Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	4141.20
True Name	Bovine Rhinotracheitis-Virus Diarrhea Vaccine, Modified Live Virus, Campylobacter Fetus-Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Express FP 3-VL5 - 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	Bovine Virus Diarrhea (BVD)
Study Purpose	Demonstration of efficacy against persistent infection of calves with BVD Type 1
Product Administration	Pregnant heifers
Study Animals	Bovine
Challenge Description	BVD Type 1a isolate BJ
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 19, 2003

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea (BVD)
Study Purpose	Demonstration of efficacy against BVD Type 1 (respiratory disease)
Product Administration	
Study Animals	Bovine
Challenge Description	BVD Type 1 isolate NY-1
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	November 9, 1998

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	
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 2, 2002; September 25, 2002

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bovine Virus Diarrhea Type 1 (BVD1)</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of 12 month duration of immunity against BVD1 (respiratory and reproductive)</td></tr>
<tr><td>Product Administration</td><td>One dose, subcutaneously</td></tr>
<tr><td>Study Animals</td><td>Heifers (22 Vaccinates and 23 Controls), 12-15 months of age</td></tr>
<tr><td>Challenge Description</td><td>Challenged with noncytopathic BVD1b BJ strain, 12 months (368 days) after vaccination and approximately 93 days of gestation.</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed for 14 days after challenge. Blood collected on days 0, 2, 4, 6, 8, 10, 12 and 14 after challenge to evaluate viremia and leukopenia. Fetuses collected on day 72 after challenge.</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 no greater than 40% of pre-challenge baseline count).

Positive for Viremia and Leukopenia:
<table>
<tr><th></th><th>Viremia</th><th>Leukopenia</th></tr>
<tr><td>Vaccinates</td><td>0/22 (0%)</td><td>8/22 (36%)</td></tr>
<tr><td>Controls</td><td>19/23 (83%)</td><td>21/23 (91%)</td></tr>
</table>

Calves (fetuses) were considered positive for persistent BVD infection if at least one fetal tissue was positive or if heifers were open when the fetuses were harvested. The fetal tissues spleen, thymus, heart blood, and cerebellum were evaluated for the presence of BVD1 by virus isolation.

Positive for BVD Persistent Infection:
<table>
<tr><td>Vaccinates</td><td>1/22 (5%)</td></tr>
<tr><td>Controls</td><td>20/23 (87%)</td></tr>
</table>

See tables on the following pages for data.</td></tr>
<tr><td>USDA Approval Date</td><td>October 3, 2011</td></tr>
</table>

Viremia

Vaccinates (22 bovine)

Animal ID	Days Post-Challenge							
	0	2	4	6	8	10	12	14
5	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-
29	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-
56	-	-	-	-	-	-	-	-
64	-	-	-	-	-	-	-	-
77	-	-	-	-	-	-	-	-
92	-	-	-	-	-	-	-	-
120	-	-	-	-	-	-	-	-
125	-	-	-	-	-	-	-	-
149	-	-	-	-	-	-	-	-
152	-	-	-	-	-	-	-	-
156	-	-	-	-	-	-	-	-
181	-	-	-	-	-	-	-	-
185	-	-	-	-	-	-	-	-
201	-	-	-	-	-	-	-	-
223	-	-	-	-	-	-	-	-
250	-	-	-	-	-	-	-	-
260	-	-	-	-	-	-	-	-
263	-	-	-	-	-	-	-	-
277	-	-	-	-	-	-	-	-
300	-	-	-	-	-	-	-	-

Controls (23 bovine)

Animal ID	Days Post-Challenge							
	0	2	4	6	8	10	12	14
17	-	-	-	-	+	-	-	-
22	-	-	-	-	-	-	-	-
51	-	-	-	-	+	-	-	-
53	-	-	-	-	-	-	-	-
58	-	-	-	-	+	-	-	-
66	-	-	-	+	-	-	-	-
94	-	-	-	-	+	+	-	-
103	-	-	-	-	+	-	-	-
111	-	-	-	+	+	-	-	-
134	-	-	-	-	+	-	-	-
135	-	-	-	+	-	-	-	-
136	-	-	-	-	+	-	-	-
141	-	-	-	-	-	-	-	-
179	-	-	-	+	+	-	-	-
198	-	-	-	-	+	-	-	-
225	-	-	-	+	+	-	-	-
230	-	-	-	-	+	-	-	-
236	-	-	-	-	+	-	-	-
241	-	-	-	+	+	-	-	-
243	-	-	+	+	+	-	-	-
259	-	-	-	-	+	-	-	-
262	-	-	-	-	+	-	-	-
283	-	-	-	-	-	-	-	-

