



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	4X29.20
True Name	Bovine Rhinotracheitis-Virus Diarrhea Vaccine, Modified Live Virus, Mannheimia Haemolytica Toxoid
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Pyramid 3 + Presponse SQ - No distributor specified
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

Study Type	Efficacy									
Pertaining to	Bovine Virus Diarrhea (BVD)									
Study Purpose	Demonstration of efficacy against BVD Type 1 (respiratory disease) 217 days after vaccination									
Product Administration	One dose, subcutaneously									
Study Animals	46 bovine calves (23 vaccinates and 23 controls), 25 to 37 days of age									
Challenge Description	Challenged with BVD Type 1b, Isolate CA0401186A, 217 days (7 months) after vaccination									
Interval observed after challenge	Calves were observed and blood was collected for 14 days after challenge to evaluate viremia and leukopenia.									
Results	<p>Results of the study are summarized as follows:</p> <p>Blood was evaluated for viremia (the presence of virus) and leukopenia (at least one white blood cell count below 60% of pre-challenge baseline).</p> <p>Positive for Viremia and Leukopenia:</p> <table border="1"> <thead> <tr> <th></th> <th>Viremia</th> <th>Leukopenia</th> </tr> </thead> <tbody> <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> </tbody> </table> <p>See tables on the following pages for data.</p>		Viremia	Leukopenia	Vaccinates	0/23 (0%)	6/23 (26%)	Controls	22/23 (96%)	21/23 (91%)
	Viremia	Leukopenia								
Vaccinates	0/23 (0%)	6/23 (26%)								
Controls	22/23 (96%)	21/23 (91%)								
USDA Approval Date	July 14, 2014									

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/ μ L
- 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/ μ L
- 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 2 clinical 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	<i>Mannheimia haemolytica</i>
Study Purpose	Demonstration of efficacy against <i>Mannheimia haemolytica</i>
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	July 17, 1996

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

Study Type	Safety										
Pertaining to	All fractions										
Study Purpose	To demonstrate safety under field conditions										
Product Administration	One dose, subcutaneously										
Study Animals	217 Bovine calves, 5 – 6.6 months of age										
Challenge Description	Not applicable										
Interval observed after challenge	Not applicable										
Results	<p>There were no local or systemic adverse reactions related to vaccination noted in any of the 217 calves during the 14 day post-vaccination observation period. The demographics of the calves is summarized as follows:</p> <table border="1"> <thead> <tr> <th>Months of Age</th> <th>Number of Calves</th> </tr> </thead> <tbody> <tr> <td>5</td> <td>27</td> </tr> <tr> <td>5.5</td> <td>90</td> </tr> <tr> <td>6</td> <td>94</td> </tr> <tr> <td>6.6</td> <td>6</td> </tr> </tbody> </table>	Months of Age	Number of Calves	5	27	5.5	90	6	94	6.6	6
Months of Age	Number of Calves										
5	27										
5.5	90										
6	94										
6.6	6										
USDA Approval Date	October 22, 2007										