



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Bimeda Biologicals, Inc.
USDA Vet Biologics Establishment Number	290
Product Code	1121.22
True Name	Bovine Rhinotracheitis-Parainfluenza 3 Vaccine, Modified Live Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Stimulator 2 - No distributor specified
Date of Compilation Summary	December 04, 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 Rhinotracheitis (IBR)																														
Study Purpose	Demonstrate efficacy against respiratory disease																														
Product Administration	Single dose administered subcutaneously																														
Study Animals	33 mixed-breed beef calves, 4 to 5 months of age, randomly divided into 22 vaccinates and 11 controls																														
Challenge Description	IBR virus administered 28 days following vaccination																														
Interval observed after challenge	Observed daily for 14 days. Vaccinates and controls were monitored daily for nasal lesions) daily, and a nasal swab was collected from each animal daily as well. Swabs were evaluated for IBR virus by cell culture and polymerase chain reaction (PCR).																														
Results	<p>Presence of nasal lesions: 11/11 Controls 4/22 Vaccinates</p> <p>Severity of nasal lesions: Controls All 11 calves had with lesions affecting more than 50% of the visible nasal mucus membrane Vaccinates The 4 affected calves had nasal lesions that did not exceed 10% of the visible nasal mucus membrane</p> <p>Duration of nasal lesions Controls 10/11 controls had unresolved nasal lesions at the end of the observation period Vaccinates No lesions evident by the end of the study.</p> <p>Duration of nasal shedding of virus, in days:</p> <table border="1"> <thead> <tr> <th></th> <th>Min</th> <th>1st Quartile</th> <th>Median</th> <th>3rd Quartile</th> <th>Max</th> </tr> </thead> <tbody> <tr> <td>Control (CPE*)</td> <td>9</td> <td>10</td> <td>11</td> <td>12</td> <td>13</td> </tr> <tr> <td>Vaccinate (CPE)</td> <td>6</td> <td>8</td> <td>9</td> <td>10</td> <td>14</td> </tr> <tr> <td>Control (PCR)</td> <td>10</td> <td>10</td> <td>11</td> <td>12</td> <td>13</td> </tr> <tr> <td>Vaccinate (PCR)</td> <td>6</td> <td>8</td> <td>9</td> <td>10</td> <td>14</td> </tr> </tbody> </table> <p>*CPE= cytopathic effect in cell culture</p> <p>See Next Page for Raw Data.</p>		Min	1 st Quartile	Median	3 rd Quartile	Max	Control (CPE*)	9	10	11	12	13	Vaccinate (CPE)	6	8	9	10	14	Control (PCR)	10	10	11	12	13	Vaccinate (PCR)	6	8	9	10	14
	Min	1 st Quartile	Median	3 rd Quartile	Max																										
Control (CPE*)	9	10	11	12	13																										
Vaccinate (CPE)	6	8	9	10	14																										
Control (PCR)	10	10	11	12	13																										
Vaccinate (PCR)	6	8	9	10	14																										
USDA Approval Date	September 25, 2012																														

Bovine Nasal Lesion Scores

Calf ID	Group	Observation Day (Challenge administered on Day 0)																	
		Day -2	Day -1	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	
2	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	Vaccinate	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0
11	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	Vaccinate	0	0	0	0	0	0	1	1	1	1	1	1	1	1	0	0	0	0
15	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
27	Vaccinate	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0
28	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
29	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
101	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
108	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
111	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
112	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
115	Vaccinate	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
117	Vaccinate	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0	0
1	Control	0	0	0	0	0	0	1	4	4	4	4	4	4	4	4	4	4	4
4	Control	0	0	0	0	0	1	2	4	4	4	4	4	4	4	4	4	4	3
9	Control	0	0	0	0	0	0	1	1	3	4	3	3	2	1	0	0	0	0
17	Control	0	0	0	0	0	1	2	3	4	4	4	4	4	4	4	2	1	1
21	Control	0	0	0	0	0	1	1	3	4	4	4	4	4	4	3	3	3	3
22	Control	0	0	0	0	0	1	3	3	4	4	4	4	3	3	3	2	2	2
23	Control	0	0	0	0	0	1	3	4	4	4	4	4	4	4	4	4	3	3
30	Control	0	0	0	0	0	1	2	3	4	4	4	4	4	4	4	4	4	2
116	Control	0	0	0	0	0	1	3	4	4	4	4	4	3	3	3	3	2	2
118	Control	0	0	0	0	0	0	1	3	4	4	4	4	4	4	3	2	2	2
124	Control	0	0	0	0	0	0	1	2	3	4	4	4	4	4	4	3	2	1

Score Description

- 0 Absence of definitive lesions of IBR virus disease.
- 1 The presence of lesions characteristic of IBR disease not to exceed 10% of the visible nasal mucous membrane.
- 2 The presence of lesions characteristic of IBR disease affecting 11-25% of the visible nasal mucous membrane.
- 3 The presence of lesions characteristic of IBR disease affecting 26-50% of the visible nasal mucous membrane.
- 4 The presence of lesions characteristic of IBR disease affecting greater than 50% of the visible nasal mucous membrane.