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

Leukopenia in Vaccinates (22 bovine)

Animal ID	White Blood Cell Count per each Day Post-Challenge									Overall Result
	Baseline (-2)	0	2	4	6	8	10	12	14	
5	6.8	7.5	6	8.9	7	10	6.6	7.7	6.7	-
11	8.8	8.1	4.9	7.3	5.4	5.6	4.9	4	5.9	+
29	7.2	6.2	3.6	4.6	5	4.5	4.7	5	4.3	+
37	8.9	7.3	6.2	6.9	6.1	4.4	7.1	4.1	3.9	+
56	6.5	5.3	6.4	4.9	5	5.3	6.8	4.8	5.1	-
64	8.8	7	7.2	8.9	8.1	6.7	5.3	7.4	6.6	-
77	5	7.1	3.3	5	5.9	5.8	3.1	3.9	2.7	+
92	6	7.1	4.6	4	5.7	5.6	4.8	5.2	4.4	-
120	8.1	4.8	5.6	7.5	5	4.9	4.7	4.7	6.9	+
125	4.6	7.8	8.3	5.3	5.3	5.7	4.8	5.1	4.1	-
149	9.1	8.3	7.4	6.7	6.6	6.2	8.4	5.9	5.5	-
152	9.4	12	8.6	5.4	6.9	6.8	5.3	7.9	7.8	+
156	8.1	10	7.3	7.1	7.3	7.9	6.6	7.1	6.6	-
181	6.8	5.7	4.9	4.6	4.2	4.5	6	3.9	2.8	+
185	7.2	4.9	5.8	5.4	7.7	7.8	5.8	5.6	5.1	-
201	7.2	8.2	6.2	5.6	6.2	6.5	5.9	6.3	8.1	-
223	7.8	7.8	8	7.6	6	5.1	5.7	5	6	-
250	7.9	6	6.2	5	5	8.5	5.6	6	5.7	-
260	9.3	6.3	5.9	6.1	7.3	5.9	6.1	6.2	6.1	-
263	7	9.7	7.2	6.8	7.6	7	7.7	6.3	8.3	-
277	11.3	5.6	6	5.9	4.9	4.5	6.8	4.1	4.1	+
300	6.2	7.2	5.2	4.4	6.3	6.7	5.5	6.5	6.9	-

White Blood Cell Count:

- Numerical values = white blood cell count in thousands of cells per cubic millimeter of blood (i.e. 6.8 equals 6,800 cells/mL^3)

Overall Result:

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

Leukopenia in Controls (23 bovine)

Animal ID	White Blood Cell Count per each Day Post-Challenge									Overall Result
	Baseline (-2)	0	2	4	6	8	10	12	14	
17	7.4	7.6	5.3	2.4	3.5	2.7	6.6	8.2	5.7	+
22	7.2	7.3	6.4	2.5	3.6	3.2	5.1	5.2	5.9	+
51	4	6.6	5.4	2.7	4.1	4	4.5	4.8	3.9	-
53	7.3	8.1	6.9	2.5	3.2	5.9	8.8	4.2	4.5	+
58	11.5	10.2	8	4	4.7	4.7	9.5	5	7.5	+
66	8.3	6.2	3.5	3.7	2.7	5	6.5	3.8	5.6	+
94	8.3	6.8	6.7	4.5	6.2	6.3	9.5	9.4	8.4	+
103	12.5	7.2	5.8	3.5	4.3	4.9	5	4.2	6.6	+
111	8.9	5.6	6.8	3.6	5.5	5.6	6.8	6.5	3.8	+
134	8.6	9.6	6.1	4.5	3.8	6.3	5.7	7.4	11.4	+
135	6.4	6.1	5.8	3.4	4	3.7	3.9	5.3	6.7	+
136	7.1	6.4	5.9	3.4	4.8	5.5	6.8	7.4	7.1	+
141	19.3	16	10.5	4.9	5.8	6.7	5.9	6.7	6.3	+
179	5.5	6.8	6.7	2	2.5	5	2.9	3.2	5.8	+
198	12.8	9	8.1	2.6	2.8	3.5	4.5	4.4	4.6	+
225	8.3	8.4	9.6	4.7	4.4	5.3	4.3	3.6	5.1	+
230	7.7	9.2	7.9	3.5	4.9	6.4	5.9	6	8	+
236	11.4	11.8	9.2	3.6	4.4	5.5	7.8	7.2	5.5	+
241	9.4	7.7	5.9	3.2	4	5.7	8.7	5.4	6.4	+
243	5	5	5.7	2.9	3.4	8.1	3.5	3.4	5.4	+
259	5.2	6.4	8.4	3.7	5.6	10.1	8.5	8.9	6.8	-
262	8.6	8.1	7.7	3.7	6.3	6.8	3.9	8.5	4.8	+
283	4.8	5.5	5.5	1.5	3	4.6	2.9	2.8	2.5	+

