Summary of Studies Supporting USDA Product Licensure

Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	4560.24
True Name	Bovine Rhinotracheitis-Virus Diarrhea-Parainfluenza 3 Vaccine, Modified Live Virus, Campylobacter Fetus-Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	PregGuard GOLD FP 10 - No distributor specified
Date of Compilation Summary	February 16, 2023

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 Viral Diarrhea Virus, type 1 (BVDV1)
Study Purpose	Demonstrate efficacious against persistently infected calves caused by BVDV1
Product Administration	
Study Animals	
Challenge Description	Non-cytopathic BVDV1 strain 816317(b)
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	02/06/2002

Study Type	Efficacy
Pertaining to	Bovine viral diarrhea virus, type 1 (BVDV1)
Study Purpose	Demonstrate 1-year duration of immunity against persistently infected calves caused by BVDV1
Product Administration	
Study Animals	
Challenge Description	Non-cytopathic BVDV1 strain 816317(b)
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	07/08/2005

Study Type	Efficacy
Pertaining to	Bovine viral diarrhea virus type 1 (BVDV1)
Study Purpose	Demonstrate efficacy against respiratory disease caused by BVDV1
Product Administration	
Study Animals	
Challenge Description	Non-cytopathic BVDV1b 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	06/27/2005

Study Type	Efficacy
Pertaining to	Bovine Virus Diarrhea (BVD) Type 1
Study Purpose	To demonstrate fetal protection against persistent infection of calves
Product Administration	One dose administered intramuscularly (IM) 35 days prior to breeding to heifers
Study Animals	20 IM vaccinated, and 10 control heifers, 13–17 months of age, seronegative to BVD1 and BVD2 (serum neutralizing antibody titers < 2) and negative for BVD persistent infection (ear notch immunohistochemistry).
Challenge Description	BVD1b (non-cytopathic) seeder calf challenge 124-138 days post vaccination
Interval observed after challenge	Dams were observed daily up to 83 days after challenge. Fetuses were assessed for persistent infection on or after 150 days of gestation
Results	Fetuses were considered persistently infected if the they were seropositive for BVD (serum neutralizing antibody titers ