Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	1181.26
True Name	Bovine Rhinotracheitis-Virus Diarrhea-Parainfluenza 3-Respiratory Syncytial Virus Vaccine, Modified Live Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Boehringer Ingelheim (Canada) Ltd. Pyramid 5 - No distributor specified Pyramid FP 5 - Boehringer Ingelheim (Canada) Ltd.
Date of Compilation Summary	April 08, 2019

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	Demonstration of efficacy against BVD Type 1 clinical disease, leukopenia, and viremia
Product Administration	
Study Animals	Bovine
Challenge Description	BVD1b NY-1 strain
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	June 14, 1994

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea (BVD)
Study Purpose	Demonstration of efficacy against persistent infection of calves with BVD Type 1
Product Administration	Pregnant heifers or cows prior to breeding
Study Animals	Bovine
Challenge Description	BVD1b 97B1415 strain
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 10, 2003

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bovine Virus Diarrhea (BVD)</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of efficacy against BVD Type 1 (respiratory disease) 217 days after vaccination</td></tr>
<tr><td>Product Administration</td><td>One dose, subcutaneously</td></tr>
<tr><td>Study Animals</td><td>46 bovine calves (23 vaccinates and 23 controls), 25 to 37 days of age</td></tr>
<tr><td>Challenge Description</td><td>Challenged with BVD Type 1b, Isolate CA0401186A, 217 days (7 months) after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Calves were observed and blood was collected for 14 days after challenge to evaluate viremia and leukopenia.</td></tr>
<tr><td>Results</td><td>Results of the study are summarized as follows:

Blood was evaluated for viremia (the presence of virus) and leukopenia (at least one white blood cell count below 60% of pre-challenge baseline).

Positive for Viremia and Leukopenia:
<table>
<tr><th></th><th>Viremia</th><th>Leukopenia</th></tr>
<tr><td>Vaccinates</td><td>0/23 (0%)</td><td>6/23 (26%)</td></tr>
<tr><td>Controls</td><td>22/23 (96%)</td><td>21/23 (91%)</td></tr>
</table>

See tables on the following pages for data.</td></tr>
<tr><td>USDA Approval Date</td><td>July 14, 2014</td></tr>
</table>

Viremia in Vaccinates (23 bovine)

Animal ID	Days Post-Challenge														Overall Result
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
21	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
34	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
41	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
49	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
51	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
57	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
61	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
64	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
67	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
68	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
73	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
82	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
86	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
87	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
94	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
97	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

+ = positive for virus (highlighted yellow)
- = negative for virus

Viremia in Controls (23 bovine)

Animal ID	Days Post-Challenge														Overall Result
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
31	-	-	-	-	-	+	+	-	+	-	-	-	-	-	+
33	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+
36	-	+	+	+	-	+	-	-	-	-	-	-	-	-	+
38	-	-	-	+	+	+	+	-	+	-	-	-	-	-	+
44	-	-	-	+	+	+	-	-	-	-	-	-	-	-	+
47	-	-	-	+	+	-	-	-	-	-	-	-	-	-	+
50	-	-	-	-	-	+	+	-	-	-	-	-	-	-	+
53	-	-	-	-	+	+	+	+	+	-	-	-	-	-	+
56	-	-	-	+	+	+	+	-	-	-	-	-	-	-	+
58	-	-	-	+	+	+	+	-	-	-	-	-	-	-	+
59	-	-	-	+	+	+	+	+	+	-	-	-	-	-	+
62	-	-	-	-	+	-	+	-	-	-	-	-	-	-	+
66	-	-	-	-	+	+	-	+	-	-	-	-	-	-	+
69	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+
70	-	-	-	-	+	+	+	-	-	-	-	-	-	-	+
74	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
85	-	-	-	-	+	+	-	-	-	-	-	-	-	-	+
89	-	-	-	-	+	+	+	-	-	-	-	-	-	-	+
92	-	-	-	-	-	+	+	-	-	-	-	-	-	-	+
98	-	-	-	-	+	+	+	-	-	-	-	-	-	-	+
101	-	-	-	-	-	+	+	+	-	-	-	-	-	-	+
106	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+
107	-	-	-	-	+	+	+	-	-	-	-	-	-	-	+

+ = positive for virus (highlighted yellow)
- = negative for virus

Leukopenia in Vaccinates (23 bovine)

