Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	2668.00
True Name	Leptospira Canicola-Grippotyphosa-Icterohaemorrhagiae-Pomona Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	
Date of Compilation Summary	May 17, 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	Demonstrate efficacy against leptospirosis and leptospiruria due to *L. canicola*
Product Administration	Animals received two doses subcutaneously, 3 weeks apart.
Study Animals	Thirty-seven puppies, 47 to 88 days old Vaccinates: 19 Controls: 18
Challenge Description	Challenged 21 days after second vaccination against *Leptospira canicola*
Interval observed after challenge	Urine samples were collected 14 days prior to challenge and 13, 15, 17, 20, 22 and 34 days after challenge. Tissues were examined 35 days after challenge.
Results	**Leptospirosis:** An animal was considered to have leptospirosis *if L. canicola* was isolated from the urine on one or more occasions and if abnormal renal histopathologic changes were observed, or if *L. canicola* was isolated on multiple occasions from the urine. Animals with leptospirosis: Vaccinates: 0/19 Controls: 16/18 **Leptospiruria** was defined as shedding *Leptospira* organisms in the urine on multiple occasions after challenge Animals with leptospiruria: Vaccinates: 0/19 Controls: 14/18 See raw data on attached page.
USDA Approval Date	August 22, 2007

Table 1: Individual Leptospiruria

Group	Puppy ID	Days Post-Challenge (Study Day)						
		-14 (28)	13 (55)	15 (57)	17 (59)	20 (62)	22 (64)	34 (76)
Cont.	13001	-	+	-	+	+	-	-
Cont.	13104	-	+	+	-	-	-	+
Cont.	12607	-	+	+	-	+	-	-
Cont.	12910	-	+	-	-	+	-	-
Cont.	82204	-	+	+	-	+	-	-
Cont.	12903	-	-	+	-	+	+	-
Cont.	82106	-	+	+	+	+	+	+
Cont.	13106	-	-	+	+	+	-	-
Cont.	82201	-	-	+	-	+	-	+
Cont.	82704	-	-	-	-	-	+	-
Cont.	12606	-	+	+	+	+	+	+
Cont.	82105	-	+	+	+	+	-	-
Cont.	12907	-	+	-	-	-	-	-
Cont.	82206	-	-	-	-	-	-	-
Cont.	82302	-	+	+	-	-	+	-
Cont.	13003	-	+	-	+	+	+	+
Cont.	82703	-	-	-	-	-	-	-
Cont.	12905	-	-	+	-	+	-	+
Vacc.	**82203**	-	-	-	-	-	-	-
Vacc.	**12909**	-	-	-	-	-	-	-
Vacc.	**82702**	-	-	-	-	-	-	-
Vacc.	**12908**	-	-	-	-	-	-	-
Vacc.	**13103**	-	-	-	-	-	-	-
Vacc.	**82303**	-	-	-	-	-	-	-
Vacc.	**82601**	-	-	-	-	-	-	-
Vacc.	**12902**	-	-	-	-	-	-	-
Vacc.	**82701**	-	-	-	-	-	-	-
Vacc.	**82202**	-	-	-	-	-	-	-
Vacc.	**12906**	-	-	-	-	-	-	-
Vacc.	**12904**	-	-	-	-	-	-	-
Vacc.	**82107**	-	-	-	-	-	-	-
Vacc.	**13105**	-	-	-	-	-	-	-
Vacc.	**82205**	-	-	-	-	-	-	-
Vacc.	**13002**	-	-	-	-	-	-	-
Vacc.	**12602**	-	-	-	-	-	-	-
Vacc.	**82705**	-	-	-	-	-	-	-
Vacc.	**12604**	-	-	-	-	-	-	-

+ indicates *Leptospira* organisms were re-isolated from the urine
- indicates no *Leptospira* organisms were re-isolated from urine

Table 2: Individual Renal Histopathology Results

Histopathological findings	Score
No histopathological changes; normal	0
Presence of rare and discrete clusters of inflammatory cells (lymphocytes, plasma cells) within cortical interstitium; no tubular or glomerular abnormalities noted	1
Multiple clusters of inflammatory cells (lymphocytes, plasma cells) lymphocytes within cortical interstitium; clusters are large enough that they obliterate some tubules	2
More than one of the following criteria: ▪ Extensive mononuclear cells inflammatory infiltrates throughout cortex, may also include neutrophils ▪ Renal function is visibly impaired as evidenced by protein within tubules or tubular degeneration, or glomerular senescence ▪ Cortical fibrosis with pitting may be present	3

A score of ≥1 is considered abnormal.

