Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	2668.05
True Name	Leptospira Canicola-Grippotyphosa-Icterohaemorrhagiae-Pomona Bacterial Extract
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	LeptoVax 4 - Boehringer Ingelheim (Canada) Ltd. LeptoVax 4 - No distributor specified
Date of Compilation Summary	December 16, 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	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 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. See the next page for data.
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.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Leptospira grippotyphosa</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness against Leptospira grippotyphosa in 6-week-old dogs.</td></tr>
<tr><td>Product Administration</td><td>Two doses were administered subcutaneously (SC) 3 weeks apart.</td></tr>
<tr><td>Study Animals</td><td>Twenty (20) 6-week-old puppies were randomized into one group of 10 SC vaccinates and one group of 10 controls.</td></tr>
<tr><td>Challenge Description</td><td>Fifteen (15) days after second vaccination all animals were challenged with Leptospira grippotyphosa organisms.</td></tr>
<tr><td>Interval observed after challenge</td><td>Dogs were observed daily for 21 days after challenge</td></tr>
<tr><td>Results</td><td>Efficacy was based on the reduction in spirochetemia in vaccinates when compared to controls.

Leptospira was not isolated in any of the vaccinates receiving vaccine by SC route.

Leptospira was isolated from blood collected from dogs in the control group after challenge, as shown in the following table for Days 0 – 14 (post-challenge):
<table>
<tr><th>Dog</th><th>0</th><th>3</th><th>4</th><th>5</th><th>6</th><th>7</th><th>8</th><th>9</th><th>10</th><th>11</th><th>12</th><th>13</th><th>14</th></tr>
<tr><td>1</td><td></td><td></td><td></td><td></td><td></td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>2</td><td></td><td></td><td></td><td></td><td>+</td><td></td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>3</td><td></td><td></td><td></td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>4</td><td></td><td></td><td></td><td></td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>5</td><td></td><td></td><td></td><td>+</td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>6</td><td></td><td></td><td></td><td></td><td></td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>NA</td><td>NA</td><td>NA</td></tr>
<tr><td>7</td><td></td><td></td><td></td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td></tr>
<tr><td>8</td><td></td><td></td><td></td><td></td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>NA</td><td>NA</td><td>NA</td></tr>
<tr><td>9</td><td></td><td></td><td></td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>NA</td><td>NA</td><td>NA</td></tr>
<tr><td>10</td><td></td><td></td><td></td><td></td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>+</td><td>NA</td><td>NA</td><td>NA</td></tr>
</table>
NA is Animal Dead or euthanized / no sample taken
+ is Positive for Leptospira</td></tr>
<tr><td>USDA Approval Date</td><td>January 12, 1999</td></tr>
</table>

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. See the next page for data.
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.

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

Leptospira was not isolated from blood in any of the vaccinates receiving vaccine by SC route.

Leptospira was isolated from blood collected from dogs in the control group after challenge, as shown in the following table for Days 0 – 14 (post-challenge):
<table>
<tr><th>Dog</th><th>0</th><th>1</th><th>2</th><th>3</th><th>4</th><th>5</th><th>6</th><th>7</th><th>8</th><th>9</th><th>10</th><th>11</th><th>12</th><th>13</th><th>14</th></tr>
<tr><td>1</td><td></td><td></td><td>+</td><td>+</td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>2</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>3</td><td></td><td></td><td>+</td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>4</td><td></td><td></td><td></td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>5</td><td></td><td></td><td>+</td><td>+</td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>6</td><td></td><td></td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>7</td><td></td><td>+</td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>8</td><td></td><td></td><td>+</td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>9</td><td></td><td>+</td><td>+</td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>10</td><td></td><td>+</td><td></td><td>+</td><td>+</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
</table>
+ is Positive for Leptospira</td></tr>
<tr><td>USDA Approval Date</td><td>January 12, 1999</td></tr>
</table>

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>All fractions</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate safety of product under typical use conditions</td></tr>
<tr><td>Product Administration</td><td>Two doses were administered subcutaneously (SC) at 2-3 week intervals in dogs 6 weeks of age or older.</td></tr>
<tr><td>Study Animals</td><td>A total of 624 dogs, privately owned and from commercial kennels, were enrolled in the study. From these dogs, 341 were 6 weeks of age or younger, at first vaccination.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>No challenge. Dogs were observed for 30 minutes following each vaccination and daily for two weeks after each vaccination.</td></tr>
<tr><td>Results</td><td>Frequency of adverse events:
<table>
<tr><th colspan="7">Post Vaccination Reaction Occurrence by doses. Total Doses = 1223</th></tr>
<tr><th rowspan="2">Reaction Category</th><th colspan="2">≤ 6 Week old Dogs</th><th colspan="2">> 6 Weeks old Dogs</th><th colspan="2">Total Doses</th></tr>
<tr><th>#</th><th>Percent</th><th>#</th><th>Percent</th><th>#</th><th>Percent</th></tr>
<tr><td>No adverse events</td><td>673</td><td>99.26%</td><td>538</td><td>98.72%</td><td>1211</td><td>99.02%</td></tr>
<tr><td>lethargy</td><td>0</td><td>0.00%</td><td>1</td><td>0.18%</td><td>1</td><td>0.08%</td></tr>
<tr><td>Swelling</td><td>0</td><td>0.00%</td><td>3</td><td>0.55%</td><td>3</td><td>0.25%</td></tr>
<tr><td>Injection Site pain</td><td>5</td><td>0.74%</td><td>1</td><td>0.18%</td><td>6</td><td>0.49%</td></tr>
<tr><td>Pruritus</td><td>0</td><td>0.00%</td><td>2</td><td>0.37%</td><td>2</td><td>0.16%</td></tr>
<tr><td>Increased Thirst</td><td>0</td><td>0.00%</td><td>1</td><td>0.18%</td><td>1</td><td>0.08%</td></tr>
</table>
*25 dogs only received one vaccination. Either they did not return for follow-up or were removed for health reasons confirmed by the study cooperator to be unrelated to vaccination.</td></tr>
<tr><td>USDA Approval Date</td><td>November 2, 1998</td></tr>
</table>