White Blood Cell Count:

- Numerical values = white blood cell count in thousands of cells per cubic millimeter of blood (i.e. 6.8 equals 6,800 cells/mL^3)

Overall Result:

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

Persistent Infection of Calves

Vaccinates (22 bovine)

Animal ID	Result	Virus Isolation: BVD Type 1			
		Spleen	Thymus	Heart Blood	Brain
5	Negative	-	-	-	-
11	Negative	-	-	-	-
29	Negative	-	-	-	-
37	Negative	-	-	-	-
56	Negative	-	-	-	-
64	Negative	-	-	-	-
77	Negative	-	-	-	-
92	Negative	-	-	-	-
120	Negative	-	-	-	-
125	Negative	-	-	-	-
149	Negative	-	-	-	-
152	Negative	-	-	-	-
156	Negative	-	-	-	-
181	Positive	NA	NA	NA	NA
185	Negative	-	-	-	-
201	Negative	-	-	-	-
223	Negative	-	-	-	-
250	Negative	-	-	-	-
260	Negative	-	-	-	-
263	Negative	-	-	-	-
277	Negative	-	-	-	-
300	Negative	-	-	-	-

Controls (23 bovine)

Animal ID	Result	Virus Isolation: BVD Type 1			
		Spleen	Thymus	Heart Blood	Brain
17	Positive	+	+	+	+
22	Negative	-	-	-	-
51	Positive	+	+	+	+
53	Negative	-	-	-	-
58	Positive	+	+	+	+
66	Positive	+	+	+	+
94	Positive	+	+	+	+
103	Positive	-	+	+	+
111	Positive	+	+	+	+
134	Positive	+	+	+	+
135	Positive	NA	NA	NA	NA
136	Positive	+	+	+	+
141	Positive	NA	NA	NA	NA
179	Positive	+	+	+	+
198	Negative	-	-	-	-
225	Positive	NA	NA	NA	NA
230	Positive	NA	NA	NA	NA
236	Positive	+	+	+	+
241	Positive	-	+	+	+
243	Positive	+	+	+	+
259	Positive	+	+	+	+
262	Positive	NA	NA	NA	NA
283	Positive	+	+	+	+

Result:
Positive = positive for BVD persistent infection because at least one fetal tissue was positive, or heifer was open
Negative = negative for BVD persistent infection because all fetal tissues were negative

Virus Isolation:
+ = fetal tissue positive for BVD1 by virus isolation
- = fetal tissue negative for BVD1 by virus isolation
NA = not applicable because heifer was open

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea (BVD)
Study Purpose	Demonstration of efficacy against BVD Type 2 (persistently infected calves)
Product Administration	Pregnant heifers
Study Animals	Bovine
Challenge Description	BVD Type 2a isolate PA131
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 24, 2006

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea (BVD)
Study Purpose	Demonstration of efficacy against BVD Type 2 (respiratory disease)
Product Administration	
Study Animals	Bovine
Challenge Description	BVD Type 2a isolate BVD 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	November 9, 1998

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
Study Animals	Bovine
Challenge Description	BVD Type 2 isolate PA131
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 19, 2003

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
Study Animals	Bovine
Challenge Description	BVD Type 2a isolate NY-93
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 2, 2002; September 25, 2002

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bovine Virus Diarrhea Type 2 (BVD2)</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of 12 month duration of immunity against BVD2 (respiratory and persistent infection of calves)</td></tr>
<tr><td>Product Administration</td><td>One dose, subcutaneously</td></tr>
<tr><td>Study Animals</td><td>Heifers (18 Vaccinates and 22 Controls), 13-16 months of age</td></tr>
<tr><td>Challenge Description</td><td>Challenged with noncytopathic BVD2 PA131 strain, 12 months (374 days) after vaccination and at approximately 90 days of gestation</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed for 14 days after challenge. Blood collected on days 0, 2, 4, 6, 8, 10, 12 and 14 after challenge to evaluate viremia and leukopenia. Fetuses collected on day 65 after challenge.</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 no greater than 40% of pre-challenge baseline count).