Isolation of IBR virus from nasal swabs

Calf	Group	4/11/2012	4/12/2012	4/13/2012	4/14/2012	4/15/2012	4/16/2012	4/17/2012	4/18/2012	4/19/2012	4/20/2012	4/21/2012	4/22/2012	4/23/2012	4/24/2012	4/25/2012
		Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
2	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	+/+	-/-	-/-
7	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	+/+
11	Vaccinate	-/-	+/+	+/+	-/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-
12	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	+/+	-/-
13	Vaccinate	-/-	+/+	+/+	-/-	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-
14	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	-/-
15	Vaccinate	-/-	+/+	+/+	+/+	-/-	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-
16	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	-/-	-/-
19	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-
20	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	-/-
25	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-
27	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/+	-/-	-/-	-/-	-/-	-/-
28	Vaccinate	-/-	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	-/-
29	Vaccinate	-/-	-/-	-/-	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	-/-
31	Vaccinate	-/-	+/+	+/+	+/+	-/-	+/+	-/-	+/+	-/-	-/-	-/-	-/-	-/-	-/-	-/-
101	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-
103	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	-/-
108	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	-/+	-/-	+/+	-/-	-/-	-/-	-/-	-/-	-/-
111	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-
112	Vaccinate	-/-	+/+	-/-	-/-	-/-	+/+	+/+	+/+	-/-	+/+	+/+	-/+	-/-	-/-	-/-
115	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	-/-	+/+	-/-	+/+	-/+	-/-	-/-	-/-
117	Vaccinate	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	-/-	-/-

1	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-
4	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-
9	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-
17	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-
21	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-
22	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-
23	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-
30	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-
116	Control	-/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-	-/-
118	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	-/-	-/-	-/-	-/-
124	Control	-/-	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	-/-	+/+	+/+	-/-

- / - = Neg CPE/Neg PCR, - / + = Neg CPE / Pos PCR, + / + = Pos CPE / Pos PCR

Study Type	Efficacy
Pertaining to	Parainfluenza Virus Type 3.
Study Purpose	Pivotal Efficacy against PI3
Product Administration	Single Dose administered subcutaneously
Study Animals	30 mixed breed beef calves, 4 to 5 months of age randomly divided into 20 vaccinates and 10 controls
Challenge Description	PI3 administered 28 days following vaccination
Interval observed after challenge	Observed daily for 14 days clinical signs and a nasal swab was collected from each animal daily as well.
Results	<p>An animal was considered affected if virus was detected from cultured nasal swabs. Results are provided in the tables below.</p> <p>There were no clinical signs observed in either group.</p>
USDA Approval Date	January 24, 2013

Viral Isolation determined by Cytopathic Event (CPE)

Calf	Grp	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Total Days
1	v	-	+	+	+	-	+	+	-	-	-	-	-	-	-	-	5
2	v	-	+	+	+	+	+	-	-	-	-	-	-	-	-	-	5
4	v	-	+	+	+	+	+	+	-	-	-	-	-	-	-	-	6
5	v	-	-	+	+	-	+	-	-	-	-	-	-	-	-	-	4
6	v	-	+	+	+	-	+	-	-	-	-	-	-	-	-	-	3
10	v	-	+	+	+	+	+	+	-	-	-	-	-	-	-	-	5
11	v	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	2
13	v	-	+	+	+	-	-	-	+	-	-	-	-	-	-	-	4
15	v	-	-	+	+	-	+	+	-	-	-	-	-	-	-	-	5
16	v	-	+	+	+	-	+	+	-	-	-	-	-	-	-	-	4
17	v	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-	2
18	v	-	-	+	+	+	+	-	-	-	-	-	-	-	-	-	3
19	v	-	+	+	+	-	-	-	+	-	-	-	-	-	-	-	3
20	v	-	+	+	+	-	+	+	-	-	-	-	-	-	-	-	4
21	v	-	+	+	+	-	-	+	-	-	-	-	-	-	-	-	4
22	v	-	+	+	+	-	+	-	-	-	-	-	-	-	-	-	3
25	v	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-	4
26	v	-	+	+	-	-	-	-	-	+	-	-	-	-	-	-	2
27	v	-	+	+	+	+	-	-	-	-	+	-	-	-	-	-	4
30	v	-	+	+	+	+	-	+	-	-	-	-	-	-	-	-	5
3	c	-	-	+	+	+	+	+	-	+	+	+	-	-	-	-	8
7	c	-	+	+	+	+	+	+	+	-	-	-	-	-	-	-	7
8	c	-	+	+	+	+	+	+	+	+	+	+	-	-	-	-	10
9	c	-	-	+	+	+	+	+	+	+	+	+	-	-	-	-	8
12	c	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	13
14	c	-	+	+	+	-	+	+	+	+	+	+	-	-	-	-	8
23	c	-	-	+	+	+	+	+	+	+	+	+	-	-	-	-	8
24	c	-	+	+	+	+	+	+	+	+	+	+	+	-	-	-	10
28	c	-	-	+	+	+	+	+	+	+	+	+	-	-	-	+	10
29	c	-	-	+	+	+	+	+	+	+	+	+	+	+	-	-	10

