Summary of Studies Supporting USDA Product Licensure

Establishment Name	Diamond Animal Health, Inc.
USDA Vet Biologics Establishment Number	213
Product Code	4439.20
True Name	Bovine Rhinotracheitis-Virus Diarrhea-Parainfluenza 3 Vaccine, Modified Live Virus, Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Diamond Animal Health, Inc. Elanco US, Inc. - Diamond Animal Health, Inc. Titanium 4 L5 - Elanco Animal Health - Diamond Animal Health, Inc. Titanium 4 L5 - Elanco US, Inc. - Diamond Animal Health, Inc.
Date of Compilation Summary	September 22, 2021

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 Type 1
Study Purpose	To demonstrate effectiveness against disease caused by bovine virus diarrhea type 1
Product Administration	1 dose to calves 6-8 months of age.
Study Animals	Bovine
Challenge Description	BVDV NY-1 Strain non-cytopathic Type 1b
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	July 14, 1998

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea Virus (BVDV) Type 2
Study Purpose	To demonstrate effectiveness against disease caused by bovine virus diarrhea type 2
Product Administration	
Study Animals	Bovine
Challenge Description	BVDV Type 2a strain 890
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	July 14, 1998

Study Type	Efficacy
Pertaining to	Infectious Bovine Rhinotracheitis (IBR) Virus
Study Purpose	To demonstrate effectiveness against disease caused by infectious bovine rhinotracheitis virus.
Product Administration	1 dose to calves 6-8 months of age.
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 requires publication of data submitted after that date.
USDA Approval Date	July 13, 1998

Study Type	Efficacy
Pertaining to	Leptospira canicola
Study Purpose	Demonstrate efficacy against L. canicola
Product Administration	One dose
Study Animals	Bovine
Challenge Description	NA
Interval observed after challenge	NA
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	January 5, 1983

Study Type	Efficacy
Pertaining to	Leptospira grippotyphosa
Study Purpose	Demonstrate efficacy against L. grippotyphosa
Product Administration	One dose
Study Animals	Bovine
Challenge Description	NA
Interval observed after challenge	NA
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	January 5, 1983

Study Type	Efficacy
Pertaining to	Leptospira hardjo
Study Purpose	Demonstrate efficacy against L. hardjo
Product Administration	One dose
Study Animals	Bovine
Challenge Description	Leptospira hardjo, Clay Center isolate
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	January 5, 1983

Study Type	Efficacy
Pertaining to	Leptospira icterohaemorrhagiae
Study Purpose	Demonstrate efficacy against L. icterohaemorrhagiae
Product Administration	One dose
Study Animals	Bovine
Challenge Description	NA
Interval observed after challenge	NA
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	January 5, 1983

Study Type	Efficacy
Pertaining to	Leptospira pomonaa
Study Purpose	Demonstrate efficacy against L. pomona
Product Administration	One dose
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 requires publication of data submitted after that date.
USDA Approval Date	January 5, 1983

Study Type	Efficacy
Pertaining to	Infectious Parainfluenza$_3$ (PI_3) Virus
Study Purpose	To demonstrate effectiveness against disease caused by infectious Parainfluenza$_3$ Virus
Product Administration	1 dose to calves 6-8 months of age.
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 requires publication of data submitted after that date.
USDA Approval Date	May 15, 1998

Study Type	Safety
Pertaining to	ALL
Study Purpose	Demonstrate safety of product under typical use conditions
Product Administration	One dose
Study Animals	Bovine
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	July 13, 1998

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>ALL</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate safety in pregnant cows and calves nursing pregnant cows</td></tr>
<tr><td>Product Administration</td><td>Two doses administered subcutaneously to heifers and cows, 1 dose prior to breeding and 1 dose during pregnancy at different trimesters. Heifers and cows were confirmed to be pregnant at administration during pregnancy.</td></tr>
<tr><td>Study Animals</td><td>Heifers and cows-separate groups vaccinated during each trimester. Similar sized groups in each trimester were maintained as controls.</td></tr>
<tr><td>Challenge Description</td><td>NA</td></tr>
<tr><td>Interval observed after challenge</td><td>Heifers and cows observed from pre-breeding vaccination through birth of calves. Nursing calves observed through 4 weeks of age.</td></tr>
<tr><td>Results</td><td>Summary of Calving Rates
(Normal calves delivered/Total deliveries)

<table>
<tr><td>Trimester</td><td>Vaccinates</td><td>Controls</td></tr>
<tr><td>1</td><td>200/208 (96%)</td><td>205/213 (96%)</td></tr>
<tr><td>2</td><td>302/313 (96%)</td><td>293/308 (95%)</td></tr>
<tr><td>3</td><td>193/205 (94%)</td><td>195/208 (94%)</td></tr>
<tr><td>Total</td><td>695/726 (96%)</td><td>693/729 (95%)</td></tr>
</table>

First Trimester (≤93 days of gestation)
<table>
<tr><td></td><td>Vaccinate</td><td>Control</td></tr>
<tr><td>Enrolled</td><td>209</td><td>213</td></tr>
<tr><td>Excluded (not related to vaccination)</td><td>1</td><td>0</td></tr>
<tr><td>Aborted or stillborn</td><td>6</td><td>5</td></tr>
<tr><td>Died at or after birth</td><td>2</td><td>3</td></tr>
</table>

Second Trimester (94-187 days of gestation)
<table>
<tr><td></td><td>Vaccinate</td><td>Control</td></tr>
<tr><td>Enrolled</td><td>315</td><td>310</td></tr>
<tr><td>Excluded (not related to vaccination)</td><td>2</td><td>2</td></tr>
<tr><td>Aborted or stillborn</td><td>7</td><td>9</td></tr>
<tr><td>Died at or after birth</td><td>4</td><td>6*</td></tr>
</table>
*one death was from a set of twins; the other was normal

Third Trimester (188-250 days of gestation)
<table>
<tr><td></td><td>Vaccinate</td><td>Control</td></tr>
<tr><td>Enrolled</td><td>205</td><td>208</td></tr>
<tr><td>Aborted or stillborn</td><td>9</td><td>9*</td></tr>
<tr><td>Died at or after birth</td><td>3</td><td>4**</td></tr>
</table>
*one stillborn was from a set of twins; the other was normal
**one dead was from a set of twins; the other was normal</td></tr>
</table>

USDA Approval Date	March 5, 2013