

Summary of Studies Supporting USDA Product Licensure

Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	26M7.01
True Name	Leptospira Hardjo Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Spirovac - No distributor specified Spirovac - Zoetis Japan Inc. Spirovac - Zoetis Mexico Spirovac - Zoetis de Uruguay S.R.L.
Date of Compilation Summary	February 25, 2023

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 borgpetersenii serovar hardjo isolate (L. Hardjo)
Study Purpose	Demonstration of efficacy against <i>L. hardjo</i> in calves.
Product Administration	Two doses administered 28 days apart subcutaneously.
Study Animals	Calves between 8-9 months of age, 10 controls and 11 vaccinates
	with two doses (28-42 days apart). All animals were
	seronegative for Leptospira serovars hardjo, pomona, canicola,
	icterohaemorrhagiae, and grippotyphosa.
Challenge Description	Animals were challenged with L. hardjo 35 days after the second
	vaccination.
Interval observed after	Urine cultures collected weekly following 14 days after
challenge	challenge until the study finalized. Kidney tissues were
	examined 36 days following the challenge.
Results	Animals were considered positive for L. hardjo if at least one
	urine sample was positive for L. hardjo, left kidney culture result
	was positive for <i>L. hardjo</i> , or a gross lesion was present on the
	left or right kidney.
	Urine Culture Results:
	Controls: 10/10 (100%) positive
	Vaccinates: 0/11 (0%) positive
	PCR identity testing confirmed the presence of <i>L. hardjo</i> in all
	culture positive urine samples.
	Kidney Culture Results:
	Controls: 10/10 (100%) positive
	Vaccinates: 0/11 (0%) positive
	Kidney Gross Lesion Results:
	Controls: 6/10 (60%) positive
	Vaccinates: 6/11 (55%) positive
	See the following tables for the raw data.
USDA Approval Date	05/29/2009

Control ID	Day 14	Day 21	Day 28	Day 35	
5892	-	+	+	+	
5895	+	+	+	+	
5896	-	+	+	+	
5903	+	+	+	+	
5910	-	+	+	+	
5911	+	+	+	+	
5917	+	+	+	+	
5920	-	+	+	+	
5927	-	+	+	+	
5929	+	+	+	+	
All vaccinates were negative at all sampling points.					

Kidney Gross Lesion Data

Control	Left	Right
ID	Kidney	Kidney
5892	+	+
5895	+	+
5896	+	-
5903	+	+
5910	-	-
5911	-	-
5917	-	-
5920	+	+
5927	-	+
5929	-	-
Vaccinate	Left	Right
ID	Kidney	Kidney
5884	-	+
5886	-	-
5890	-	-
5899	+	+
5905	-	-
5907	-	+
5915	-	-
5922	+	+
5922 5925	+	+
5922 5925 5931	+ - +	+ - + +

Study Type	Efficacy					
Pertaining to	Leptospira borgpetersenii serovar hardjo type hardjo bovis					
	(Leptospira interrogans serovar hardjo, L. Hardjo)					
Study Purpose	Demonstration of duration of immunity against kidney infection					
	and leptospiuria caused by L. hardjo in calves.					
Product Administration	Two doses administered 4 weeks apart subcutaneously.					
Study Animals	Cattle 7-10 months of age, 9 controls and 9 vaccinates with two					
	doses. All animals were seronegative for Leptospira serovar					
	hardjo.					
Challenge Description	Animals were challenged with L. interrogans serovar hardjo					
	bovis, strain 033, 54 weeks following first vaccination.					
Interval observed after	Urine samples were collected weekly from day of challenge for 4					
challenge	weeks for culture and dark field microscopy testing. Kidneys					
	from cattle and from hamsters inoculated with concentrated urine					
	(5 and 10 fold) from the study animals were collected for culture.					
Results	Animals were considered positive for <i>L. hardjo</i> if at least one					
	urine or kidney sample yielded positive per the following tests:					
	- Urine: Culture and darkfield microscope					
	- Kidney Tissue: Culture. Only one control cattle was included					
	in culture in kidney.					
	Urine Results:					
	Controls: $9/9(100\%)$ positive					
	vaccinates: 0/9 (0%) positive					
	Vidnov Doculta					
	$\frac{\text{Kidley Kesults}}{\text{Controls: } 1/1 (100\%) \text{ positive}}$					
	Vaccinates: $0/9$ (0%) positive					
	See the following tables for individual raw data					
	see the renowing mores for marriadul fur dum.					
USDA Approval Date	05/10/2000					