ID	White Blood Cell Count per each Day Post-Challenge															Overall Result
	Base -line	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
21	13.5	10.4	11.3	11.6	11.9	11.3	12.4	12.2	11.6	12.4	9.6	9.6	9.3	9.7	10.4	-
32	8.4	8.1	7.8	7.9	NA	9.9	8.9	9.7	8.9	7.1	6.6	8	8.4	10.7	12	-
34	8.9	8.7	9	9.3	9.5	8.5	8.9	9	8.6	8	8.2	4.7	5.1	6.9	8.6	+
37	13.9	12.4	12.7	12.6	11.9	11.6	11	11.4	9.4	9.3	9	9.9	10.1	10.1	9.9	-
41	8.1	8.3	7.8	9.1	8.3	7.5	7.3	7.4	7.5	5.4	5.3	5.1	6.2	7.8	8.1	-
43	8.0	7.7	8	8.8	8.1	8.6	8	8.9	7.8	8.2	6	6.9	8.1	7.4	6.8	-
48	6.2	6.6	6.8	7	6.7	6.5	6.5	6.8	7.2	3.1	3.8	5	5.6	5.8	6.1	+
49	11.1	10.6	10.9	11.1	11.8	10.5	9.4	10.1	10.4	10.5	8	8.8	8.6	10.9	11.9	-
51	8.0	8.5	9.4	10.8	10.4	11.3	9.7	10.1	10.3	8.7	5.5	6.7	7.4	7.5	8.2	-
57	8.5	9.4	9.6	9.1	9.7	8.8	9.4	9.1	9	8.8	8.4	7	8	7.5	7.3	-
61	7	7	6.8	7.9	4.6	3.9	4.5	6.6	7	6.8	6.3	8.2	8.8	8	7.9	+
64	8.1	6.6	6.1	6.6	7.2	6.2	6.9	7.2	7.1	7.4	7.1	6.8	7.8	9.5	9	-
67	6.2	5.8	5.9	6.6	6.7	6.3	3.5	4.7	5	5.1	5.4	6.4	6.4	8.2	6.1	+
68	7.6	8.2	8.5	8.7	8.7	7	5.1	5.6	6.3	6.6	7.2	7.9	8.1	9.3	9.4	-
73	8.0	8	7.9	8	8.1	7.8	7.7	6.1	5.7	5.8	5.9	6.1	7.3	7.4	9.2	-
82	11.6	11.1	11.2	17.2	12.1	11.6	11.6	11	11.5	11.4	5.7	8.1	9.6	11.5	10.8	+
86	6.6	7.2	7.1	6.8	6.8	5.9	6.3	6.1	5.8	6.7	4.2	4.6	5.9	5.9	7.2	-
87	9.2	9.4	9.9	10	7.4	8.3	7.5	10.4	8.8	8.6	9.7	9.1	8.9	9.1	9.6	-
94	11.6	11.2	11.4	10.6	10.1	9.3	9.3	9.4	9.9	10.2	8.3	8.6	9.4	11.4	11.8	-
97	6.4	6.8	7	8.1	8.3	7.7	7.4	7.9	8.3	7.5	4.8	5.3	5.7	6.6	5.8	-
102	8.7	8.3	8.8	8.7	8.9	8.2	8.2	8.5	8	6	3.8	5.5	6.3	7.1	8.1	+
104	8.3	8.4	8.6	9.2	8.9	7.9	8.1	8.9	8.5	6.9	5.3	6.7	6.7	9.9	7.9	-
108	8.1	8.1	9	7.7	8.4	11.4	7.8	9.3	11.9	10.3	10.3	8	12.7	10.6	10.2	-

White Blood Cell Count:

- Baseline is the average white blood cell (WBC) counts from 3 consecutive days, prior to challenge
- Numerical values = white blood cell count in K/µL
- Highlighted yellow = positive for leukopenia, meaning a 40% or more reduction in the total WBC count compared to baseline on that day
- NA = not applicable / no measurement on that day

Overall Result:

+ = positive for leukopenia at least one day (highlighted yellow)
- = negative for leukopenia on every day

Leukopenia in Controls (23 bovine)