Positive for Viremia and Leukopenia:
<table><tr><th></th><th>Viremia</th><th>Leukopenia</th></tr><tr><td>Vaccinates</td><td>1/18 (6%)</td><td>1/18 (6%)</td></tr><tr><td>Controls</td><td>20/22 (91%)</td><td>14/22 (50%)</td></tr></table>
Calves (fetuses) were considered positive for persistent BVD infection if at least one fetal tissue was positive. The fetal tissues spleen, thymus, heart blood, and cerebellum were evaluated for the presence of BVD2 by virus isolation.

Positive for BVD Persistent Infection:
<table><tr><td>Vaccinates</td><td>0/18 (0%)</td></tr><tr><td>Controls</td><td>21/22 (95%)</td></tr></table>
See tables on the following pages for data.</td></tr>
<tr><td>USDA Approval Date</td><td>October 4, 2011</td></tr>
</table>

Viremia

Vaccinates (18 bovine)

Animal ID	Days Post-Challenge							
	0	2	4	6	8	10	12	14
9	-	-	-	-	-	-	-	-
21	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-
57	-	-	-	-	-	-	-	-
70	-	-	-	-	-	-	-	-
82	-	-	-	-	-	-	-	-
90	-	-	-	-	-	-	-	-
97	-	-	-	-	-	-	-	-
106	-	-	-	-	-	-	-	-
114	-	-	-	-	-	-	-	-
130	-	-	-	+	-	-	-	-
137	-	-	-	-	-	-	-	-
191	-	-	-	-	-	-	-	-
196	-	-	-	-	-	-	-	-
227	-	-	-	-	-	-	-	-
242	-	-	-	-	-	-	-	-
271	-	-	-	-	-	-	-	-
272	-	-	-	-	-	-	-	-

Controls (22 bovine)

Animal ID	Days Post-Challenge							
	0	2	4	6	8	10	12	14
2	-	-	-	-	+	-	-	-
3	-	-	-	+	+	+	-	-
7	-	-	-	+	+	-	-	-
12	-	-	-	-	-	-	-	-
20	-	-	-	-	+	+	-	-
24	-	-	-	+	+	-	-	-
27	-	-	-	-	-	-	-	-
81	-	-	-	+	+	-	-	-
88	-	-	-	+	+	+	+	-
91	-	-	-	+	-	-	-	-
145	-	-	-	+	+	+	-	-
157	-	-	-	-	+	-	-	-
159	-	-	+	+	+	+	-	+
168	-	-	-	+	+	-	-	-
170	-	-	-	+	+	-	-	-
199	-	-	-	+	+	-	-	-
202	-	-	-	+	+	-	-	-
211	-	-	-	-	+	+	-	-
224	-	-	+	+	+	+	-	-
248	-	-	-	+	+	-	-	-
269	-	-	-	+	+	+	-	-
279	-	-	-	+	+	-	-	-

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

Leukopenia in Vaccinates (18 bovine)

Animal ID	White Blood Cell Count per each Day Post-Challenge									Overall Result
	Baseline (-2)	0	2	4	6	8	10	12	14	
9	4.9	4.3	6.5	8.8	6.8	7.4	8.6	8.5	6.4	-
21	7	6.6	9	5.4	7.2	7	5.4	5.9	6.7	-
43	4	5.2	9.8	9.1	3.7	7.9	6.5	6.3	7.5	-
57	5.4	6.6	6.8	5.2	5	6.6	8.3	6.2	7.6	-
70	4.6	8.6	6.2	6	4.5	6.4	6.1	9.6	5.4	-
82	6	6.7	8.4	10.2	5.5	9.9	6.8	7.3	6.9	-
90	5	6.5	5.9	9.6	4.9	6.3	6.6	6	7.1	-
97	5.2	6.7	6.8	7.7	6.4	5.5	6.8	7	4.6	-
106	3.8	8.1	6.3	6.5	4.7	8	7.2	5.8	6.6	-
114	6.4	6.9	6.1	5.1	6.3	6.9	6.9	5.3	5.3	-
130	5.4	4.5	7.2	5.5	3.6	9.4	6.4	5.2	6.6	-
137	8	5.1	4.9	6.5	10	7.4	9.1	6.4	4.7	+
191	3.6	7.6	7.9	7.2	4.3	7.2	5.7	6.5	5.5	-
196	4.2	8.2	4.3	6.5	8.4	8.3	5	4.9	4.8	-
227	3.7	4.8	5.8	4.8	5.3	8.2	6.2	9.2	6.5	-
242	8.7	10	9	7.1	5.6	8.8	7.4	5.4	5.5	-
271	5.4	6.1	5.6	5.9	5.8	10.9	6.7	7.1	10.1	-
272	5.9	5.3	4.2	5.8	4.7	5.1	5.9	5.7	7.1	-