				Wee	eks Post	t-Challer	ige		
Treatment Animal Group ID		Dark Field Microscopy Results			Culture Results				
		2	3	4	5	2	3	4	5
	11	-	-	-	-	+	+	+	+
	12	-	+	+	+	+	+	+	+
LS.	13	-	-	-	-	+	+	+	+
IO1	14	+	+	+	+	+	+	+	+
TR	15	-	+	+	+	+	+	+	+
NC	16	-	-	-	-	+	+	+	+
č	17	-	+	+	+	+	+	+	+
	18	-	+	+	+	+	-	+	+
	19	-	-	+	+	+	+	+	+
	1	-	-	-	-	-	-	-	-
70	3	-	-	-	-	-	-	-	-
LES	4	-	-	-	-	-	-	-	-
LA	5	-	-	-	-	-	-	-	-
NI	6	-	-	-	-	-	-	-	-
CC	7	-	-	-	-	-	-	-	-
٧A	8	-	-	-	-	-	-	-	-
-	9	-	-	-	-	-	-	-	-
	10	-	-	-	-	-	-	-	-

Analysis of Urine for detection of Leptospires:

+: Leptopires detected; -: Leptopires not detected

Culture Results of Kidney in Cattle for detection of Leptospires

Treatment	Animal ID	Ki	idney Secti	on
Group	Animai ID	1	2	3
CONTROL*	14	+	+	+
	1	-	-	-
	3	-	-	-
LEC	4	-	-	-
LA ^T	5	-	-	-
NI	6	-	-	-
CC	7	-	-	-
/A	8	-	-	-
-	9	-	-	-
	10	-	-	-

* Only one control animal was included in culture in kidney.

+: Leptopires detected; -: Leptopires not detected

<u>Culture Results of Kidney in Hamsters inoculated with concentrated urine for detection of Leptospires:</u>

Treatment Group	Cattle ID	Hamster ID	Cattle Urine Concentrated x Fold	Hamster Kidney Result
CONTROL*	14	19	10	+
	1	1	10	-
		2	5	-
	2	3	10	-
	3	4	5	-
	Λ	5	10	-
	4	6	5	-
S	5	7	10	-
E.		8	5	-
NA	6	9	10	-
CI		10	5	-
AC	7	11	10	-
\mathbf{V}_{I}		12	5	-
	o	13	10	-
	0	14	5	-
	0	15	10	-
	9	16	5	-
	10	17	10	-
	10	18	5	-

* Only one control cattle was included in culture in kidney in hamsters and test was conducted with urine concentrated at 10 fold only. +: Leptopires detected; -: Leptopires not detected