Treatment group	ID	Kidney A	Kidney B
Cont.	12606	0	1
Cont.	12607	0	1
Cont.	12903	2	1
Cont.	12905	0	0
Cont.	12907	2	2
Cont.	12910	1	1
Cont.	13001	2	2
Cont.	13003	1	1
Cont.	13104	2	1
Cont.	13106	1	0
Cont.	82105	1	1
Cont.	82106	1	1
Cont.	82201	1	0
Cont.	82204	2	1
Cont.	82206	0	0
Cont.	82302	1	0
Cont.	82703	1	0
Cont.	82704	0	1

Treatment group	ID	Kidney A	Kidney B
Vacc.	12602	0	0
Vacc.	12604	0	0
Vacc.	12902	0	0
Vacc.	12904	0	0
Vacc.	12906	0	0
Vacc.	12908	0	0
Vacc.	12909	0	0
Vacc.	13002	0	0
Vacc.	13103	0	0
Vacc.	13105	0	0
Vacc.	82107	0	0
Vacc.	82202	0	0
Vacc.	82203	0	0
Vacc.	82205	0	0
Vacc.	82303	0	0
Vacc.	82601	0	0
Vacc.	82701	0	0
Vacc.	82702	0	0
Vacc.	82705	0	0

Study Type	Efficacy
Pertaining to	*Leptospira grippotyphosa*
Study Purpose	Demonstrate efficacy against leptospirosis and leptospiruria due to *L. grippotyphosa*
Product Administration	Animals received two doses subcutaneously, 3 weeks apart.
Study Animals	Thirty-seven puppies, 60 to 70 days old Vaccinates: 18 Controls: 19
Challenge Description	Challenged 17 days after second vaccination against *Leptospira grippotyphosa*
Interval observed after challenge	Urine samples were collected 10 days prior to challenge and 14, 16, 18, 20, 27 and 31 days after challenge. Tissue samples were examined 31 days after challenge.
Results	**Leptospirosis:** An animal was considered to have leptospirosis *if L. grippotyphosa* was isolated from the urine on one or more occasions and if abnormal renal histopathologic changes were observed, or if *L. grippotypho*sa was isolated on multiple occasions from the urine. Animals with leptospirosis: Vaccinates: 0/18 Controls: 16/19 **Leptospiruria** was defined as shedding *L. grippotyphosa* organisms in the urine on multiple occasions after challenge Animals with leptospiruria: Vaccinates: 0/18 Controls: 16/19 See raw data on attached page.
USDA Approval Date	July 17, 2007