v = vaccinate
c = control
+ = positive
- = negative

Viral Isolation determine by Polymerase Chain Reaction (PCR)

caif	grp	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Total Days
1	V	-	+	+	+	-	+	+	-	-	-	-	-	-	-	-	5
2	V	-	+	+	+	+	+	-	-	-	-	-	-	-	-	-	5
4	V	-	+	+	+	+	+	+	-	-	-	-	-	-	-	-	6
5	V	-	-	+	+	-	+	-	+	-	-	-	-	-	-	-	4
6	V	-	+	+	+	-	+	-	-	-	-	-	-	-	-	-	3
10	V	-	+	+	+	+	-	+	-	-	+	-	-	-	-	-	6
11	V	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	2
13	V	-	+	+	+	-	-	-	+	-	-	-	-	-	-	-	5
15	V	-	-	+	+	-	+	+	-	-	-	-	-	-	-	-	5
16	V	-	+	+	+	-	-	+	-	-	-	-	-	-	-	-	4
17	V	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-	2
18	V	-	+	+	+	+	+	-	-	-	-	-	-	-	-	-	4
19	V	-	+	+	+	-	-	-	+	-	-	-	-	-	-	-	3
20	V	-	+	+	+	-	+	+	-	-	-	-	-	-	-	-	4
21	V	-	+	+	+	-	-	+	-	-	-	-	-	-	-	-	4
22	V	-	+	+	+	-	+	-	-	-	-	-	-	-	-	-	3
25	V	-	+	+	+	-	-	-	-	+	-	-	-	-	-	-	5
26	V	-	+	+	-	-	-	-	-	-	+	-	-	-	-	-	3
27	V	-	+	+	+	-	-	-	-	-	+	-	-	-	-	-	4
30	V	-	+	+	+	+	-	+	-	-	+	-	-	-	-	-	6
3	C	-	-	+	+	+	+	+	-	+	+	+	-	-	-	-	8
7	C	-	+	+	+	+	+	+	+	-	-	-	-	-	-	-	7
8	C	-	+	+	+	+	+	+	+	+	+	+	+	-	-	-	10
9	C	-	-	+	+	+	+	+	+	+	+	+	+	-	-	-	8
12	C	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	13
14	C	-	+	+	+	+	+	+	+	+	+	+	+	-	-	-	8
23	C	-	-	+	+	+	+	+	+	+	+	+	+	-	-	-	8
24	C	-	+	+	+	+	+	+	+	+	+	+	+	-	-	-	11
28	C	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	11
29	C	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	10

v = vaccinate
c = control
+ = positive
- = negative

Study Type	Safety																																
Pertaining to	All																																
Study Purpose	Demonstrate safety under typical field conditions																																
Product Administration	1 dose subcutaneously																																
Study Animals	776 head of cattle ranging in age of 3 to 9 months with 70% at or below the minimum age of 5 months.																																
Challenge Description	NA																																
Interval observed after challenge	Observed daily for 21 days after vaccination																																
Results	<p>No local or systemic reactions or adverse events related to vaccination were observed.</p> <p style="text-align: center;">Summary of Field Safety Test</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th>Group</th> <th>No. Head</th> <th>Treated*</th> <th>Deaths</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>86</td> <td>0</td> <td>0</td> </tr> <tr> <td>2</td> <td>61</td> <td>0</td> <td>0</td> </tr> <tr> <td>3**</td> <td>83</td> <td>1</td> <td>2</td> </tr> <tr> <td>4</td> <td>257</td> <td>8</td> <td>0</td> </tr> <tr> <td>5</td> <td>135</td> <td>0</td> <td>0</td> </tr> <tr> <td>6***</td> <td>154</td> <td>1</td> <td>0</td> </tr> <tr> <td>Total</td> <td>776</td> <td>10</td> <td>2</td> </tr> </tbody> </table> <p>*Calves treated for pneumonia; unrelated to vaccine as affirmed by licensee. ** Two calves died of polioencephalomalacia during the study; unrelated to vaccine as affirmed by licensee. ***An umbilical hernia was observed in one calf, 2 days post vaccination; this calf was removed from the other calves for the remainder of the study, and never exhibited any adverse events related to vaccine.</p>	Group	No. Head	Treated*	Deaths	1	86	0	0	2	61	0	0	3**	83	1	2	4	257	8	0	5	135	0	0	6***	154	1	0	Total	776	10	2
Group	No. Head	Treated*	Deaths																														
1	86	0	0																														
2	61	0	0																														
3**	83	1	2																														
4	257	8	0																														
5	135	0	0																														
6***	154	1	0																														
Total	776	10	2																														
USDA Approval Date	May 7, 2013																																