Study Type	Efficacy					
Pertaining to	Leptospira borgpetersenii serovar hardjo type hardjo bovis					
	(Leptospira interrogans serovar hardjo, L. Hardjo)					
Study Purpose	Demonstration of efficacy against fetal infection					
Product Administration	Two doses administered 4 weeks apart subcutaneously.					
Study Animals	Heifers between 12-15 months of age, 16 vaccinates and 8 that					
	were seronegative for <i>Leptospira</i> serovar hardjo and were bred					
	post-vaccination.					
Challenge Description	Animals were challenged at 4.5 to 5.5 months of gestation by					
	vaginal and conjunctival inoculation for 3 consecutive days with					
	L. borgpetersenii serovar hardjo mixed strains 203 and 197.					
Interval observed after	Urine samples were collected every 2 weeks beginning 2 weeks					
challenge	post challenge. Maternal kidney and placenta, and calf kidney,					
	liver and lung tissues were collected at calving time (or abortion					
	if happened).					
Results	Urine or tissue sample evaluated per the following tests:					
	- Urine: Leptospiral culture and immunofluorescence					
	- Tissue: Leptospiral culture, immunofluorescence, and					
	histologic examination					
	Urine Results from Heifers:					
	Controls: 8/8 (100%) positive					
	Vaccinates: 0/16 (0%) positive					
	<u>Issue Results for Maternal Kidneys:</u>					
	Controls: $8/8 (100\% \text{ positive})$					
	vaccinates: 0/16 (0%) positive					
	Tissue Results for placental and/or fetal infection (calf kidney					
	liver. or lung):					
	Controls: 5/8 (62.5 %) positive					
	Vaccinates: 0/16 (0%) positive					
	Individual raw data is not available.					
USDA Approval Date	September 12, 2002					

Study Type	Efficacy				
Pertaining to	Leptospira borgpetersenii serovar hardjo type hardjo bovis				
_	(Leptospira interrogans serovar hardjo, L. Hardjo)				
Study Purpose	Efficacy against renal infection and leptospiuria caused by L.				
	borgpetersenii serovar hardjo bovis in calves.				
Product Administration	Two doses administered 4 weeks apart subcutaneously.				
Study Animals	Twenty-two (22) vaccinated and 13 control seronegative calves				
	included in 2 trials:				
	- Trial 1: 10 vaccinates; 6 controls				
	- Trial 2: 12 vaccinates; 7 controls				
Challenge Description	In Trial 1, calves were challenged 13 weeks post first				
	vaccination, and in Trial 2, calves were challenged 6 weeks post				
	vaccination with <i>L. interrogans</i> serovar hardjo type hardjo				
	bovis.				
Interval observed after	In Trial 1, urine samples were collected on days 28, 34 and 41				
challenge	post-challenge. Kidney were cultured.				
	In Trial 2, urine samples were collected on days 14, 21, 28, and				
	35 post-challenge. Kidneys were cultured.				
	Kidneys (4 sections) were cultured from calves with negative				
	leptospiuria only.				
Results	Summary of results are as follows:				
	<u>Urine Culture Results Trial 1</u> :				
	Controls: 4/6 (67 %) positive				
	Vaccinates: 0/10 (0%) positive				
	Urine Culture Results Trial 2.				
	Controls: $7/7$ (100 %) positive				
	Vaccinates: $0/11*(0\%)$ positive				
	* Only 11 vaccinates from trial 2 were tested				
	Kidney Culture Results Trial 1*:				
	Controls: 2/2 (100 %) positive				
	Vaccinates: 0/12 (0%) positive				
	*kidneys were only collected from leptospiuria negative animals				
	Kidney Culture Degulte Trial 2*:				
	$\frac{\text{Kincy Cutture Results IIIai 2}}{\text{Vaccinates: } 0/12 (0\%) \text{ positive}}$				
	*kidneys were only collected from leptospiuria negative animals				
	Combined Urine and Kidney Culture Results for both Trial 1 and				
	<u>Trial 2</u> :				
	Controls: 13/13 (100 %) positive				
	Vaccinates: 0/22 (0 %) positive				
	See the following tables for individual raw data				

USDA Approval Date 05/10/2000

<u>Results from Urine Culture for detection of Leptospires (Trial 1)</u>:

Tuestment Cuern	A nimal ID	Study Day (Challenge was on Day 0)			
Treatment Group	Allilla ID	28	34	41	
	62	+	-	+	
	64	-	-	-	
CONTROLS	67	+	+	+	
CONTROLS	69	+	-	+	
	77	-	-	-	
	78	-	-	+	
	49	-	-	-	
	50	-	-	-	
	52	-	-	-	
	65	-	-	-	
VACCINATES	68	-	-	-	
VACCINATES	71	-	-	-	
	74	-	-	-	
	75	-	-	-	
	76	-	-	-	
	79	-	-	-	