Table 1: Individual Leptospiruria

Group	Puppy ID	Days Post-Challenge (Study Day)						
		-10 (28)	14 (52)	16 (54)	18 (56)	20 (58)	27 (65)	31 (69)
Cont.	85001	-	+	-	-	+	+	-
Cont.	15001	-	-	-	-	-	-	-
Cont.	15205	-	+	-	+	+	+	-
Cont.	85204	-	-	+	+	-	-	-
Cont.	15102	-	-	-	-	-	-	-
Cont.	14903	-	+	+	+	+	-	-
Cont.	85202	-	+	+	+	+	+	-
Cont.	85203	-	+	+	+	+	-	-
Cont.	14902	-	-	+	+	-	+	-
Cont.	85304	-	-	-	-	-	+	-
Cont.	85005	-	+	+	+	+	+	-
Cont.	15206	-	+	+	+	-	+	-
Cont.	85103	-	+	-	+	+	+	-
Cont.	85003	-	+	-	+	+	+	-
Cont.	15103	-	-	-	+	-	+	-
Cont.	85303	-	+	+	+	+	+	-
Cont.	85104	-	+	+	+	+	+	-
Cont.	85306	-	+	-	+	+	+	-
Cont.	15203	-	+	+	+	+	+	-
Vacc.	**85006**	-	-	-	-	-	-	-
Vacc.	**15201**	-	-	-	-	-	-	-
Vacc.	**85201**	-	-	-	-	-	-	-
Vacc.	**85205**	-	-	-	-	-	-	-
Vacc.	**85106**	-	-	-	-	-	-	-
Vacc.	**85102**	-	-	-	-	-	-	-
Vacc.	**15202**	-	-	-	-	-	-	-
Vacc.	**85002**	-	-	-	-	-	-	-
Vacc.	**85302**	-	-	-	-	-	-	-
Vacc.	**85004**	-	-	-	-	-	-	-
Vacc.	**85305**	-	-	-	-	-	-	-
Vacc.	**15204**	-	-	-	-	-	-	-
Vacc.	**85105**	-	-	-	-	-	-	-
Vacc.	**15207**	-	-	-	-	-	-	-
Vacc.	**15002**	-	-	-	-	-	-	-
Vacc.	**15101**	-	-	-	-	-	-	-
Vacc.	**15104**	-	-	-	-	-	-	-
Vacc.	**14901**	-	-	-	-	-	-	-

+ indicates *Leptospira* organisms were re-isolated from the urine
- indicates no *Leptospira* organisms were re-isolated from urine

Table 2: Individual Renal Histopathology Results

Histopathological findings	**Score**
No histopathological changes; normal	0
Presence of rare and discrete clusters of inflammatory cells (lymphocytes, plasma cells) within cortical interstitium; no tubular or glomerular abnormalities noted	1
Multiple clusters of inflammatory cells (lymphocytes, plasma cells) lymphocytes within cortical interstitium; clusters are large enough that they obliterate some tubules	2
More than one of the following criteria: ▪ Extensive mononuclear cells inflammatory infiltrates throughout cortex, may also include neutrophils ▪ Renal function is visibly impaired as evidenced by protein within tubules or tubular degeneration, or glomerular senescence ▪ Cortical fibrosis with pitting may be present	3

A score of $\geq$1 is considered abnormal.

Treatment group	ID	Kidney A	Kidney B
Cont.	14902	0	1
Cont.	14903	2	1
Cont.	15001	0	0
Cont.	15102	0	0
Cont.	15103	0	0
Cont.	15203	1	2
Cont.	15205	2	1
Cont.	15206	2	2
Cont.	85001	2	2
Cont.	85003	2	2
Cont.	85005	1	0
Cont.	85103	2	2
Cont.	85104	1	1
Cont.	85202	1	1
Cont.	85203	2	1
Cont.	85204	1	2
Cont.	85303	2	1
Cont.	85304	0	0
Cont.	85306	1	2

Treatment group	ID	Kidney A	Kidney B
Vacc.	**14901**	**0**	**0**
Vacc.	**15002**	**0**	**0**
Vacc.	**15101**	**0**	**0**
Vacc.	**15104**	**0**	**0**
Vacc.	**15201**	**0**	**0**
Vacc.	**15202**	**0**	**0**
Vacc.	**15204**	**0**	**0**
Vacc.	**15207**	**0**	**0**
Vacc.	**85002**	**0**	**1**
Vacc.	**85004**	**0**	**0**
Vacc.	**85006**	**0**	**0**
Vacc.	**85102**	**0**	**0**
Vacc.	**85105**	**0**	**0**
Vacc.	**85106**	**0**	**0**
Vacc.	**85201**	**0**	**0**
Vacc.	**85205**	**0**	**0**
Vacc.	**85302**	**0**	**0**
Vacc.	**85305**	**0**	**0**

