.4 11.7 8.5 7.3 9.3 8.2 9.7 11.8 11.8 10.5 8DPC 16.5 19.2 11.4 20.7 9.8 9.3 6.4 8.3 7DPC 12.5 20.7 12.5 17.4 13.1 9.4 9.7 7.5 9.2 13.4 7.3 13.6 12.2 10.2 13.2 13.9 60PC 11.7 2 7.2 00 6 11 SDPC 15.5 11.5 10.7 12.7 19.3 10.1 14.1 9.4 9.9 6 00 4DPC 14.6 20.3 10.5 12.2 10.2 7.6 9.5 8.2 8.4 8.4 14 3DPC 12.7 11.8 12.9 15.1 9.6 7.6 10.1 12.1 17 9.1 9.1 2DPC 12.3 12.8 10.6 10.7 15.1 9.6 9.3 9.5 9.5 9.4 00 1DPC 25.8 19.8 15.6 12.4 13.2 11.4 15.8 10.5 89 16.1 8.4 (Avg -2DPC, Baseline -1DPC, 0DPC) 22.1 12.3 21.7 13.3 14.3 8.9 11.2 10.2 14 # 11 Dog 12 13 14 15 16 17 18 19 2 22 21

DPC = Day post-challenge. Values reported as $k/\mu L$.

196 47E5.21 Page 18 of 33

		14DPC			21.9	13.9	13.3			12.2			16.9	20.2
		13DPC			29.4	12.7	11.5			16.7			17.4	15.9
		12DPC			26.2	11.5	15			12.69			26.3	15.7
		11DPC			36.7	9.6	13.9			9.2			31.5	10.9
		10DPC			36.6	16.6	11.3			11.4			20.5	15.3
Leptospira canicola White Blood Cell Count Post Challenge		9DPC			28.1	13.8	7.9			8.7			22.8	17.3
unt Post		8DPC			26	11.7	16.2			10.4			22.8	12.6
od Cell Co	sjo.	7DPC		20.5	17		21			11.1			13	12
White Blo	Controls	6DPC		14.6	13.6	8	19.4	13.2	17.5	10.6		15.8	8.7	9
canicola \		SDPC		15.6	12.6	6.7	8.6	19.4	5.3	7.9	10.3	9.9	4.4	3.8
eptospira		4DPC	21.7	11.5	10	5.7	5.2	7	5	6.1	9	9	5.3	5.6
Ľ		зорс	7.4	6.1	8.3	5.6	4.1	3.9	4.2	3.2	4	5.3	2.6	3.4
		2DPC	14.2	16.7	13	9.6	5.5	6.4	7.8	9.5	6.4	11.5	6.1	10.1
		1DPC	21.7	20	11.3	7.9	8.9	18.4	19.4	11.9	10.6	12.2	17.5	9.6
		Baseline (Avg -2DPC, -1DPC, 0DPC)	18.3	16.1	17.1	9	10.4	9.6	12.2	9.5	8.9	11.9	11.8	7
		Dog	23	24	25	26	27	28	29	30	31	32	33	34

DPC = Day post-challenge. Values reported as $k/\mu L$.