+: Leptospires detected; -: Leptospires not detected

Results from Urine Culture for detection of Leptospires (Trial 2):

Tuestment Cusur	Animal	Study D	Study Day (Challenge was on						
Treatment Group	ID	14	21	28	35				
	1	-	+	+	+				
	2	-	+	+	+				
	3	-	-	+	+				
CONTROLS	4	-	-	+	+				
	5	-	+	+	+				
	6	-	-	-	+				
	7	-	-	-	+				
	3	-	-	-	-				
	10								
	10	-	-	-	-				
	10	-	-	-	-				
VACCINATES	10 11 2	- - ND	- - ND	- - ND	- - ND				
VACCINATES		- - ND -	- - ND -	- - ND -	- - ND -				
VACCINATES	$ \begin{array}{r} 10\\ 11\\ 2\\ 8\\ 14\\ \end{array} $	- - ND -	- - ND - -	- ND -	- - ND -				
VACCINATES	$ \begin{array}{r} 10 \\ 11 \\ 2 \\ 8 \\ 14 \\ 5 \\ 5 \end{array} $	- ND - -	- - ND - - -	- ND - -	- ND - -				
VACCINATES	$ \begin{array}{r} 10 \\ 11 \\ 2 \\ 8 \\ 14 \\ 5 \\ 12 \\ \end{array} $	- ND - - -	- ND - - -	- ND - -	- ND - -				

4	-	ND	-	-
7	-	-	-	-
9	-	-	-	-

+: Leptospires detected; -: Leptopires not detected ND: Not Done

<u>Results from Kidney Culture for detection of Leptospires (Trial 1)</u>:

Treatment	Animal	Kidney Section						
Group*	ID	1	2	3	4			
CONTROL S	64	-	-	+	+			
CONTROLS	77	+	+	+	+			
	49	-	-	-	-			
	50	-	-	-	-			
	52	-	-	-	-			
	65	-	-	-	-			
VACCINATES	68	-	-	-	-			
VACCINATES	71	-	-	-	-			
	74	-	-	-	-			
	75	-	-	-	-			
	76	-	-	-	-			
	79	-	-	-	-			

*: Only calves with negative leptospiuria were tested

+: Leptospires detected; -: Leptospires not detected

Results from Kidney Culture for detection of Leptospires (Trial 2):

T	Animal		Kidney Section						
I reatment Group	ID	1	2	3	4				
	3	-	-	-	-				
	10	-	-	-	-				
	11	-	-	-	-				
	2	-	-	-	-				
	8	-	-	-	-				
VACCINATES*	14	-	-	-	-				
	5	-	-	-	-				
	12	-	-	-	-				
	15	-	-	-	-				
	4	-	-	-	-				
	7	-	-	-	-				
	9	-	-	-	-				

*: Only calves with negative leptospiuria were tested

+: Leptospires detected; -: Leptospires not detected

Study Type	Efficacy
Pertaining to	Leptospira borgpetersenii serovar hardjo type hardjo bovis
	(Leptospira interrogans serovar hardjo, L. Hardjo)
Study Purpose	Demonstration of efficacy against renal infection and
	leptospiuria caused by L. hardjo.
Product Administration	Two doses administered 4 weeks apart subcutaneously.
Study Animals	Heifers between 8-12 months of age, 8 controls and 8 vaccinates
	received two doses of vaccine. All animals were seronegative
	for Leptospira serovar hardjo.
Challenge Description	Animals were challenged 16 weeks following second
	vaccination by intraperitoneal or conjunctival inoculation for 3
	consecutive days with L. borgpetersenii serovar hardjo strain
	type 203.
Interval observed after	Urine samples collected once or twice weekly from day of
challenge	challenge to necropsy day. Kidney tissues were obtained
	between 11 and 14 weeks after challenge.
Results	Urine or tissue sample evaluated per the following tests:
	- Urine: Culture, immunofluorescence, and darkfield microscope
	- Kidney Tissue: Culture, immunofluorescence, histology and
	silver staining or immunochemistry
	$\frac{\text{Urine Results:}}{(1-1)^{1/2}}$
	Controls: $6/8 (75\%)$ positive
	vaccinates: 0/8 (0%) positive
	Vidnov Doculta:
	$\frac{\text{Kincy Kesuits}}{\text{Controls: } 8/8 (100\%) \text{ positive}}$
	Vaccinates: $0/8$ ($100/0$) positive
	See the following tables for individual raw data.
USDA Approval Date	03/29/2000