Study Type	Efficacy
Pertaining to	*Leptospira grippotyphosa*
Study Purpose	Demonstrate efficacy against leptospirosis and leptospiruria due to *L. grippotyphosa* 15 months after vaccination to establish a minimum duration of immunity
Product Administration	Animals received two doses subcutaneously, 3 weeks apart.
Study Animals	Forty-one puppies, 47 to 73 days old Vaccinates: 20 Controls: 21
Challenge Description	Challenged 15 months after second vaccination against *Leptospira grippotyphosa*
Interval observed after challenge	Urine samples were collected prior to challenge and 15, 18, 20, 22, 25, 29 and 33 days after challenge. Tissues were examined 34 days after challenge.
Results	**Leptospirosis:** An animal was considered to have leptospirosis *if L. grippotyphosa* was isolated from the urine on one or more occasions and if abnormal renal histopathologic changes were observed, or if *L. grippotypho*sa was isolated on multiple occasions from the urine. Animals with leptospirosis: Vaccinates: 0/20 Controls: 16/21 **Leptospiruria** was defined as shedding *Leptospira* organisms in the urine on any day sampled after challenge. Animals with leptospiruria: Vaccinates: 1/20 Controls: 16/21 See raw data on attached page.
USDA Approval Date	June 16, 2008

Table 1: Individual Leptospiruria and Renal Histopathology Score

Group	Dog ID	Leptospiruria - Days Post-challenge (Study Day)								Individual Renal Histopathology Score[b]
		-1 (490)	15 (506)	18 (509)	20 (511)	22 (513)	25 (516)	29 (520)	33 (524)	
Cont.	17901	-	-	-	-	-	-	-	-	0
Cont.	18103	-	-	-	-	+	-	-	-	2
Cont.	87403	-	-	-	-	-	-	-	-	0
Cont.	87504	-	+	-	+	+	+	+	-	2
Cont.	18403	-	+	-	-	+	-	+	-	2
Cont.	87405	-	+	-	+	+	+	+	-	1
Cont.	87503	-	-	-	-	-	-	-	-	0
Cont.	18303	-	+	+	+	+	-	+	+	2
Cont.	87603	-	-	-	-	-	+	+	-	0
Cont.	18204	-	-	-	+	-	+	-	+	2
Cont.	18504	-	-	-	-	-	+	+	-	3
Cont.	87702	-	+	-	+	+	+	+	+	3
Cont.	18101	-	+	+	+	+	+	+	+	3
Cont.	18401	-	-	-	+	+	+	-	-	3
Cont.	87606	-	+	+	-	+	+	-	+	3
Cont.	18201	-	-	-	-	-	-	-	-	0
Cont.	87501	-	-	-	-	-	-	-	-	0
Cont.	18505	-	-	-	+	+	+	+	-	0
Cont.	87604	-	+	+	+	-	+	+	-	1
Cont.	18302	-	-	+	-	-	+	+	+	0
Cont.	17904	-	-	-	+	-	-	-	+	3
Vacc.	**18102**[a]	-	-	-	-					0
Vacc.	**18104**	-	-	-	-	-	-	-	-	0
Vacc.	**87703**	-	-	-	-	-	-	-	-	0
Vacc.	**18501**	-	-	-	-	-	-	-	-	0
Vacc.	**87701**	-	-	-	-	-	-	-	-	0
Vacc.	**87506**	-	-	-	-	-	-	-	-	2
Vacc.	**18402**	-	-	-	-	-	-	+	-	0
Vacc.	**18503**	-	-	-	-	-	-	-	-	0
Vacc.	**18603**	-	-	-	-	-	-	-	-	0
Vacc.	**18404**	-	-	-	-	-	-	-	-	0
Vacc.	**18304**	-	-	-	-	-	-	-	-	0
Vacc.	**18604**	-	-	-	-	-	-	-	-	1
Vacc.	**87505**	-	-	-	-	-	-	-	-	0
Vacc.	**17902**	-	-	-	-	-	-	-	-	0
Vacc.	**87404**	-	-	-	-	-	-	-	-	0
Vacc.	**18202**	-	-	-	-	-	-	-	-	0
Vacc.	**18301**	-	-	-	-	-	-	-	-	0
Vacc.	**87605**	-	-	-	-	-	-	-	-	1
Vacc.	**87607**	-	-	-	-	-	-	-	-	0
Vacc.	**18203**	-	-	-	-	-	-	-	-	0

