Summary of Studies Supporting USDA Product Licensure

Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	2863.02
True Name	Campylobacter Fetus-Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	StayBred VL5 - No distributor specified StayBred VL5 - Zoetis Argentina StayBred VL5 - Zoetis C.A.
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.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Campylobacter fetus (C. fetus)</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against Campylobacteriosis caused by C. fetus</td></tr>
<tr><td>Product Administration</td><td>Two doses intramuscularly 30 days apart</td></tr>
<tr><td>Study Animals</td><td>Forty-four (44) heifers, 22 vaccinates and 22 controls; heifers were negative for C. fetus var. veneralis culture.</td></tr>
<tr><td>Challenge Description</td><td>Bulls infected with C. fetus var. veneralis per intrapreputial inoculation: Bulls were placed with heifers 4 weeks post second vaccination. Before infection, bulls tested negative for C. fetus var. veneralis culture and trichomoniasis examination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Cervical mucus was collected before vaccination, and days 26, 43, 58, 63 and 108 past beginning of breeding for C. fetus var. veneralis culture. Pregnancy status was checked on day 82 past beginning of breeding.</td></tr>
<tr><td>Results</td><td><u>C. fetus Isolation Summary for at Least One Positive Results:</u>
Controls: 14/22 (64%)
Vaccinates: 6/22 (27%)

<u>Total Pregnancies per Treatment Group and Estrus Cycle Summary:</u>

<table>
<tr><th>Length of Pregnancies / Estrus Cycle</th><th>Treatment Group</th><th>Pregnancies per Estrus</th><th>Cumulative Pregnancies</th><th>% Cumulative Animals Pregnant</th></tr>
<tr><td rowspan="2">66 to 86 days pregnancy (1st Estrus)</td><td>Controls</td><td>6/22</td><td>6/22</td><td>27%</td></tr>
<tr><td>Vaccinates</td><td>14/22</td><td>14/22</td><td>64%</td></tr>
<tr><td rowspan="2">45 to 65 days pregnancy (2nd Estrus)</td><td>Controls</td><td>6/22</td><td>12/22</td><td>55%</td></tr>
<tr><td>Vaccinates</td><td>5/22</td><td>19/22</td><td>86%</td></tr>
<tr><td rowspan="2">24 to 44 days pregnancy (3rd Estrus)</td><td>Controls*</td><td>2/22</td><td>14/22</td><td>64%</td></tr>
<tr><td>Vaccinates</td><td>0/22</td><td>19/22</td><td>86%</td></tr>
</table>
* Two heifers' length of pregnancy was set at 40 days (either early 3rd or late 2nd cycle).

See next table for individual data</td></tr>
<tr><td>USDA Approval Date</td><td>02/21/1980</td></tr>
</table>

Campylobacter fetus isolation and pregnancy status results:

Treatment Group	Animal ID	Culture Isolation					Pregnancy Status	Number of Days of Pregnancy	Conception Cycle
		Days past beginning of breeding							
		26	43	58	63	108			
Controls	124	+	+	+	+	+	P	55	2nd
	140	+	+	-	-	-	O	0	O
	144	-	-	-	-	-	P	40	3rd*
	146	-	-	-	+	-	P	75	1st
	151	-	-	-	-	-	P	70	1st
	177	-	+	-	+	-	P	60	2nd
	187	+	+	-	-	-	O	0	O
	104	-	-	-	+	-	P	75	1st
	131	-	+	-	-	-	O	0	O
	132	-	+	-	+	-	O	0	O
	133	-	+	+	+	-	O	0	O
	143	+	+	-	-	-	P	50	2nd
	159	+	+	-	+	-	O	0	O
	169	-	+	-	+	-	O	0	O
	125	-	-	-	-	-	P	65	2nd
	152	-	-	-	-	-	P	60	2nd
	154	-	-	-	-	-	P	75	1st
	168	-	+	-	+	-	O	0	O
	173	-	-	-	-	-	P	75	1st
	178	-	-	-	-	-	P	70	1st
	186	-	-	-	-	-	P	60	2nd
	191	-	+	-	-	-	P	40	3rd*
Vaccinates	117	-	-	+	-	-	P	70+	1st
	118	-	+	-	-	-	O	0	O
	134	-	-	+	-	+	O	0	O
	161	-	-	-	-	-	P	70	1st
	163	-	-	-	-	-	P	70+	1st
	164	-	-	-	-	-	P	70+	1st
	179	-	-	-	-	-	P	75+	1st
	189	-	-	-	-	-	P	75+	1st
	110	-	-	-	-	-	P	75	1st
	142	-	-	-	-	-	P	65	2nd
	145	-	-	-	-	-	P	70+	1st
	160	-	-	-	-	-	P	50	2nd
	174	-	-	-	-	-	P	70+	1st
	183	-	-	-	+	-	O	0	O
	185	-	-	-	-	-	P	65	2nd
	102	-	-	-	+	-	P	55	2nd
	103	-	-	-	-	-	P	75+	1st

	111	-	-	-	-	-	P	75+	1st
	128	-	-	-	-	-	P	70	1st
	137	-	-	-	-	-	P	70	1st
	156	-	-	-	-	-	P	65	2nd
	162	-	-	-	-	-	P	70	1st

+: Positive Isolation; -: No Isolation
P: Pregnant; O: Open
* Early 3rd or late 2nd conception cycle

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 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

<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 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 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	Safety
Pertaining to	All fractions
Study Purpose	Demonstrate safety under field conditions
Product Administration	One dose administrated intramuscularly
Study Animals	A total of 2,797 cattle representing different ages and breeds, including 2191 vaccinates, from 22 different herds
Challenge Description	N/A
Interval observed after vaccination	Animals were observed on days 1-3, 7-14, and 21 post vaccination.
Results	Transient swellings at the injection site following vaccination were reported in 5 of the 22 groups that received the vaccine.
USDA Approval Date	02/01/1989