Treatment	Animal		Study Day Post Challenge (Challenge was on Day 193)																
Group	ID	2	4	6	8	10	12	14	17	21	24	28	35	42	45	49	51	56	63*
	15	-	-	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+
\sim	23	-	-	-	+	-	-	-	-	+	+	+	+	+	+	+	+	+	+
)L.	24	-	-	+	-	-	-	-	+	+	+	+	+	+	+	+	+	+	+
RC	28	-	-	-	+	I	I	+	+	+	+	+	+	+	+	+	+	+	+
L	2	-	-	-	-	I	I	I	I	I	I	I	I	I	I	-	-	-	-
0	7	-	-	-	-	I	I	+	+	+	+	+	+	+	+	+	+	+	+
\cup	16	-	-	-	-	1	I	-	-	I	1	+	+	+	+	+	+	+	+
	22	-	-	-	-	-	-	-	-	I	-	-	-	-	-	-	-	-	-
	11	-	1	-	-	I	I	1	I	1	I	I	1	1	I	-	-	-	-
S	13	-	-	-	-	1	I	-	-	I	1	I	I	I	1	-	-	-	1
T	14	-	-	-	-	1	I	-	-	I	1	I	I	I	1	-	-	-	1
NA	20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CI	12	-	-	-	I	I	1	1	1	-	I	1	1	1	I	1	1	-	-
AC	17	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Λ ⁷	18	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	19	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Analysis of Urine for detection of Leptospires:

*Results for urine samples are available until Day 63 post challenge and on necropsy day (see table below) only.

Analysis of Kidney and Urine at Necropsy:

Treatment	Animal ID	Detection of	leptospires	Kidney Lesion
Group		Urine	Kidney	Score *
	15	+	+	1
	23	+	+	0
	24	+	+	1.5
T S	28	+	+	2
go	2	-	+	0
	7	+	+	3.5
õ	16	+	+	1.5
C	22	-	+	2.5
	11	-	-	1
	13	-	-	2
E N	14	-	-	2
I	20	-	-	0
Z	12	-	-	0
ACCI	17	ND	-	0.5
	18	ND	-	2.5
\rightarrow	19	-	-	1

* Lesion Score: 0= no lesions detected; 1=focal or multi focal 1- to 2-mm pale foci of lymphocytic interstitial nephritis in renal cortex; 2=multiple 2- to 5-mm foci of lymphocytic interstitial nephritis in renal cortex; 3=multiple 5- to 10-mm foci in renal cortex and medulla, with extensive lymphocytic interstitial nephritis and tubular degeneration; 4=pale foci > 10 mm foci in renal cortex and medulla, with severe lymphocytic interstitial nephritis, tubular degeneration, and fibrosis ** ND: Not Done

