Summary of Studies Supporting USDA Product Licensure

Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	2665.01
True Name	Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Leptoferm 5 - No distributor specified Leptoferm 5 - Zoetis Argentina Leptoferm 5 - Zoetis Colombia S.A.S. Leptoferm 5 - Zoetis Mexico Leptoferm 5 - Zoetis Panama Leptoferm 5/2 mL - Zoetis Industria de Produtos
Date of Compilation Summary	February 16, 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 interrogans* serovar c*anicola* (*L canicola*)
Study Purpose	Demonstration of efficacy against leptospirosis caused by *L. canicola*
Product Administration	One dose administered intramuscularly
Study Animals	15 Calves approximately 6 months of age; 10 vaccinates and 5 controls. All animals were seronegative for *Leptospira canicola, icterohaemorrhagiae, hardjo, grippotyphosa, pomona*.
Challenge Description	Animals were challenged 3 weeks following vaccination.
Interval observed after challenge	Animals were observed post challenge for 8 days. Body temperatures and blood samples were collected daily.
Results	Leptospira Isolation Results in Blood: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive Temperature Results: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive See the following tables for individual raw data
USDA Approval Date	09/13/1977

Blood culture for isolation of Leptospires:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)							
		1	2	3	4	5	6	7	8
CONTROLS	45	+	+	+	-	-	-	-	-
	68	+	+	-	-	-	-	-	-
	75	+	+	+	-	-	-	-	-
	86	+	+	-	-	-	-	-	-
	106	+	+	+	-	-	-	-	-
VACCINATES	39	-	-	-	-	-	-	-	-
	57	-	-	-	-	-	-	-	-
	63	-	-	-	-	-	-	-	-
	67	-	-	-	-	-	-	-	-
	82	-	-	-	-	-	-	-	-
	85	-	-	-	-	-	-	-	-
	92	-	-	-	-	-	-	-	-
	99	-	-	-	-	-	-	-	-
	103	-	-	-	-	-	-	-	-
	104	-	-	-	-	-	-	-	-

+: Leptopires detected; -: Leptopires not detected

Temperature in ºF:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)								
		0	1	2	3	4	5	6	7	8
CONTROLS	45	102.4	101.0	104.4	107.2	106.2	103.6	103.8	101.6	100.8
	68	102.2	102.0	106.6	106.8	103.6	101.2	102.8	101.0	100.6
	75	102.0	102.0	102.0	106.6	106.4	101.4	101.6	101.6	101.8
	86	102.4	103.4	105.6	106.4	105.2	101.8	102.4	102.0	102.0
	106	102.0	102.0	104.0	104.8	104.4	102.8	101.6	101.4	101.0
VACCINATES	39	102.2	101.6	102.0	102.0	102.0	102.0	102.6	103.0	102.2
	57	101.2	102.0	101.4	101.0	101.0	100.2	100.8	100.8	100.2
	63	101.6	101.0	101.0	100.8	100.6	100.4	101.0	101.0	101.4
	67	102.0	102.0	101.6	101.0	101.4	101.8	101.8	101.6	102.0
	82	102.4	102.4	101.6	100.8	101.4	101.0	101.8	102.2	100.2
	85	100.8	102.8	101.4	100.4	100.6	100.2	100.6	101.0	100.8
	92	102.0	101.6	101.0	100.6	100.8	100.0	101.4	101.6	101.2
	99	102.0	102.0	101.4	101.8	102.0	101.4	101.6	101.6	100.6
	103	102.8	102.0	102.0	101.4	100.8	100.0	101.0	101.0	100.8
	104	101.8	101.6	102.0	101.2	101.2	101.2	101.4	101.4	100.6

Temperature >103 ºF was considered as pyrexia

Study Type	Efficacy
Pertaining to	*Leptospira canicola*
Study Purpose	Demonstrate effectiveness against *Leptospira canicola*
Product Administration	
Study Animals	Swine
Challenge Description	
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	March 15, 1978

Study Type	Efficacy
Pertaining to	*Leptospira interrogans* serovar *grippotyphosa* (*L Grippotyphosa*)
Study Purpose	Demonstration of efficacy against leptospirosis caused by *L. Grippotyphosa*
Product Administration	One dose
Study Animals	15 Calves; 10 vaccinates and 5 controls. All animals were seronegative for *Leptospira Grippotyphosa, hardjo, pomona*.
Challenge Description	Animals were challenged 8 weeks following vaccination.
Interval observed after challenge	Animals were observed for 8 days post challenge. Body temperatures and blood samples were collected daily.
Results	Leptospira Isolation Results in Blood: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive Temperature Results: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive See the following tables for individual raw data
USDA Approval Date	12/09/1975