White Blood Cell Count:

- Numerical values = white blood cell count in thousands of cells per cubic millimeter of blood (i.e. 4.9 equals 4,900 cells/mL^3)

Overall Result:

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

Leukopenia in Controls (22 bovine)

Animal ID	White Blood Cell Count per each Day Post-Challenge									Overall Result
	Baseline (-2)	0	2	4	6	8	10	12	14	
2	4.5	6.4	8.1	2.6	4.8	3.3	4.5	7.3	8.2	+
3	10.4	6	8.9	4.8	6.7	6.1	8.3	6.4	6.7	+
7	3.7	3.8	5.4	3.9	3.6	5.2	4.3	5.1	5.1	-
12	3.4	4.6	6.2	3.7	3.7	5.4	4.5	4.9	5.5	-
20	6.3	3.4	7.5	3.5	4.3	4.8	5.5	4.3	4.5	-
24	4.5	6	7	3.1	3.6	4.4	6.2	5.1	6.9	+
27	1.5	4.3	6	2.5	1.4	2.5	5	2.8	2.9	+
81	3.2	4	7.6	2.7	3.2	4	5.6	4.4	4.3	-
88	7.2	7.9	7.3	5.9	7.5	5.4	5	6.3	5.6	-
91	5.9	7.8	9.7	3.7	4.3	7.3	12.7	9.9	11	+
145	4.3	4.2	5.5	2.9	4.5	3.6	4.3	5.7	6.7	-
157	6.4	8.6	12.1	3.1	4.9	6.9	3.8	4.5	6.5	+
159	4.8	5.6	8.3	4.4	7	4.7	4	5.1	4.1	-
168	7.7	7	5.6	4	3.4	3.8	3.7	3.9	6.6	+
170	5.2	5.5	7	3	3.7	3.8	4	4.3	4.8	+
199	3.5	4.6	4.3	3.6	3.2	5.7	3.2	3.7	5.6	-
202	5.6	5.6	6	2	5.2	2.5	1.1	3.3	4.8	+
211	5.2	8.6	7.3	3.4	3.3	2.8	6.1	4.1	5.9	+
224	2.7	6.9	5	5	6.3	3	2.2	5.3	4.8	+
248	5.9	6.4	8.2	3.4	6.2	5.5	4.2	4.1	6.6	+
269	7.2	8.1	6.4	4.8	2.6	ND	4.2	3.9	4.7	+
279	5.7	7.4	6	3	4.2	3.1	4.7	3.3	3.2	+

White Blood Cell Count:

- Numerical values = white blood cell count in thousands of cells per cubic millimeter of blood (i.e. 4.9 equals 4,900 cells/mL^3)

Overall Result:

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

Persistent Infection of Calves

Vaccinates (18 bovine)

Animal ID	Result	Virus Isolation: BVD Type 2			
		Spleen	Thymus	Heart Blood	Brain
9	Negative	-	-	-	-
21	Negative	-	-	-	-
43	Negative	-	-	-	-
57	Negative	-	-	-	-
70	Negative	-	-	-	-
82	Negative	-	-	-	-
90	Negative	-	-	-	-
97	Negative	-	-	-	-
106	Negative	-	-	-	-
114	Negative	-	-	-	-
130	Negative	-	-	-	-
137	Negative	-	-	-	-
191	Negative	-	-	-	-
196	Negative	-	-	-	-
227	Negative	-	-	-	-
242	Negative	-	-	-	-
271	Negative	-	-	-	-
272	Negative	-	-	-	-

Controls (22 bovine)

Animal ID	Result	Virus Isolation: BVD Type 2			
		Spleen	Thymus	Heart Blood	Brain
2	Positive	+	-	+	+
3	Positive	+	+	+	+
7	Positive	+	+	+	+
12	Positive	+	+	+	+
20	Positive	+	+	+	+
24	Positive	+	+	+	+
27	Positive	+	+	+	+
81	Negative	-	-	-	-
88	Positive	+	+	+	+
91	Positive	+	+	+	+
145	Positive	+	+	+	+
157	Positive	-	+	+	+
159	Positive	+	+	+	+
168	Positive	+	+	+	+
170	Positive	+	+	+	+
199	Positive	+	+	+	+
202	Positive	+	+	+	+
211	Positive	+	+	+	+
224	Positive	+	+	+	+
248	Positive	+	+	+	+
269	Positive	+	+	+	+
279	Positive	+	+	+	+