Study Type	Efficacy
Pertaining to	Leptospira borgpetersenii serovar hardjo type hardjo bovis
	(Leptospira interrogans serovar hardjo, L. Hardjo)
Study Purpose	Demonstration of efficacy against renal and reproductive tract
	infection and leptospiuria caused by <i>L. hardjo</i> in heifers.
Product Administration	Two doses administered 4 weeks apart subcutaneously.
Study Animals	Heifers 12 months of age, 12 controls and 12 vaccinates that
	received two doses of vaccine. All animals were seronegative
	for Leptospira serovar hardjo.
Challenge Description	Animals were challenged 19 weeks following second
	vaccination by conjunctival and vaginal inoculation for 3
	consecutive days with L. borgpetersenii serovar hardjo strain
	203 type A or 197 type B.
Interval observed after	Urine samples were collected weekly from two weeks post-
challenge	challenge to necropsy day. Tissues (kidney, uterus, oviduct)
	were obtained at necropsy between 10 and 12 weeks after
	challenge.
Results	Urine or tissue sample evaluated per the following tests:
	- Urine: Culture, immunofluorescence, PCR, and darkfield
	microscopy
	- Tissue: Culture, immunofluorescence, histopathology and
	immunochemistry
	Summary of results
	<u>Urine Results</u>
	Controls: 12/12 (100%) positive
	Vaccinates: 0/11* (0%) positive
	<u>Kidney Results (leptospires and/or lesion score ≥ 1):</u>
	Controls: 12/12 (100%) positive
	Vaccinates: 4/11 (36%) positive
	Denne dusting Tas at Desults.
	<u>Contrologi 10/12 (82%) positivo</u>
	$V_{\text{assignators}} = 0/11^* (09/) \text{ positive}$
	vaccinates: 0/11 (0%) positive
	* One heifer from vaccinated group died of unrelated causes (bloat) before the end of study.
	See the following tables for individual raw data
USDA Annroval Data	03/29/2000
USDA Approval Date	03/27/2000

Treatment	Animal	Study Day (Challenge was on Day 0)								
Group	ID	0	14	21	28	35	42	49	56	63 [¥]
	123	-	-	+	+	+	+	+	+	+
	124	-	-	+	+	+	+	+	+	+
	131	-	+	+	+	+	+	+	+	+
	132	-	+	+	+	+	+	+	+	+
)L.	138	-	-	+	+	+	+	+	+	+
RC	143	-	+	+	+	+	+	+	+	+
E	144	-	-	+	+	+	+	+	+	+
O	146	-	-	+	+	+	+	+	+	+
U	150	-	+	+	+	+	+	+	+	+
	128*	-	+	+	+	+	+	+	+	+
	135*	-	-	+	+	+	+	+	+	+
	148^{*}	-	-	-	-	+	+	+	+	+
	125	-	-	-	-	-	-	-	-	-
	127	-	-	-	-	-	-	-	-	ND**
	130	-	-	-	-	-	-	-	-	-
N S	133	-	-	-	-	-	-	-	-	-
	136	-	-	-	-	-	-	-	-	-
NA	139	-	-	-	-	-	-	-	-	-
CI	142	-	-	-	-	-	-	-	-	-
AC	145	-	-	-	-	-	-	-	-	-
Ĩ →	149	-	-	-	-	-	-	-	-	-
	129*	-	-	-	-	-	-	-	-	-
	137*	-	-	-	-	-	-	-	-	-
	140^{*}	-	-	-	-	-	-	-	-	-

Analysis of Urine for detection of Leptospires:

+: Leptospires detected; -: Leptospires not detected *: Heifers with * were challenged with *L. borgpetersenii* serovar *hardjo* strain type A 203. The other animals were challenged with *L.* borgpetersenii serovar hardjo strain type B 197.

¥: Results for urine samples are available until Day 63 post challenge and on necropsy day (see table below) only.

** Heifer 127 died of unrelated causes (bloat) before the end of study.

ND: Not Done

Analysis of Kidney, Urine, and Reproductive Tract at Necropsy:

Treatment	Animal	Detection	Kidney Lesion			
Group	ID	Urine	Kidney	Uterus	Oviduct	Score €
	123	+	+	+	+	0
	124	+	+	-	+	3
	131	+	+	-	+	0
S	132	+	+	+	-	0
IO:	138	+	+	-	+	1
TR	143	+	+	+	+	0
NC	144	-	+	-	-	0
č	146	+	+	+	+	2
	150	+	+	+	-	0
	128*	+	+	-	+	ND
	135*	+	+	-	-	0

	148^{*}	+	+	+	+	3
	125	-	-	-	-	0
	127**	ND	ND	ND	ND	ND
	130	-	-	-	-	0
S [7]	133	-	-	-	-	0
E.	136	-	-	-	-	0
NA	139	ND	-	-	-	1
CI	142	-	-	-	-	0
AC	145	-	-	-	-	0
V.	149	-	-	-	-	1
	129*	-	-	-	-	0
	137*	-	-	-	-	0
	140^{*}	-	-	-	-	3

+: Leptospires detected; -: Leptospires not detected

* Heifers with * were challenged with *L. borgpetersenii* serovar *hardjo* strain type A 203. The other animals were challenged3 with *L. borgpetersenii* serovar *hardjo* strain type B 197.