[a]Dog #18102 (vaccinate) was euthanized on Study Day 512 due to an acute painful abdomen with transudate fluid-filled peritoneal cavity thought to be due to uroperitoneum based on necropsy histopathology reports.
[b]From the 2 kidneys the highest histopathologic score was taken to classify the dog

Leptospiruria
+ indicates *Leptospira* organisms were re-isolated from the urine
- indicates that no *Leptospira* organisms were re-isolated from the urine

Renal histopathology score
Renal histopathology scoring chart found in Table 2.

Table 2: Renal Histopathology Scoring Chart

Histopathological findings	**Score**
No histopathological changes; normal	0
Presence of rare and discrete clusters of inflammatory cells (lymphocytes, plasma cells) within cortical interstitium; no tubular or glomerular abnormalities noted	1
Multiple clusters of inflammatory cells (lymphocytes, plasma cells) lymphocytes within cortical interstitium; clusters are large enough that they obliterate some tubules	2
More than one of the following criteria: ▪ Extensive mononuclear cells inflammatory infiltrates throughout cortex, may also include neutrophils ▪ Renal function is visibly impaired as evidenced by protein within tubules or tubular degeneration, or glomerular senescence ▪ Cortical fibrosis with pitting may be present	3

A score of $\geq$1 is considered abnormal.

Study Type	Efficacy
Pertaining to	*Leptospira icterohaemorrhagiae*
Study Purpose	Demonstrate efficacy against leptospirosis and leptospiruria due to *L. icterohaemorrhagiae*
Product Administration	Animals received two doses subcutaneously, 3 weeks apart.
Study Animals	Thirty-six puppies, 9-12 weeks of age Vaccinates: 18 Controls: 18
Challenge Description	Challenged 7 weeks after second vaccination against *Leptospira icterohaemorrhagiae*
Interval observed after challenge	Urine samples were collected 7 days prior to challenge and 12, 14, 16, 20, 24 and 36 days after challenge. Tissues were examined 36 days after challenge.
Results	**Leptospirosis:** An animal was considered to have leptospirosis *if L. icterohaemorrhagiae* was isolated from the urine on one or more occasions and if abnormal renal histopathologic changes were observed, or if *L. icterohaemorrhagiae* was isolated on multiple occasions from the urine, or if an animal was euthanized for clinical signs of leptospirosis. Animals with leptospirosis: Vaccinates: 0/18 Controls: 17/18 **Leptospiruria** was defined as shedding *Leptospira* organisms in the urine on any day sampled after challenge Animals with leptospiruria: Vaccinates: 0/18 Controls: 16/18 See raw data on attached page.
USDA Approval Date	May 1, 2007