Result:
Positive = positive for BVD persistent infection because at least one fetal tissue was positive, or heifer was open
Negative = negative for BVD persistent infection because all fetal tissues were negative

Virus Isolation:
+ = fetal tissue positive for BVD2 by virus isolation
- = fetal tissue negative for BVD2 by virus isolation

Study Type	Efficacy
Pertaining to	*Campylobacter fetus*
Study Purpose	Demonstration of efficacy against infertility, delayed conception, or abortion caused by *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 requires publication of data submitted after that date.
USDA Approval Date	August 20, 1971

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	May 4, 1994

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Infectious Bovine Rhinotracheitis (IBR)</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of efficacy against IBR (reproductive disease) 12 months after vaccination</td></tr>
<tr><td>Product Administration</td><td>One dose, subcutaneously approximately five months prior to breeding</td></tr>
<tr><td>Study Animals</td><td>32 bovine (13 vaccinates and 19 controls), 7 - 9 months of age</td></tr>
<tr><td>Challenge Description</td><td>Challenged with IBR Cooper strain 386 days after vaccination at approximately 7 months of gestation</td></tr>
<tr><td>Interval observed after challenge</td><td>Cattle were observed daily after challenge and until calving for signs of abortion. Fetal tissues were evaluated for the presence of IBR and other causes of abortion.</td></tr>
<tr><td>Results</td><td>Cattle were considered affected if the fetus was aborted and testing results of the fetus were negative for other causes of abortion (Bovine viral diarrhea virus (BVDV) and abortifacient bacteria).

Results of the study are summarized as follows:

Abortions in vaccinates and controls:
<table>
<tr><th></th><th>Non-Aborted</th><th>Aborted</th></tr>
<tr><td>Vaccinates</td><td>11/13 (84.6%)</td><td>2/13 (15.4%)</td></tr>
<tr><td>Controls</td><td>1/19 (5.3%)</td><td>18/19 (94.7%)</td></tr>
</table>

See table on the following page for data.</td></tr>
<tr><td>USDA Approval Date</td><td>October 5, 2011</td></tr>
</table>

Abortion status and evaluation of fetal tissues:

Treatment	Animal	Abortion	IBR by PCR	IBR by Virus Isolation (VI)					BVDV by VI
				Brain	Kidney	Liver	Lung	Thymus	Same tissues
Vaccinates (13 bovine)	6	No	NA	NA	NA	NA	NA	NA	NA
	10	Yes	Negative	-	-	-	-	-	-
	34	No	NA	NA	NA	NA	NA	NA	NA
	45	No	NA	NA	NA	NA	NA	NA	NA
	89	No	NA	NA	NA	NA	NA	NA	NA
	117	No	NA	NA	NA	NA	NA	NA	NA
	155	No	NA	NA	NA	NA	NA	NA	NA
	176	Yes	Positive	-	-	-	-	+	-
	180	No	NA	NA	NA	NA	NA	NA	NA
	206	No	NA	NA	NA	NA	NA	NA	NA
	209	No	NA	NA	NA	NA	NA	NA	NA
	228	No	NA	NA	NA	NA	NA	NA	NA
	276	No	NA	NA	NA	NA	NA	NA	NA
Controls (19 bovine)	18	Yes	Positive	+	-	-	-	-	-
	26	Yes	Positive	-	-	-	-	-	-
	30	Yes	Positive	-	-	-	-	-	-
	41	Yes	Positive	-	-	-	-	-	-
	42	Yes	Positive	-	-	-	-	-	-
	47	Yes	Positive	-	-	-	-	-	-
	48	Yes	Positive	-	-	-	-	-	-
	62	Yes	Positive	-	-	-	+	-	-
	119	Yes	Positive	-	-	-	+	-	-
	128	No	NA	NA	NA	NA	NA	NA	NA
	154	Yes	Positive	-	-	-	-	-	-
	161	Yes	Positive	-	-	-	-	-	-
	174	Yes	Positive	-	-	-	-	-	-
	187	Yes	Positive	-	-	-	+	-	-
	194	Yes	Positive	-	-	-	-	-	-
	210	Yes	Positive	-	-	-	-	-	-
	219	Yes	Positive	-	+	-	-	-	-
	257	Yes	Positive	+	-	-	-	-	-
	282	Yes	Positive	+	-	-	+	-	-

NA = Not applicable since calf was not aborted.