196 47E5.21 Page 19 of 33

		14DPC	470	467	640	461	390	278	572	524	469	583	593
		13DPC	511	510	802	463	399	257	554	516	464	474	495
		12DPC	483	550	508	438	428	232	406	418	462	429	497
		11DPC	381	616	568	260	302	261	480	414	601	521	200
		10DPC	512	501	267	482	519	270	405	381	493	501	492
llenge		9DPC	631	470	695	497	512	288	483	476	662	581	297
: Post Cha		8DPC	478	565	693	576	655	314	463	379	704	650	473
let Counts	inates	7DPC	582	636	604	633	558	351	247	375	706	514	469
ola Plate	SC Vaco	бррс	531	467	497	612	555	389	542	376	538	441	517
pira canio		5DPC	512	539	536	503	492	329	453	375	523	469	576
Leptos		4DPC	473	576	444	421	456	324	398	403	483	447	478
		3DPC	452	573	202	543	452	311	381	324	530	476	581
		2DPC	480	559	452	381	409	247	356	353	497	354	455
		1DPC	538	679	571	407	377	243	331	330	494	332	413
		Baseline (Avg -2DPC, -1DPC, 0DPC)	444.3	551.3	473.3	459.7	477.3	318	425.7	348.7	555.3	378.3	469.3
		Dog	12	13	14	15	16	17	18	19	20	21	22
Leptospira canicola Platelet Counts Post Challenge	SC Vaccinates	Baseline (Avg-2DPC, -1DPC, 0DPC) 3DPC 4DPC 5DPC 6DPC	444.3 538 480 452 473 512 531	551.3 679 559 573 576 539 467	473.3 571 452 505 444 536 497	459.7 407 381 543 421 503 612	477.3 377 409 452 456 492 555	318 243 247 311 324 329 389	425.7 331 356 381 398 453 542	348.7 330 353 324 403 375 376	555.3 494 497 530 483 523 538	378.3 332 354 476 447 469 441	

DPC = Day post-challenge. Values reported as $k/\mu L$.

196 47E5.21 Page 20 of 33

					Leptos	pira canic	Leptospira canicola Platelet Counts Post Challenge	et Counts	Post Cha	llenge					
							Controls	rols							
Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	зорс	4DPC	5DPC	ОРС	7DPC	8DPC	90РС	10DPC	11DPC	12DPC	13DPC	14DPC
23	300	238	148	11	7.7	O	O	O	O	O	O	O	Q	O	D
24	342	204	161	1.49	40.5	45.3	123	207	D	Q	D	Q	Q	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	O	Q	Q	O	Q	Q	O	D
29	529.7	521	305	195	37.6	15.8	42.2	D	D	Q	D	O	Q	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	O	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)ata														
D = dead															

DPC = Day post-challenge. Values reported as $k/\mu L$.

196 47E5.21 Page 21 of 33

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 <i>Leptospira grippotyphosa</i> organisms.
Interval observed after	Dogs were observed daily for 21 days after challenge
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

196 47E5.21 Page 22 of 33

Isolation of Leptospira from Blood Collected from Dogs Post Challenge

						Contro	l 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

196 47E5.21 Page 23 of 33

^{+ -} 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 <i>Leptospira</i>
	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 <i>Leptospira icterohaemorrhagiae</i> organisms.
Interval observed after	Dogs were observed daily for 21 days after challenge for clinical
challenge	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 leadronesis if the platelet count
	A dog was considered to have leukopenia if the platelet count dropped below 6 $k/\mu L$ and the count was less than 50% of the
	baseline value.
	baseline value.
	Data tables are appended to the end of this summary.
	Data tables are appended to the end of this summary.
USDA Approval Date	March 31, 1998

196 47E5.21 Page 24 of 33

		100PC 110PC 120PC 130PC 140PC 150PC 150PC 170PC 180PC 190PC 200PC 210PC			В		Е										
		19DPC 2				ш		A									
		18DPC			٥	٥				٥							
		C 17DP(ш												
		C 16DP										E					
		PC 15D															
		DPC 14D			ш							E					
		DPC 130			_		0										
98		1DPC 12										0					
hallen		.0DPC 1:															
Post C		9DPC 1															
erved		90														bserved	
Signs Obs	SC Vaccinates	8DPC				٦	3						rine	3.0°F		Blank - no clinical Sign observed	
ero Clinica	SC	7DPC											K - Bloody Urine	L - Fever >103.0°F	M - Death	Blank - no c	
Leptospira Ictero Clinical Signs Observed Post Challenge		6DPC	A			E					В	0				stool)	()0
a		SDPC			Q							0	large Serous	narge Mucoid	H- Diarrhea Mild (loose stool)	derate (Watery stool)	J - Diarrhea Severe (bloody stool)
		4DPC											F - Nasal Discharge Serous	G - Nasal Discharge Mucoid	H- Diarrhea Mi	I- Diarrhea Moderate (\	J - Diarrhea Se
		3DPC			ш	п						0					-
		2DPC										0			thargy	ge Serous	ge Mucoi
		1DPC					A,E						ance	500	sion/Le	Discharg	Dischar
		0DPC 1											A-inappetance	B-Vomiting	C - Depression/Lethargy	D- Ocular Discharge Serous	E - Ocular Discharge Mucoid
		Dog	11	12	13	14	15	16	17	18	19	20					