Table 1: Individual Leptospiruria

Group	Puppy ID	Days Post-Challenge (Study Day)						
		- 7 (63)	12 (82)	14 (84)	16 (86)	20 (90)	24 (94)	36 (106)
Cont.	418503	-	+	+	+	-	+	-
Cont.	580105	-	+	+	+	+	+	-
Cont.	580201	-	+	+	+	+	+	-
Cont.	510107	-	+	+	+	+	+	-
Cont.	487205	-	+	+	+	+	+	-
Cont.	418505	-	+	+	+	-	+	-
Cont.	418506	-	+	+	+	+	+	-
Cont.	487001	-	-	+	+	+	+	-
Cont.	*487003*	-	+*	E	E	E	E	E
Cont.	580102	-	+	+	+	+	+	-
Cont.	510101	-	+	+	+	+	-	-
Cont.	*510103*	-	+	+	+	+	E	E
Cont.	487201	-	+	+	+	+	+	-
Cont.	*418601*	-	-*	E	E	E	E	E
Cont.	418501	-	+	+	+	-	+	-
Cont.	487103	-	+	+	+	+	+	-
Cont.	418401	-	+	+	+	-	+	-
Cont.	418402	-	+	+	+	-	-	-
Vacc.	**510106**	-	-	-	-	-	-	-
Vacc.	**580106**	-	-	-	-	-	-	-
Vacc.	**418603**	-	-	-	-	-	-	-
Vacc.	**487204**	-	-	-	-	-	-	-
Vacc.	**418504**	-	-	-	-	-	-	-
Vacc.	**418606**	-	-	+	-	-	-	-
Vacc.	**487105**	-	-	+	-	-	-	-
Vacc.	**486907**	-	-	-	-	-	-	-
Vacc.	**487002**	-	-	-	-	-	-	-
Vacc.	**580101**	-	-	-	-	-	-	-
Vacc.	**580104**	-	-	-	-	-	-	-
Vacc.	**510102**	-	-	-	-	-	-	-
Vacc.	**487202**	-	-	-	-	-	-	-
Vacc.	**487203**	-	-	-	-	-	-	-
Vacc.	**418602**	-	-	-	-	-	-	-
Vacc.	**418502**	-	-	-	-	-	-	-
Vacc.	**487104**	-	-	-	-	-	-	-
Vacc.	**418403**	-	-	-	-	-	-	-

* Actual sample collected on Day 6 post-challenge prior to euthanasia.
E indicates no data as Control Dogs 418601 and 487003 were euthanized on Study Day 76 and control Dog 510103 was euthanized on Study Day 94 due to severe clinical signs (hyperthermia, icterus, dehydration and prostration).
+ indicates *Leptospira* organisms were re-isolated from the urine
- indicates no *Leptospira* organisms were re-isolated from urine

Table 2: Individual Renal Histopathology Results

Histopathological findings	**Score**
No histopathological changes; normal	0
Presence of rare and discrete clusters of inflammatory cells (lymphocytes, plasma cells) within cortical interstitium; no tubular or glomerular abnormalities noted	1
Multiple clusters of inflammatory cells (lymphocytes, plasma cells) lymphocytes within cortical interstitium; clusters are large enough that they obliterate some tubules	2
More than one of the following criteria: ▪ Extensive mononuclear cells inflammatory infiltrates throughout cortex, may also include neutrophils ▪ Renal function is visibly impaired as evidenced by protein within tubules or tubular degeneration, or glomerular senescence ▪ Cortical fibrosis with pitting may be present	3

A score of $\geq$1 is considered abnormal.

Treatment group	ID	Kidney Score
Cont.	418401	2
Cont.	418402	2
Cont.	418501	2
Cont.	418503	2
Cont.	418505	2
Cont.	418506	2
Cont.	418601	2
Cont.	487001	2
Cont.	487003	3
Cont.	487103	2
Cont.	487201	2
Cont.	487205	2
Cont.	510101	2
Cont.	510103	3
Cont.	510107	2
Cont.	580102	2
Cont.	580105	2
Cont.	580201	2

Treatment group	ID	Kidney Score
Vacc.	418403	0
Vacc.	418502	0
Vacc.	418504	0
Vacc.	418602	0
Vacc.	418603	0
Vacc.	418606	0
Vacc.	486907	0
Vacc.	487002	0
Vacc.	487104	0
Vacc.	487105	0
Vacc.	487202	0
Vacc.	487203	0
Vacc.	487204	0
Vacc.	510102	0
Vacc.	510106	0
Vacc.	580101	0
Vacc.	580104	0
Vacc.	580106	0