Positive = Positive for the presence of IBR virus by PCR in all fetal tissues examined.
Negative = Negative for the presence of IBR virus by PCR in all fetal tissues (brain, kidney, liver, lung, and thymus).

+ = Positive for the presence of IBR or BVDV by virus isolation.
- = Negative for the presence of IBR or BVDV by virus isolation.
The same tissues were assessed for BVDV (brain, kidney, liver, lung, thymus).

Tissues were negative for abortifacient bacteria. Data not shown.

Study Type	Efficacy
Pertaining to	*Leptospira canicola*
Study Purpose	Demonstration of efficacy against leptospirosis caused by *Leptospira canicola*
Product Administration	
Study Animals	Bovine and Porcine
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 14, 1981

Study Type	Efficacy
Pertaining to	*Leptospira grippotyphosa*
Study Purpose	Demonstration of efficacy against leptospirosis caused by *Leptospira grippotyphosa*
Product Administration	
Study Animals	Bovine and Porcine
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 14, 1981

Study Type	Efficacy
Pertaining to	*Leptospira hardjo*
Study Purpose	Demonstration of efficacy against leptospirosis caused by *Leptospira hardjo*
Product Administration	
Study Animals	Bovine and Porcine
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 14, 1981

<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>32 bovine (21 vaccinates, 11 controls), 6 months of age</td></tr>
<tr><td>Challenge Description</td><td>Challenged with Leptospira borgpetersenii serovar hardjo-bovis on 84, 85 and 86 days after the second vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Cattle were observed daily after challenge. Urine samples were taken weekly for 8 weeks. On day 56 and 57 after challenge, kidneys, ovaries, and uterine tissues were cultured for Leptospira isolation.</td></tr>
<tr><td>Results</td><td>An animal was considered affected if urine cultures were positive at one or more points after challenge.

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></tr>
<tr><td>Vaccinates</td><td>0 / 21</td><td>0%</td></tr>
<tr><td>Controls</td><td>11 / 11</td><td>100%</td></tr>
</table>
Kidney cultures were positive for Leptopsira at necropsy:
<table>
<tr><th>Group</th><th># Positive / Total</th><th>% Affected</th></tr>
<tr><td>Vaccinates</td><td>0 / 21</td><td>0%</td></tr>
<tr><td>Controls</td><td>10 / 11</td><td>91%</td></tr>
</table>
Ovary cultures were positive for Leptopsira at necropsy:
<table>
<tr><th>Group</th><th># Positive / Total</th><th>% Affected</th></tr>
<tr><td>Vaccinates</td><td>0 / 21</td><td>0%</td></tr>
<tr><td>Controls</td><td>2 / 11</td><td>18%</td></tr>
</table>
No Leptospira was cultured from the uterine tissue of any of the vaccinated or control heifers at necropsy.

See tables on the following pages for data.</td></tr>
<tr><td>USDA Approval Date</td><td>April 5, 2010</td></tr>
</table>

Urine, Kidney and Ovary Cultures:

Vaccinates:

Animal #	Weekly Urine Observations								Overall Urine Outcome	Kidney Outcome	Ovary Outcome
	1	2	3	4	5	6	7	8			
2	-	-	-	-	-	-	-	-	Negative	Negative	Negative
7	-	-	-	-	-	-	-	-	Negative	Negative	Negative
10	-	-	-	-	-	-	-	-	Negative	Negative	Negative
11	-	-	-	-	-	-	-	-	Negative	Negative	Negative
12	-	-	-	-	-	-	-	-	Negative	Negative	Negative
13	-	-	-	-	-	-	-	-	Negative	Negative	Negative
14	-	-	-	-	-	-	-	-	Negative	Negative	Negative
15	-	-	-	-	-	-	-	-	Negative	Negative	Negative
16	-	-	-	-	-	-	-	-	Negative	Negative	Negative
17	-	-	-	-	-	-	-	-	Negative	Negative	Negative
30	-	-	-	-	-	-	-	-	Negative	Negative	Negative
32	-	-	-	-	-	-	-	-	Negative	Negative	Negative
37	-	-	-	-	-	-	-	-	Negative	Negative	Negative
41	-	-	-	-	-	-	-	-	Negative	Negative	Negative
42	-	-	-	-	-	-	-	-	Negative	Negative	Negative
43	-	-	-	-	-	-	-	-	Negative	Negative	Negative
49	-	-	-	-	-	-	-	-	Negative	Negative	Negative
50	-	-	-	-	-	-	-	-	Negative	Negative	Negative
51	-	-	-	-	-	-	-	-	Negative	Negative	Negative
53	-	-	-	-	-	-	-	-	Negative	Negative	Negative
54	-	-	-	-	-	-	-	-	Negative	Negative	Negative

