Summary of Studies Supporting USDA Product Licensure

Establishment Name	Elanco US Inc.
USDA Vet Biologics Establishment Number	196
Product Code	4145.22
True Name	Bovine Rhinotracheitis-Virus Diarrhea Vaccine, Killed Virus, Campylobacter Fetus-Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Vira Shield 4 + VL5 HB - Elanco US Inc.
Date of Compilation Summary	December 02, 2020

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	Bovine Virus Diarrhea (BVD)
Study Purpose	To demonstrate effectiveness against Bovine Virus Diarrhea Type 1b
Product Administration	
Study Animals	Bovine
Challenge Description	BVD isolate NY-1, BVD1b
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 require publication of data submitted after that date.
USDA Approval Date	July 16, 2003

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea (BVD)
Study Purpose	To demonstrate effectiveness against Bovine Virus Diarrhea Type 2a
Product Administration	
Study Animals	Bovine
Challenge Description	BVD isolate 890, Type BVD2a
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 require publication of data submitted after that date.
USDA Approval Date	November 3, 1998

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea
Study Purpose	To demonstrate effectiveness against Bovine Virus Diarrhea Type 2a at 11 months post-vaccination
Product Administration	
Study Animals	Bovine
Challenge Description	BVD Isolate 890, Type BVD2a
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 require publication of data submitted after that date.
USDA Approval Date	September 24, 1996

Study Type	Efficacy
Pertaining to	*Campylobacter fetus*
Study Purpose	To demonstrate effectiveness against *Campylobacter fetus*
Product Administration	
Study Animals	Bovine
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 require publication of data submitted after that date.
USDA Approval Date	January 14, 1986

Study Type	Efficacy
Pertaining to	*Campylobacter fetus*
Study Purpose	To demonstrate effectiveness against *Campylobacter fetus* for one year duration of immunity
Product Administration	
Study Animals	Bovine
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 require publication of data submitted after that date.
USDA Approval Date	March 15, 1989

Study Type	Efficacy
Pertaining to	Bovine Rhinotracheitis
Study Purpose	To demonstrate effectiveness against Bovine Rhinotracheitis.
Product Administration	
Study Animals	Bovine
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 require publication of data submitted after that date.
USDA Approval Date	October 22, 1986

Study Type	Efficacy
Pertaining to	*Leptospira canicola, Leptospira grippotyphosa, Leptospira icterohaemorrhagiae, Leptospira pomona*
Study Purpose	To demonstrate effectiveness against *Leptospira spp.*
Product Administration	
Study Animals	Bovine
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 require publication of data submitted after that date.
USDA Approval Date	March 18, 1983

Study Type	Efficacy
Pertaining to	*Leptospira hardjo* type *hardjo-bovis*
Study Purpose	To demonstrate effectiveness against *Leptospira hardjo* type *hardjo-bovis*
Product Administration	
Study Animals	Bovine
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 require publication of data submitted after that date.
USDA Approval Date	July 24, 2001 / November 9, 2001

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Leptospira hardjo type hardjo-bovis</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness against Leptospira hardjo type hardjo-bovis at 12 months post vaccination.</td></tr>
<tr><td>Product Administration</td><td>Two doses, given subcutaneously, 28 days apart</td></tr>
<tr><td>Study Animals</td><td>18 vaccinates and 18 placebo controls</td></tr>
<tr><td>Challenge Description</td><td>L. hardjo Bovis (10^7 bacteria/1 mL) administered 397 days after first vaccination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily after challenge for 57 days. Tissues and organs evaluated at 57 days post challenge.</td></tr>
<tr><td>Results</td><td>The primary outcome for the study was the isolation of L. hardjo bovis organisms from urine, kidney, and reproductive tissues.