** Heifer 127 died of unrelated causes (bloat) before the end of study.

 \in Lesion Score: 0= no lesions detected; 1=focal or multi focal 1- to 2-mm pale foci of lymphocytic interstitial nephritis in renal cortex; 2=multiple 2- to 5-mm foci of lymphocytic interstitial nephritis in renal cortex; 3=multiple 5- to 10-mm foci in renal cortex and medulla, with extensive lymphocytic interstitial nephritis and tubular degeneration; 4=pale foci > 10 mm foci in renal cortex and medulla, with severe lymphocytic interstitial nephritis, tubular degeneration, and fibrosis

ND: Not Done

<u>Summary Table for Kidney, Urine, and Reproductive Tract (Consolidation results from</u> <u>urine samples and samples from necropsy day)</u>:

Two stress and	Animal	Detection	Detection of leptospires						
Group	ID	Urine	Kidney	Reproductive Tract					
	123	+	+	+					
	124	+	+	+					
	131	+	+	+					
	132	+	+	+					
)L.	138	+	+	+					
RC	143	+	+	+					
L	144	+	+	-					
	146	+	+	+					
Ŭ	150	+	+	+					
	128*	+	+	+					
	135*	+	+	-					
	148^{*}	+	+	+					
	125	-	-	-					
	127**	ND	ND	ND					
N S	130	-	-	-					
	133	-	-	-					
NA	136	-	-	-					
CI	139	ND	-	-					
VAC	142	-	-	-					
	145	-	-	-					
	149	-	-	-					
	129*	-	-	-					

137*	-	-	-
140*	-	-	-

* Reproductive tract includes oviduct and uterus.** Heifer 127 died of unrelated causes (bloat) before the end of study.

Study Type	Safety
Pertaining to	Leptospira borgpetersenii serovar hardjo bovis (L. hardjo)
Study Purpose	Demonstrate safety in cattle under field conditions
Product Administration	
Study Animals	Bovine, including pregnant and lactating cattle
Challenge Description	NA
Interval observed after	
challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	September 4, 2003

Study Type	Safety				
Pertaining to	Leptospira borgpetersenii serovar hardjo type hardjo bovis (Leptospira				
	interrogans serovar hardjo, L. Hardjo)				
Study Purpose	Demonstrate safety u	nder field c	onditions in minimu	n age, weaned and	
	high-stress calves, lac	ctating and	pregnant cows		
Product	One dose followed 4 weeks later by a second dose administered				
Administration	subcutaneously (SC)				
Study Animals	A total of 2151 cattle	$(\leq 4 \text{ weeks})$	s of age calves, $> 4 \text{ w}$	eeks of age calves,	
	open and pregnant ca	open and pregnant cattle in all three trimesters of pregnancy) were			
	enrolled at 3 geograp	hic location	s. The animals were	distributed as	
	follows: 720 controls	and 1431 v	vaccinates.		
	Category	Controls	Vaccinates	Total animals included in study	
	≤4 weeks of age calves	89	162		
	> 4 weeks of age Calves*	216	453		
	Total Calves per treatment group	305	615	920 calves	
	Open Cows	7	12		
	Pregnant Cows	408	804		
	Total Cows per treatment group	415	816	1231 cows	
	Total Animals per Treatment Group	720	1431	2151	
	*: 224 vaccinated calves we	re ≤ 4 ½ weeks	of age.		