Controls:

Animal #	Weekly Urine Observations								Overall Urine Outcome	Kidney Outcome	Ovary Outcome
	1	2	3	4	5	6	7	8			
4	-	-	+	+	+	+	+	-	Positive	Negative	Negative
5	-	-	+	+	+	+	+	+	Positive	Positive	Positive
6	-	-	+	+	+	+	+	+	Positive	Positive	Negative
9	-	-	-	+	+	+	+	+	Positive	Positive	Negative
23	-	-	-	+	+	-	+	+	Positive	Positive	Negative
27	-	-	+	+	+	-	-	+	Positive	Positive	Negative
28	-	-	+	+	+	+	+	-	Positive	Positive	Positive
31	-	-	-	-	-	+	+	-	Positive	Positive	Negative
34	-	-	+	-	+	+	+	+	Positive	Positive	Negative
35	-	-	-	+	+	-	+	+	Positive	Positive	Negative
52	-	-	-	+	+	+	+	-	Positive	Positive	Negative

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

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

Study Type	Efficacy
Pertaining to	*Leptospira icterohaemorrhagiae*
Study Purpose	Demonstration of efficacy against leptospirosis caused by *Leptospira icterohaemorrhagiae*
Product Administration	
Study Animals	Bovine and Porcine
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 14, 1981

Study Type	Efficacy
Pertaining to	*Leptospira pomona*
Study Purpose	Demonstration of efficacy against leptospirosis caused by *Leptospira pomona*
Product Administration	
Study Animals	Bovine and Porcine
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 14, 1981

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	November 16, 2006

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>All fractions</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate safety in pregnant heifers/cows and nursing calves</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered subcutaneously. First vaccination given 1 – 2 months prior to breeding. Second vaccination given during a specified trimester of pregnancy.</td></tr>
<tr><td>Study Animals</td><td><u>Site 1:</u>
2,063 cows and heifers received vaccine prior to breeding.
1,586 cows and heifers received vaccine or a placebo during pregnancy and are included in this summary.
<u>Site 2:</u>
120 calves from dams that received vaccine in the 2nd or 3rd trimester.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>Not applicable</td></tr>
<tr><td>Results</td><td>All cows and heifers were observed from pre-breeding vaccination through calving and calves were observed for 4 weeks postpartum. Results of the study are summarized as follows:

Fetal Loss (Site 1):
<table>
<tr><th rowspan="2">Trimester</th><th colspan="2">Vaccinates</th><th colspan="2">Controls (Placebo)</th></tr>
<tr><th>Enrolled</th><th>Fetal Loss (%)</th><th>Enrolled</th><th>Fetal Loss (%)</th></tr>
<tr><td>1st</td><td>306</td><td>7 (2.3%)</td><td>274</td><td>6 (2.2%)</td></tr>
<tr><td>2nd</td><td>237</td><td>1 (0.4%)</td><td>235</td><td>3 (1.3%)</td></tr>
<tr><td>3rd</td><td>267</td><td>5 (1.9%)</td><td>267</td><td>6 (2.2%)</td></tr>
</table>
The number of animals during pregnancy was reduced due to normal losses including dystocia, lameness, and non-study related causes (as affirmed by licensee).
Fetal loss was due to abortion or open (non-pregnant). For all three trimesters, no cows or heifers (0.0%) in either group were diagnosed as having aborted due to Infectious Bovine Rhinotracheitis (IBR) or Bovine Virus Diarrhea Virus (BVDV). All tests for viral detection and isolation of IBR and BVDV on all fetal tissues were negative.

<u>Fetal Infection (Site 2):</u>
Serum samples were collected from calves prior to receiving colostrum. 61 calves were from cows vaccinated in the 2nd trimester and 59 calves were from cows vaccinated in the 3rd trimester. 6 serum samples were removed from the study due to equipment malfunction or concerns that colostrum was received. All valid samples tested negative for antibodies to IBR, BVD1 and BVD2. Serum samples were also negative for IBR by virus isolation and negative for BVD1 and BVD2 by PCR.</td></tr>
</table>

USDA Approval Date	January 11, 2008