Blood culture for isolation of Leptospires:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)							
		1	2	3	4	5	6	7	8
CONTROLS	161	+	+	+	+	+	-	-	-
	164	+	+	+	+	-	-	-	-
	165	+	+	+	+	-	-	-	-
	241	+	+	-	-	-	-	-	-
	248	+	+	+	-	-	-	-	-
VACCINATES	130	-	-	-	-	-	-	-	-
	137	-	-	-	-	-	-	-	-
	143	-	-	-	-	-	-	-	-
	145	-	-	-	-	-	-	-	-
	155	-	-	-	-	-	-	-	-
	247	-	-	-	-	-	-	-	-
	250	-	-	-	-	-	-	-	-
	255	-	-	-	-	-	-	-	-
	260	-	-	-	-	-	-	-	-
	261	-	-	-	-	-	-	-	-

+: Leptospires detected; -: Leptospires not detected

Temperature in ºF:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)								
		0	1	2	3	4	5	6	7	8
CONTROLS	161	101.6	102.4	102.2	105.4	104.8	104.4	99.4	100.6	102.8
	164	101.4	101.8	105.8	104.6	106.4	103.6	101.4	101.4	101.4
	165	102.0	102.6	102.2	104.0	104.4	104.8	101.8	102.2	102.0
	241	102.2	101.8	101.2	105.4	103.8	104.2	100.4	101.0	101.2
	248	101.6	100.4	101.8	106.0	104.4	103.6	101.0	101.2	101.6
101.4VACCINATES	130	102.0	102.0	102.0	102.4	101.6	101.4	100.2	101.4	101.8
	137	101.6	101.8	101.8	102.0	101.8	101.4	100.6	100.8	101.0
	143	102.0	101.8	101.8	101.8	102.4	101.8	100.4	99.8	101.2
	145	102.0	101.4	101.4	101.8	102.4	101.6	99.6	101.2	101.4
	155	102.2	102.0	102.0	102.4	102.2	101.2	100.0	100.4	100.8
	247	101.4	100.8	101.6	101.6	101.6	101.8	100.0	100.6	100.8
	250	101.8	102.0	102.2	101.4	101.6	101.6	101.2	101.4	101.8
	255	102.4	101.8	101.8	102.6	102.2	102.4	101.8	102.0	101.4
	260	102.0	102.6	102.8	102.4	102.0	101.6	100.0	101.2	101.2
	261	102.2	100.6	101.2	101.4	101.4	101.0	100.2	100.4	100.6

Temperature >103.5 ºF was considered as pyrexia

Study Type	Efficacy
Pertaining to	*Leptospira grippotyphosa*
Study Purpose	Demonstrate effectiveness against *Leptospira grippotyphosa*
Product Administration	
Study Animals	Swine
Challenge Description	
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	March 15, 1978

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Leptospira hardjo (L. hardjo)</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against leptospirosis caused by L. hardjo</td></tr>
<tr><td>Product Administration</td><td>One dose</td></tr>
<tr><td>Study Animals</td><td>Sera (pre-vaccination and 3 weeks post-vaccination, 1:4 diluted and undiluted) from 20 vaccinated cattle were obtained and were administered intraperitoneally to hamsters. Four hamsters were used for each sera..</td></tr>
<tr><td>Challenge Description</td><td>Hamsters were challenged with a virulent L. hardjo inoculate one day post administration of cattle sera.</td></tr>
<tr><td>Interval observed after challenge</td><td>Hamsters were humanely euthanized 14 days post challenge and kidneys examined for L. hardjo culture.</td></tr>
<tr><td>Results</td><td><u>L. hardjo Isolation in Hamster Kidneys Summary:</u>

<table>
<tr><th>Cattle Sera</th><th>L. hardjo / Tested (%)</th></tr>
<tr><td>Pre vaccination</td><td>76/80 (95%)</td></tr>
<tr><td>1:4 dilution Post-vaccination</td><td>50/80 (62.5%)</td></tr>
<tr><td>Undiluted Post-vaccination</td><td>25/80 (31.25%)</td></tr>
</table>

See table for individual data</td></tr>
<tr><td>USDA Approval Date</td><td>08/22/1978</td></tr>
</table>

Bovine Serological Titers and Hamster Passive protection testing:

Cattle ID	Bovine Serological Titers		Hamster Kidney Isolations Positive / Total
354	Pre vaccination	-	4/4
	1:4 dilution		1/4
	Undiluted	64	0/4
355	Pre vaccination	-	4/4
	1:4 dilution		4/4
	Undiluted	4	1/4
358	Pre vaccination	-	3/4
	1:4 dilution		4/4
	Undiluted	16	2/4
359	Pre vaccination	-	4/4
	1:4 dilution		4/4
	Undiluted	32	0/4
390	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	8	3/4
361	Pre vaccination	-	4/4
	1:4 dilution		1/4
	Undiluted	64	1/4
375	Pre vaccination	-	3/4
	1:4 dilution		1/4
	Undiluted	128	1/4
376	Pre vaccination	-	4/4
	1:4 dilution		2/4
	Undiluted	128	0/4
381	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	16	3/4
382	Pre vaccination	-	4/4
	1:4 dilution		2/4
	Undiluted	32	0/4
357	Pre vaccination	4	4/4
	1:4 dilution		3/4
	Undiluted	32	3/4
386	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	32	2/4
389	Pre vaccination	-	4/4
	1:4 dilution		0/4
	Undiluted	32	0/4