	Category		Controls	Vaccinates	Total animals included in study
	Brognant	First trimester	87	212	299
	Cow per	Second trimester	128	245	373
	u mester	Third trimester	91	144	235
	* Stage of Pregna confirmed if the c	ncy status was de attle were pregna	etermined only in 2 ant prior to first vac	2 out of 3 dairies, the ceination.	third dairy just
Challenge Description	N/A				
after vaccination	within six hours and the next 2 days post-vaccination. General health observations were conducted from Study Day 0 (first vaccination) and Days 3 through 56 (end of study). Pregnancy evaluations were done on Days 0 and 56. The stage of pregnancy (trimester) was determined in 2 of the 3 dairies.				
	Number of Animals with at least One Adverse Events (AEs)* Across all Animal Categories and Treatment Groups AEs Controls				nts (AEs)* ps Vaccinates
	Number of at least one Animals In study (%)	animals with AE of Total cluded in	h 50 or (6.94	f 720 4 %)	76 of 1431 (5.31 %)
	the same animal. Number of Adverse Events* per Animal Category and Treatment Groups and % Animals Included in study				
	Animai Ca	legories	Con		Vaccinates
	Calves		3	5	52
	Cows		1	5	24
	* This number does the same animal	not include Injectio	on site reactions. Mo	re than one observation	could have been made for

Animal Categories	Controls	Vaccinates
Calves	1	9
Cows	19	29
Number of animals with at least one AE of Total Animals Included in study (%)	20 of 720 (2.78 %)	38 of 1431 (2.66 %)
<u>Calves:</u> Adverse Events observ Adverse Event	ed in Calves per T Controls	reatment Grou Vaccinate
Depression [¥]	1	2
Bloat	<u> </u>	2
Pneumonia	30	41
Pneumonia and Diarrhea	0	4
Broken Leg	0	1
Culled	0	2
Total	35	52
Number of Observations fo size in Calves Controls	or Injection Site R	eactions and sw Vaccinates
1 st injection		
0		0
and inication		
	4.4.4.	

Adverse Event Mastitis Broken leg Lame Abortion* Johnes Disease	Controls	Vaccinate
Mastitis Broken leg Lame Abortion* Johnes Disease	2 0 2	1
Broken leg Lame Abortion* Johnes Disease	0	1
Lame Abortion* Johnes Disease	2	2
Abortion* Johnes Disease	2	0
Johnes Disease	11	16
	0	1
Blackleg	0	1
Culled	0	2
Heart attack	0	1
Total	15	24
found open) Number of AEs of Total	Controls 15 of 408	Vaccina 24 of 8
found open) Number of AEs of Total Animals Included in study (%)	Controls 15 of 408 (3.67 %)	Vaccina 24 of 8 (2.98 of
found open) Number of AEs of Total Animals Included in study (%) Number of Observations Swelling Size in Cows *	Controls 15 of 408 (3.67 %) for Injection Site R	Vaccina 24 of 8 (2.98 of Reactions and
found open) Number of AEs of Total Animals Included in study (%) Number of Observations Swelling Size in Cows * Controls	Controls 15 of 408 (3.67 %) for Injection Site R	Vaccina 24 of 8 (2.98 of Reactions and
found open) Number of AEs of Total Animals Included in study (%) Number of Observations Swelling Size in Cows * Controls 1 st injection	Controls 15 of 408 (3.67 %) for Injection Site R	Vaccina 24 of 8 (2.98 of Reactions and Vaccinates
found open) Number of AEs of Total Animals Included in study (%) Number of Observations Swelling Size in Cows * Controls 1 st injection 15 (0.5-2"x2"x1 inch)	Controls 15 of 408 (3.67 %) for Injection Site R 27 (0	Vaccinates
found open) Number of AEs of Total Animals Included in study (%) Number of Observations Swelling Size in Cows * Controls 1 st injection 15 (0.5-2"x2"x1 inch) 2 nd injection	Controls 15 of 408 (3.67 %) for Injection Site R 27 ((Vaccinates

	No site of injection reactions were present 28 days after second vaccination.
USDA Approval	September 4, 2003
Date	