DPC = Day post-challenge

196 47E5.21 Page 25 of 33

	_			_		_	_			_	_	_	_	_					
		100PC 110PC 120PC 130PC 140PC 150PC 160PC 170PC 180PC 190PC 200PC 210PC																	
		20DPC																	
		19DPC		3	3														
		18DPC			E						O		0	8					
		17DPC			E														
		16DPC			E								E						
		15DPC							0										
		14DPC																	
		13DPC																	
		12DPC			E				E										
nge		11DPC								M		M	E						
Challe		10DPC																	
d Post		9DPC		8														P	
serve		6																observe	
Leptospira Ictero Clinical Signs Observed Post Challenge	Controls	8DPC							A						ā),E		Blank - no clinical Sign observed	
nical S	3	7DPC													K - Bloody Urine	L - Fever >103.0°F	eath	- no clin	
ero Cli		70													K - Blo	L · Fev	M - Death	Blank	
oira lot		9DPC	A										A	E					
eptos		9															_	(atery stool)	(100
_		SDPC							ш		0				erous	Aucoid	H- Diarrhea Mild (loose stool)	(Waten	J - Diarrhea Severe (bloody stool)
		15													harge S	charge	ool) piil	oderate	evere (b
		4DPC	F	F					0	A,C,D,J		A,E			F - Nasal Discharge Serous	G - Nasal Discharge Mucoid	arrhea N	I- Diarrhea Moderate (W	irrhea Se
										A,					F - Na	9-N	Η̈́	I- Dia	J-Dia
		3DPC			1	_			Q	X		L,D	E					2	. <u>e</u> .
		2DPC			1	1			1	L,E	1		l				thargy	ge Serou	ge Muco
		1DPC													auce	500	sion/Le	Dischar	Dischar
		0DPC 1													A-inappetance	B-Vomiting	C - Depression/Lethargy	D- Ocular Discharge Serous	E - Ocular Discharge Mucoid
															A-i	<u>~</u>	ن	⇔	ய்
		Dog	21	22	23	24	25	26	27	28	29	30	31	32					

DPC = Day post-challenge

196 47E5.21 Page 26 of 33

		14DPC	6.4	12.3	8.4	9.1	10.9	8.3	7.3	6.4	6.7	8.9
		13DPC	7.2	9.1	7.8	12.8	7.5	8.3	7.5	7.8	8.8	8.1
		12DPC	9.6	6	7.8	10	11.1	10	10.2	6.5	7	7.6
		11DPC	9.7	10.2	6.7	8.6	7.7	9.5	7.1	8.1	7.8	12.6
		10DPC	8.9	7.7	10.6	13.2	10.4	8.7	11.7	9	7.7	12.5
Challenge		9DPC	8.5	8.6	8.3	8	7.5	7.7	7.6	8	8.2	8.7
Leptospira ictero White Blood Cell Count Post Challenge		8DPC	6.4	11.1	9.6	11.8	8	10.1	11.4	7.4	7.5	9.1
od Cell Co	SC Vaccinates	7DPC	6.4	8.2	9.2	7.3	10.2	8.4	9.4	8.4	10.5	6.4
White Blo	SC Vac	6DPC	6.4	15.2	8.8	6.3	11.2	9.4	10.5	7.1	6.7	14.4
ra ictero \		5DPC	10.1	12.4	14.2	11.3	8.3	9.1	7.2	7.3	8.7	14.8
Leptospii		4DPC	6.8	9.1	9.1	12.6	8	8.1	7.5	9.9	11.7	11.9
		3DPC	7.9	8.9	13.2	8.2	6	6.8	8.1	9.1	11.7	9.1
		2DPC	12.4	10.4	9.6	12.6	8.6	9.5	7.8	10.5	8.4	5.3
		1DPC	7.3	13.9	15.4	9.7	11.4	8.8	7.1	7.7	13.8.	6.6
		Baseline (Avg -2DPC, -1DPC, 0DPC)	7.2	10	7.6	13.4	8.6	9.1	9.1	7.2	9.5	13.1
		Dog	11	12	13	14	15	16	17	18	19	20

DPC = Day post-challenge. Values reported as $k/\mu L$.