Study Type	Efficacy
Pertaining to	*Leptospira pomona*
Study Purpose	Demonstrate efficacy against leptospirosis and leptospiruria due to *L. pomona*
Product Administration	Animals received two doses subcutaneously, 3 weeks apart.
Study Animals	Thirty-seven puppies, 49 to 61 days old Vaccinates: 19 Controls: 18
Challenge Description	Challenged 14 days after second vaccination against *Leptospira pomona*
Interval observed after challenge	Urine samples were collected 7 days prior to challenge and 12, 14, 17, 19, 21, 35 and 47 days after challenge. Tissues were examined 47 days after challenge.
Results	**Leptospirosis:** An animal was considered to have leptospirosis *if* *L. pomona* was isolated from the urine on one or more occasions and if abnormal renal histopathologic changes were observed, or if *L. pomona* was isolated on multiple occasions from the urine. Animals with leptospirosis: Vaccinates: 1/19 Controls: 14/18 **Leptospiruria** was defined as shedding *Leptospira* organisms in the urine on any day sampled after challenge Animals with leptospiruria: Vaccinates: 1/19 Controls: 17/18 See raw data on attached page.
USDA Approval Date	August 23, 2007

Table 1: Individual Leptospiruria

Group	Puppy ID	Days Post-Challenge (Study Day)							
		-7 (28)	12 (47)	14 (49)	17 (52)	19 (54)	21 (56)	35 (70)	47 (82)
Cont.	87205	-	-	+	-	+	-	-	-
Cont.	17604	-	-	-	-	-	-	-	-
Cont.	17505	-	-	-	-	+	+	-	-
Cont.	17509	-	-	-	+	-	-	-	-
Cont.	17507	-	+	-	+	+	+	-	-
Cont.	17504	-	-	+	-	+	-	+	-
Cont.	87301	-	-	-	-	+	+	-	-
Cont.	17409	-	-	+	-	-	+	-	-
Cont.	87206	-	+	-	+	+	+	-	-
Cont.	87201	-	-	-	-	-	+	-	-
Cont.	87202*	-	-	-	+	-	-	-	
Cont.	17702	-	+	+	+	+	+	-	-
Cont.	17501	-	-	+	-	-	-	-	-
Cont.	17603	-	-	-	+	-	+	-	-
Cont.	17402	-	+	-	+	+	+	-	-
Cont.	17404	-	-	-	-	-	+	-	-
Cont.	17405	-	-	+	+	+	-	-	-
Cont.	87302	-	-	+	+	-	+	-	-
Vacc.	**87207**	-	-	-	-	-	-	-	-
Vacc.	**17401**	-	-	-	-	-	-	-	-
Vacc.	**17701**	-	-	-	-	-	-	-	-
Vacc.	**17508**	-	-	-	-	-	-	-	-
Vacc.	**17403**	-	-	-	-	-	-	-	-
Vacc.	**87303**	-	-	-	-	-	-	-	-
Vacc.	**17506**	-	-	-	-	-	+	-	-
Vacc.	**17602**	-	-	-	-	-	-	-	-
Vacc.	**17704**	-	-	-	-	-	-	-	-
Vacc.	**17408**	-	-	-	-	-	-	-	-
Vacc.	**17503**	-	-	-	-	-	-	-	-
Vacc.	**17605**	-	-	-	-	-	-	-	-
Vacc.	**17502**	-	-	-	-	-	-	-	-
Vacc.	**87203**	-	-	-	-	-	-	-	-
Vacc.	**17407**	-	-	-	-	-	-	-	-
Vacc.	**17406**	-	-	-	-	-	-	-	-
Vacc.	**17601**	-	-	-	-	-	-	-	-
Vacc.	**87204**	-	-	-	-	-	-	-	-
Vacc.	**17703**	-	-	-	-	-	-	-	-

*There is a missing urine sample on Day 82 as no urine was in the bladder at the time of collection immediately post euthanasia.