ID	White Blood Cell Count per each Day Post-Challenge														Overall Result
	Base -line	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
31	7.8	7.7	7.3	3.8	NA	4.5	3.7	3.9	6.1	10.6	7	5.9	5.5	5.9	3.2	+
33	11.3	10.5	11.9	6.5	7	7.3	5.7	6	10.3	7.9	6.8	7	7.4	8.1	7.7	+
36	8.9	9.2	8.8	5.1	6.4	5.7	5.3	5.2	6.6	7.5	6.3	5.7	5.9	5.9	6	+
38	6.5	5.9	7	4.6	4.6	3.9	3.6	3.4	7	7.3	6.1	5.4	5.3	5.6	5	+
44	10.3	10.2	10	4.1	6.2	5.8	4.3	7.3	12.7	8	5.4	5.7	6.3	5.5	5.5	+
47	7.9	8.1	7.6	4.8	5.9	5.8	4.5	5.3	7.9	6.5	6.2	5.8	5.6	5.6	6	+
50	8.2	8.9	8.9	5.9	4.6	6	5.1	6.3	10.4	8.9	6.3	5.1	5.1	5.7	5.6	+
53	7.5	8.3	8.5	3.9	4.5	4.3	3.1	3.4	3.6	7.5	6.1	4.4	5.6	5.8	5.5	+
56	9.8	7.6	9.1	3.9	6	4.5	4.4	5.3	12.2	9.8	5.4	5.2	6	5.5	6.3	+
58	8.3	8.7	9.8	5.7	6.3	7.1	5.1	5.2	8.2	8.4	6.1	6.4	7.4	6.2	6.5	-
59	10.1	11.1	12.2	8.5	7.3	8.7	7.6	7.8	9.4	12.7	13	9.9	9.5	9.9	21.6	-
62	9.5	10.2	9.8	4.9	5.5	5.1	4.2	3.9	7.5	10.7	8.6	7	6.1	6.2	5.5	+
66	6.7	8.5	8	4.5	6	5.2	4.5	5.8	7	5.8	4.8	4.6	5.1	5.4	3.9	+
69	11.1	12.1	11.4	5.1	8.1	8.8	7.2	9.4	11.3	10.5	7.8	7.4	7.1	7.4	7.7	+
70	10.7	10.1	9	4.4	6	5.8	4.4	4.5	7.5	10.8	8.5	7.4	5.6	6.4	5.8	+
74	5.8	6.2	6.4	4.2	4.7	4.2	3.3	3	4	7	5.2	4.4	4.6	4.1	4.5	+
85	8.6	8	7.8	5.7	6.8	5.4	4.5	4.3	5	6.1	6.3	7.4	7.2	7.6	7.4	+
89	8.9	8.4	8.5	3.9	5.8	6.1	4.6	4.1	9.1	8.6	5.7	4.7	5.2	5.1	5.7	+
92	7.8	7.4	5.9	4.4	4.6	3.8	3.2	3.6	4.1	4.6	3.6	3.8	3.8	4.5	4.4	+
98	7.9	7.4	8	4.5	5.9	4.2	4.1	4.1	6.5	7.3	6.5	5.8	6.1	5.9	5.8	+
101	9.9	9.3	10.5	8.5	7.6	7.2	5.6	5.5	5.3	13.4	9.6	7.2	6.5	7	5.4	+
106	7.1	7.2	7.3	4.4	5.3	4.6	3.7	5.2	7.6	5.3	5.1	6.4	5.6	6.3	6.9	+
107	10.7	10.5	10.1	6.7	7.9	7	5.5	5.7	7.8	8.9	8.7	7.5	7.1	7.6	8.8	+

White Blood Cell Count:

- Baseline is the average white blood cell (WBC) counts from 3 consecutive days, prior to challenge
- Numerical values = white blood cell count in K/µL
- Highlighted yellow = positive for leukopenia, meaning a 40% or more reduction in the total WBC count compared to baseline on that day
- NA = not applicable / no measurement on that day

Overall Result:

+ = positive for leukopenia at least one day (highlighted yellow)
- = negative for leukopenia on every day

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea (BVD)
Study Purpose	Demonstration of efficacy against persistent infection of calves with BVD Type 2
Product Administration	Pregnant heifers or cows prior to breeding
Study Animals	Bovine
Challenge Description	BVD2a 96B2222 strain
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 10, 2003

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea (BVD)
Study Purpose	Demonstration of efficacy against BVD Type 2clinical disease, leukopenia, and viremia
Product Administration	
Study Animals	Bovine
Challenge Description	BVD2a IAF 103, BT-4A-2 strain
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	August 4, 2003

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	Bovine Parainfluenza Type 3 (PI_3)
Study Purpose	Demonstration of efficacy against PI_3
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	June 10, 2002

Study Type	Efficacy
Pertaining to	Bovine Respiratory Syncytial Virus (BRSV)
Study Purpose	Demonstration of efficacy against BRSV
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	June 14, 1994

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	December 10, 2002

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