Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	4069.20
True Name	Bovine Rhinotracheitis Vaccine, Modified Live Virus, Leptospira Hardjo-Pomona Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Pyramid IBR+LPH - No distributor specified
Date of Compilation Summary	November 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	Infectious Bovine Rhinotracheitis (IBR)
Study Purpose	Demonstration of efficacy against IBR (respiratory disease)
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 requires publication of data submitted after that date.
USDA Approval Date	September 9, 1994

Study Type	Efficacy
Pertaining to	*Leptospira hardjo*
Study Purpose	Demonstration of efficacy against *Leptospira hardjo*
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. Study data, however, are no longer available.
USDA Approval Date	October 1, 1998

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Leptospira hardjo</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of efficacy against Leptospira borgpetersenii serovar hardjo-bovis</td></tr>
<tr><td>Product Administration</td><td>Two doses, 21 days apart, Subcutaneously</td></tr>
<tr><td>Study Animals</td><td>29 bovine (16 vaccinates, 13 controls), 6-10 month old heifers</td></tr>
<tr><td>Challenge Description</td><td>Challenged with Leptospira borgpetersenii serovar hardjo-bovis on 62, 63 and 64 days after the second vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Cattle were observed daily for 10 days after challenge, then three times weekly for 7 weeks. Urine samples were taken weekly for 8 weeks. On day 62 - 63 after challenge, kidneys were cultured for Leptospira isolation.</td></tr>
<tr><td>Results</td><td>Results of the study are summarized as follows:

Urine cultures were positive for Leptospira on at least one day:
<table>
<tr><th>Group</th><th># Positive / Total</th><th>% Affected</th><th>% Unaffected</th></tr>
<tr><td>Vaccinates</td><td>1 / 16</td><td>6%</td><td>94%</td></tr>
<tr><td>Controls</td><td>13 / 13</td><td>100%</td><td>0%</td></tr>
</table>
Kidney cultures were positive for Leptospira at necropsy:
<table>
<tr><th>Group</th><th># Positive / Total</th><th>% Affected</th><th>% Unaffected</th></tr>
<tr><td>Vaccinates</td><td>0 / 16</td><td>0%</td><td>100%</td></tr>
<tr><td>Controls</td><td>13 / 13</td><td>100%</td><td>0%</td></tr>
</table>
See tables on the following pages for data.</td></tr>
<tr><td>USDA Approval Date</td><td>January 14, 2015</td></tr>
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Urine and Kidney Cultures:

Vaccinates:

Animal #	Weekly Urine Observations								Overall Urine Outcome	Overall Kidney Outcome
	1	2	3	4	5	6	7	8		
7	-	-	-	-	-	-	-	-	Negative	Negative
12	-	-	-	-	-	-	-	-	Negative	Negative
17	-	-	-	-	-	-	-	-	Negative	Negative
22	-	-	-	-	-	-	-	-	Negative	Negative
29	-	-	-	-	-	-	-	-	Negative	Negative
36	-	-	-	-	-	-	-	-	Negative	Negative
37	-	-	-	-	-	-	-	-	Negative	Negative
39	-	-	-	-	-	-	-	-	Negative	Negative
45	-	-	-	-	-	-	-	-	Negative	Negative
47	-	-	+	-	-	-	-	-	Positive	Negative
53	-	-	-	-	-	-	-	-	Negative	Negative
55	-	-	-	-	-	-	-	-	Negative	Negative
56	-	-	-	-	-	-	-	-	Negative	Negative
62	-	-	-	-	-	-	-	-	Negative	Negative
63	-	-	-	-	-	-	-	-	Negative	Negative
64	-	-	-	-	-	-	-	-	Negative	Negative

Controls:

Animal #	Weekly Urine Observations								Overall Urine Outcome	Overall Kidney Outcome
	1	2	3	4	5	6	7	8		
6	-	+	+	+	+	+	+	+	Positive	Positive
10	-	+	+	+	+	+	+	+	Positive	Positive
18	-	+	+	+	+	+	+	+	Positive	Positive
28	-	+	+	+	+	+	+	+	Positive	Positive
32	-	-	+	+	+	+	+	+	Positive	Positive
41	-	-	+	+	+	+	+	+	Positive	Positive
43	-	+	+	+	+	+	+	+	Positive	Positive
49	-	+	+	+	+	+	+	+	Positive	Positive
50	-	-	+	+	+	+	-	+	Positive	Positive
59	-	+	+	+	+	+	+	+	Positive	Positive
60	-	+	+	+	+	+	+	+	Positive	Positive
67	-	-	+	+	+	+	+	+	Positive	Positive
68	-	+	+	+	+	+	+	+	Positive	Positive

Weekly Urine Observations:
- = Urine sample was negative for *Leptospira*
+ = Urine sample was positive for *Leptospira* (highlighted yellow)

Overall Urine / Kidney Outcome:
Negative = All urine / kidney samples were negative for *Leptospira*
Positive = At least one urine / kidney sample was positive for *Leptospira* (highlighted yellow)

Study Type	Efficacy
Pertaining to	*Leptospira pomona*
Study Purpose	Demonstration of efficacy against *Leptospira pomona*
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 requires publication of data submitted after that date.
USDA Approval Date	December 3, 1997

Study Type	Safety
Pertaining to	All fractions
Study Purpose	To demonstrate safety under field conditions
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 requires publication of data submitted after that date.
USDA Approval Date	January 27, 1998

Study Type	Safety
Pertaining to	All fractions
Study Purpose	To demonstrate safety under field conditions
Product Administration	
Study Animals	Bovine: pregnant cows and calves nursing pregnant cows provided the cows were vaccinated pre-breeding
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	December 6, 2005