\+ indicates *Leptospira* organisms were re-isolated from the urine
\- indicates no *Leptospira* organisms were re-isolated from urine

Table 2: Individual Renal Histopathology Results

Histopathological findings	Score
No histopathological changes; normal	0
Presence of rare and discrete clusters of inflammatory cells (lymphocytes, plasma cells) within cortical interstitium; no tubular or glomerular abnormalities noted	1
Multiple clusters of inflammatory cells (lymphocytes, plasma cells) lymphocytes within cortical interstitium; clusters are large enough that they obliterate some tubules	2
More than one of the following criteria: ▪ Extensive mononuclear cells inflammatory infiltrates throughout cortex, may also include neutrophils ▪ Renal function is visibly impaired as evidenced by protein within tubules or tubular degeneration, or glomerular senescence ▪ Cortical fibrosis with pitting may be present	3

A score of ≥1 is considered abnormal.

Treatment group	ID	Kidney A	Kidney B
Cont.	17402	0	0
Cont.	17404	0	0
Cont.	17405	1	0
Cont.	17409	0	0
Cont.	17501	0	0
Cont.	17504	2	1
Cont.	17505	1	0
Cont.	17507	0	0
Cont.	17509	0	0
Cont.	17603	3	3
Cont.	17604	3	3
Cont.	17702	0	1
Cont.	87201	0	1
Cont.	87202	1	0
Cont.	87205	0	0
Cont.	87206	0	0
Cont.	87301	2	2
Cont.	87302	0	0

Treatment group	ID	Kidney A	Kidney B
Vacc.	17401	0	0
Vacc.	17403	0	0
Vacc.	17406	0	0
Vacc.	17407	0	0
Vacc.	17408	0	0
Vacc.	17502	0	0
Vacc.	17503	0	0
Vacc.	17506	0	1
Vacc.	17508	0	0
Vacc.	17601	1	3
Vacc.	17602	3	0
Vacc.	17605	3	3
Vacc.	17701	0	0
Vacc.	17703	0	0
Vacc.	17704	0	0
Vacc.	87203	0	0
Vacc.	87204	0	0
Vacc.	87207	0	0
Vacc.	87303	0	0

Study Type	Safety
Pertaining to	ALL
Study Purpose	Demonstrate safety under field conditions
Product Administration	Animals received two doses subcutaneously, 3-4 weeks apart.
Study Animals	A total of 925 dogs: ≤9 weeks of age: 326* >9 weeks of age: 599 *All 326 minimum age puppies were concomitantly vaccinated with a trivalent core vaccine at a separate injection site.
Challenge Description	Not applicable
Interval observed after challenge	Dogs were observed for 1 hour after vaccination. Owners observed the dogs daily for 14 days after vaccination. The veterinarian examined the dogs 5-9 days after each vaccination.
Results	Five owners did not present their dogs (n=9) for a second vaccination. Adverse events typically resolved within 1-3 days without treatment. Data on attached page.
USDA Approval Date	December 30, 2009

Table 1: Veterinarian-Reported Adverse Events

Clinical sign classification	Number of events in 1841 doses
Injection Site[a] Stinging	102
Injection Site Pain	1
Injection Site Edema	2
Injection Site Swelling (< 1.5cm)	4
Injection Site Swelling (1.5 - 5cm)	4
Vomiting	3
Diarrhea	2
Depression	1
Anemia	1
Lethargy	1
Generalized pruritus	1
Vulvar discharge[b]	1
Cystitis[b]	1

[a] Pain recorded on the day of vaccination (associated with the vaccination procedure) is reported as "injection site stinging". Pain recorded on subsequent days is reported as "injection site pain".
[b]Affirmed by licensee to have cause other than vaccination

Table 2: Owner-Reported Observations

Vaccination Dose	Number of reports	Number of Dogs with Injection Site Pain	Number of Dogs with Small Swelling (<1.5cm)	Number of Dogs with Moderate Swelling (1.5cm-5cm)	Number of Dogs with Severe Swelling (>5cm)
V1	917	85	74	35	5
V2	916	84	55	23	5
Total	1833	169 (9.2%)	129 (7.0%)	58 (3.2%)	10 (0.55%)

- The majority of swellings resolved within 1-2 days, all swellings resolved within 5-9 days. Injection site pain typically resolved within 3 days.
- Isolated and transient incidences of depression and inappetence were also reported.