394	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	16	1/4
No Ears	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	64	0/4
424	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	32	1/4
426	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	16	2/4
427	Pre vaccination	-	4/4
	1:4 dilution		4/4
	Undiluted	16	2/4
435	Pre vaccination	-	3/4
	1:4 dilution		0/4
	Undiluted	256	1/4
438	Pre vaccination	-	3/4
	1:4 dilution		3/4
	Undiluted	32	2/4

1:4 dilution Post-vaccination
Undiluted Post-vaccination
- is Negative

Study Type	Efficacy
Pertaining to	*Leptospira hardjo*
Study Purpose	Demonstrate effectiveness against *Leptospira hardjo*
Product Administration	
Study Animals	Swine
Challenge Description	
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	March 15, 1978

Study Type	Efficacy
Pertaining to	*Leptospira interrogans* serovar icterohaemorrhagiae (*L. icterohaemorrhagiae*)
Study Purpose	Demonstration of efficacy against leptospirosis caused by *L. icterohaemorrhagiae*
Product Administration	One dose administered intramuscularly
Study Animals	15 Calves approximately 6 months of age; 10 vaccinates and 5 controls. All animals were seronegative for *Leptospira canicola, icterohaemorrhagiae, hardjo, grippotyphosa, pomona*.
Challenge Description	Animals were challenged 7 weeks following vaccination.
Interval observed after challenge	Animals were observed for 8 days post challenge. Body temperatures and blood samples were collected daily.
Results	Leptospira Isolation Results in Blood: Controls: 4/5 (80 %) positive Vaccinates: 0/10 (0 %) positive Temperature Results: Controls: 5/5 (100 %) positive Vaccinates: 0/10 (0 %) positive See the following tables for individual raw data
USDA Approval Date	09/13/1977

Blood culture for isolation of Leptospires:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)							
		1	2	3	4	5	6	7	8
CONTROLS	66	+	+	-	-	-	-	-	-
	71	+	+	-	-	-	-	-	-
	79	+	+	+	-	-	-	-	-
	113	+	+	-	-	-	-	-	-
	120	-	-	-	-	-	-	-	-
VACCINATES	58	-	-	-	-	-	-	-	-
	69	-	-	-	-	-	-	-	-
	80	-	-	-	-	-	-	-	-
	102	-	-	-	-	-	-	-	-
	107	-	-	-	-	-	-	-	-
	114	-	-	-	-	-	-	-	-
	121	-	-	-	-	-	-	-	-
	122	-	-	-	-	-	-	-	-
	124	-	-	-	-	-	-	-	-
	128	-	-	-	-	-	-	-	-

+: Leptopires detected; -: Leptopires not detected

Temperature in ºF:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)								
		0	1	2	3	4	5	6	7	8
CONTROLS	66	101.0	103.6	104.8	101.0	100.8	101.2	100.0	100.4	101.0
	71	101.0	104.0	102.0	102.2	101.8	101.4	100.4	102.0	101.4
	79	101.6	103.0	104.8	103.0	102.4	102.0	102.0	101.8	102.4
	113	101.4	104.4	104.2	102.8	100.8	100.2	101.0	101.2	101.4
	120	100.0	105.4	103.0	102.6	102.0	101.2	100.6	101.0	100.8
VACCINATES	58	99.8	101.6	101.4	101.4	101.8	101.6	101.0	101.2	102.4
	69	101.0	100.2	102.4	102.4	102.0	101.2	101.2	101.2	101.6
	80	101.4	101.8	101.4	101.0	102.0	101.6	100.6	101.0	101.6
	102	101.2	101.6	101.4	102.0	102.0	100.6	101.4	101.0	102.0
	107	101.2	102.0	101.8	99.8	101.8	101.0	100.8	101.6	101.4
	114	101.0	101.8	101.6	101.6	101.6	102.0	101.0	101.4	101.4
	121	101.4	101.8	102.0	101.8	101.8	101.4	102.0	101.2	102.2
	122	101.2	100.4	101.8	102.0	101.6	101.6	101.8	101.8	101.4
	124	101.4	101.4	101.4	101.0	101.6	100.8	101.0	101.2	101.8
	128	101.2	101.4	101.2	101.4	102.4	101.4	100.8	102.2	101.2