196 47E5.21 Page 27 of 33

					Leptospir	a ictero V	Vhite Bloc	od Cell Co	unt Post	Leptospira ictero White Blood Cell Count Post Challenge					
							Cont	Controls							
Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	SDPC	брРС	7DPC	8DPC	9DРС	10DPC	11DPC	12DPC	13DPC	14DPC
21	7.4	9.9	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	6.3	8.2	5'9	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	1.7	6	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	6	7.1
26	8.4	8.6	6	3.9	11.8	12.2	15.4	11.3	11.8	6	10.2	13.3	8.6	8.9	10.5
27	7.8	7.5	9.4	15.8	14.6	10.7	8.6	7.5	8.6	12.1	9.8	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	6.6	8	10.3	10.1	6.6	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 $k/\mu L$.

196 47E5.21 Page 28 of 33

												-
		14DPC	359	517	349	281	369	294	381	287	352	378
		13DPC	471	461	337	351	290	284	373	391	406	340
		12DPC	536	473	347	263	401	286	498	283	331	325
		11DPC	586	453	415	330	288	258	417	388	383	501
		10DPC	591	487	522	431	388	316	529	406	356	488
Leptospira ictero Platelet Counts Post Challenge		9DPC	442	205	208	331	285	253	436	424	489	358
Post C		8DPC	488	480	416	376	314	281	513	327	378	392
Counts	nates	7DPC	447	435	517	335	400	268	457	419	200	352
Platelet	SC Vaccinates	бррс	457	645	445	344	435	308	542	393	459	555
ictero		SDPC	299	526	580	374	282	278	214	351	417	515
ptospira		4DPC	440	428	424	457	275	264	332	397	529	525
Lep		зррс	476	447	260	349	286	217	386	392	552	483
		2DPC	619	456	425	413	297	298	400	269	386	206
		1DPC	432	475	595	258	380	264	407	482	467	412
		Baseline (Avg -2DPC, -1DPC, 0DPC)	449.7	518.3	489.3	451.7	357.7	369	473.7	506	477	502.3
		Dog	11	12	13	14	15	16	17	18	19	20

DPC = Day post-challenge. Values reported as $k/\mu L$.

196 47E5.21 Page 29 of 33

				<u>=</u>	ptospira ictero Platelet Counts Post Challenge	ictero	Platelet	t Counts	Post C	hallenge					
							Controls	slo.							
Dog	Baseline (Avg -2DPC, -1DPC, 0DPC)	1DPC	2DPC	3DPC	4DPC	SDPC	6DPC	7DPC	SDPC	9DPC	10DPC	11DPC	12DPC	13DPC	14DPC
21	534.3	291	315	207	301	341	545	206	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	935	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]	O				
30	421.9	204	80.9	53.9	119	231	379	512	549	516	642	464	411	421	427
31	319.3	163	94.4	36.7	11.9]	O				
32	267	184	55	7.7	88.8	196	257	347	525	430	529	360	337	287	301
D = Dead	pe														

DPC = Day post-challenge. Values reported as $k/\mu L$.

196 47E5.21 Page 30 of 33

Study Type	Efficacy
Pertaining to	Leptospira pomona
Study Purpose	To demonstrate effectiveness against <i>Leptospira pomona</i> 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 <i>Leptospira</i> 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 <i>Leptospira pomona</i> 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

196 47E5.21 Page 31 of 33

Isolation of Leptospira from Blood Collected from Dogs Post Challenge

					<u> </u>										
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

196 47E5.21 Page 32 of 33

^{*}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	No challenge. Observed for 30 minutes after vaccination and					
challenge	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 u	p to 6 weeks of ag	ge		Dogs >				
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.

196 47E5.21 Page 33 of 33