<table>
<tr><th></th><th>Vaccinates
(# affected/total)</th><th>Controls
(# affected/total)</th></tr>
<tr><td>Urine isolation</td><td>4/18</td><td>18/18</td></tr>
<tr><td>Kidney isolation</td><td>0/18</td><td>18/18</td></tr>
<tr><td>Reproductive tissues isolation</td><td>0/18</td><td>5/18</td></tr>
</table>

Raw data shown on attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>February 14, 2011</td></tr>
</table>

Isolation of L. Hardjo in Urine

Vaccinates									
Calf	-1DPC	7DPC	14DPC	21DPC	28DPC	35DPC	42DPC	49DPC	56DPC
1	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
2	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
3	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
4	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
5	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Pos
6	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
7	Neg	Neg	Neg	Neg	Neg	Neg	Pos	Neg	Neg
8	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
9	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
10	Neg	Neg	Neg	Neg	Pos	Neg	Neg	Neg	Neg
11	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
12	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
13	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
14	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
15	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
16	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
17	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Pos	Neg
18	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg

Controls									
Calf	-1DPC	7DPC	14DPC	21DPC	28DPC	35DPC	42DPC	49DPC	56DPC
1	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos
2	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos
3	Neg	Neg	Neg	Neg	Pos	Pos	Neg	Pos	Pos
4	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos
5	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos
6	Neg	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos
7	Neg	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos
8	Neg	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos
9	Neg	Neg	Neg	Pos	Pos	Pos	Neg	Pos	Pos
10	Neg	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos
11	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos
12	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos
13	Neg	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos
14	Neg	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos
15	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos
16	Neg	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos
17	Neg	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos
18	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos

DPC - Days Post Challenge

Pos - Positive Isolation of L. Hardjo

Neg - No Isolation of L. Hardjo

Isolation of L. Hardjo in Kidney and Reproductive tissues

Vaccinates				
Calf	Kidney	Ovary	Oviduct	Uterus
1	Neg	Neg	Neg	Neg
2	Neg	Neg	Neg	Neg
3	Neg	Neg	Neg	Neg
4	Neg	Neg	Neg	Neg
5	Neg	Neg	Neg	Neg
6	Neg	Neg	Neg	Neg
7	Neg	Neg	Neg	Neg
8	Neg	Neg	Neg	Neg
9	Neg	Neg	Neg	Neg
10	Neg	Neg	Neg	Neg
11	Neg	Neg	Neg	Neg
12	Neg	Neg	Neg	Neg
13	Neg	Neg	Neg	Neg
14	Neg	Neg	Neg	Neg
15	Neg	Neg	Neg	Neg
16	Neg	Neg	Neg	Neg
17	Neg	Neg	Neg	Neg
18	Neg	Neg	Neg	Neg

Controls				
Calf	Kidney	Ovary	Oviduct	Uterus
1	Pos	Neg	Neg	Neg
2	Pos	Neg	Neg	Neg
3	Pos	Neg	Neg	Neg
4	Pos	Neg	Neg	Neg
5	Pos	Neg	Pos	Neg
6	Pos	Neg	Neg	Neg
7	Pos	Pos	Neg	Neg
8	Pos	Neg	Neg	Neg
9	Pos	Pos	Pos	Neg
10	Pos	Neg	Neg	Neg
11	Pos	Neg	Neg	Neg
12	Pos	Neg	Neg	Neg
13	Pos	Pos	Neg	Neg
14	Pos	Pos	Neg	Neg
15	Pos	Neg	Neg	Neg
16	Pos	Neg	Neg	Neg
17	Pos	Neg	Neg	Neg
18	Pos	Neg	Neg	Neg

Pos – Positive Isolation of L. hardjo
Neg – No isolation of L. hardjo

Study Type	Safety
Pertaining to	All fractions
Study Purpose	Safety by SQ route in cattle, including pregnant cows and heifers
Product Administration	
Study Animals	
Challenge Description	
Interval observed after challenge	
Results	Scientific data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission.

Study Type	Safety
Pertaining to	All fractions
Study Purpose	To demonstrate safety under field conditions
Product Administration	
Study Animals	Bovine, including pregnant cows and heifers
Challenge Description	
Interval observed after challenge	
Results	Scientific data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. However, study data are not available.