Temperature >103 ºF was considered as pyrexia

Study Type	Efficacy
Pertaining to	*Leptospira icterohaemorrhagiae*
Study Purpose	Demonstrate effectiveness against *Leptospira icterohaemorrhagiae*
Product Administration	
Study Animals	Swine
Challenge Description	
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	March 15, 1978

Study Type	Efficacy
Pertaining to	*Leptospira interrogans* serovar p*omona* (*L pomona*)
Study Purpose	Demonstration of efficacy against leptospirosis caused by *L. Pomona*
Product Administration	One dose
Study Animals	15 Calves; 10 vaccinates and 5 controls. All animals were seronegative for *Leptospira grippotyphosa, hardjo, pomona*.
Challenge Description	Animals were challenged 5 weeks following vaccination.
Interval observed after challenge	Animals were observed for 8 days post challenge. Body temperatures and blood samples were collected daily.
Results	Leptospira Isolation Results in Blood: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive Temperature Results: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive See the following tables for individual raw data
USDA Approval Date	12/09/1975

Blood culture for isolation of Leptospires:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)							
		1	2	3	4	5	6	7	8
CONTROLS	159	+	+	+	+	-	-	-	-
	163	+	+	+	-	-	-	-	-
	244	+	+	+	-	-	-	-	-
	252	+	+	+	-	-	-	-	-
	265	+	+	+	-	-	-	-	-
VACCINATES	134	-	-	-	-	-	-	-	-
	135	-	-	-	-	-	-	-	-
	142	-	-	-	-	-	-	-	-
	149	-	-	-	-	-	-	-	-
	151	-	-	-	-	-	-	-	-
	242	-	-	-	-	-	-	-	-
	245	-	-	-	-	-	-	-	-
	246	-	-	-	-	-	-	-	-
	257	-	-	-	-	-	-	-	-
	262	-	-	-	-	-	-	-	-

+: Leptospires detected; -: Leptospires not detected

Temperature in ºF:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)								
		0	1	2	3	4	5	6	7	8
CONTROLS	159	102.6	102.2	104.6	105.8	106.2	103.4	100.8	102.0	102.8
	163	102.6	102.2	105.6	106.0	106.6	103.2	101.0	103.0	102.6
	244	101.6	102.2	103.2	104.6	103.8	102.4	101.8	101.8	102.4
	252	102.6	102.4	103.0	107.4	104.6	103.0	102.2	103.0	103.0
	265	101.8	102.8	103.6	106.4	105.6	103.0	102.0	103.8	102.0
101.4VACCINATES	134	102.2	101.4	101.6	101.6	102.0	102.2	101.4	102.0	103.0
	135	102.6	102.6	102.6	102.4	103.2	102.8	102.0	102.8	102.4
	142	102.6	102.6	101.6	102.0	102.0	102.8	99.8	102.2	102.6
	149	102.4	102.0	102.6	102.0	101.6	102.0	101.6	102.0	102.4
	151	101.6	101.4	102.0	101.4	101.4	101.6	101.4	102.2	101.8
	242	101.6	101.2	101.6	102.0	101.6	102.0	100.8	101.4	101.0
	245	102.8	102.6	102.4	102.0	101.8	102.6	101.0	102.6	102.8
	246	102.4	101.6	102.0	102.0	102.2	102.6	101.0	102.0	102.6
	257	102.2	101.6	101.0	101.6	102.0	101.6	101.2	101.6	101.0
	262	102.6	102.0	101.0	102.0	101.6	101.8	101.0	102.6	101.4

Temperature >103.5 ºF was considered as pyrexia

Study Type	Efficacy
Pertaining to	*Leptospira pomona*
Study Purpose	Demonstrate effectiveness against *Leptospira pomona*
Product Administration	
Study Animals	Swine
Challenge Description	
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	March 15, 1978

Study Type	Safety
Pertaining to	All fractions
Study Purpose	Demonstrate safety under field conditions
Product Administration	One dose only or one dose followed 3 weeks later by a second dose
Study Animals	A total of 1253 animals from 4 different herds in one geographic location: • 850 Hereford yearling heifers • 95 Red Angus, Hereford, and Simmental cross-bred yearling heifers • 120 cross-bred Simmental yearling heifers • 107 Hereford, and Simmental cross-bred yearling heifers; 82 of these animals were vaccinated with a second dose. • 81 Longhorn and Hereford yearling bulls
Challenge Description	N/A
Interval observed after vaccination	Animals were observed at least for 14 days post vaccination.
Results	No adverse reactions were reported from any of the animals on this field trial.
USDA Approval Date	09/13/1977

Study Type	Safety
Pertaining to	ALL
Study Purpose	Demonstrate safety under field conditions
Product Administration	
Study Animals	Swine
Challenge Description	
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	February 24, 2006