Summary of Studies Supporting USDA Product Licensure

Establishment Name	Bimeda Biologicals, Inc.
USDA Vet Biologics Establishment Number	290
Product Code	1101.21
True Name	Bovine Rhinotracheitis Vaccine, Modified Live Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Stimulator IBR - No distributor specified
Date of Compilation Summary	March 02, 2021

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.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bovine Rhinotracheitis (IBR)</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against respiratory disease</td></tr>
<tr><td>Product Administration</td><td>Single dose administered subcutaneously</td></tr>
<tr><td>Study Animals</td><td>33 mixed-breed beef calves, 4 to 5 months of age, randomly divided into 22 vaccinates and 11 controls</td></tr>
<tr><td>Challenge Description</td><td>IBR virus administered 28 days following vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>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).</td></tr>
<tr><td>Results</td><td>Presence of nasal lesions:
11/11 Controls
4/22 Vaccinates

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

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.

Duration of nasal shedding of virus, in days:

<table>
<tr><th></th><th>Min</th><th>1st Quartile</th><th>Median</th><th>3rd Quartile</th><th>Max</th></tr>
<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>
</table>
*CPE= cytopathic effect in cell culture

See Next Page for Raw Data.</td></tr>
<tr><td>USDA Approval Date</td><td>September 25, 2012</td></tr>
</table>

Bovine Nasal Lesion Scores

		Observation Day (Challenge administered on Day 0)																
Calf ID	Group	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
7	Vaccinate	0	0	0	0	0	1	1	1	1	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
12	Vaccinate	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
14	Vaccinate	0	0	0	0	0	0	0	1	1	1	1	1	1	1	0	0	0
15	Vaccinate	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
19	Vaccinate	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
25	Vaccinate	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
28	Vaccinate	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
31	Vaccinate	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
103	Vaccinate	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
111	Vaccinate	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
115	Vaccinate	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
1	Control	0	0	0	0	0	0	1	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	3
9	Control	0	0	0	0	0	0	1	1	3	4	3	3	2	1	0	0	0
17	Control	0	0	0	0	0	1	2	3	4	4	4	4	4	4	4	2	1
21	Control	0	0	0	0	0	1	1	3	4	4	4	4	4	4	3	3	3
22	Control	0	0	0	0	0	0	1	3	4	4	4	4	3	3	3	2	2
23	Control	0	0	0	0	0	0	1	3	4	4	4	4	4	4	4	3	3
30	Control	0	0	0	0	0	1	1	2	3	4	4	4	4	4	4	3	2
116	Control	0	0	0	0	0	1	3	4	4	4	4	4	3	3	3	3	2
118	Control	0	0	0	0	0	0	1	3	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	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

		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
Calf	Group	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

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>All</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate safety under typical field conditions</td></tr>
<tr><td>Product Administration</td><td>1 dose subcutaneously</td></tr>
<tr><td>Study Animals</td><td>776 head of cattle ranging in age of 3 to 9 months with 70% at or below the minimum age of 5 months.</td></tr>
<tr><td>Challenge Description</td><td>NA</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for 21 days after vaccination</td></tr>
<tr><td>Results</td><td>No local or systemic reactions or adverse events related to vaccination were observed.

Summary of Field Safety Test

<table>
<tr><th>Group</th><th>No. Head</th><th>Treated*</th><th>Deaths</th></tr>
<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>
</table>
*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.</td></tr>
<tr><td>USDA Approval Date</td><td>May 7, 2013</td></tr>
</table>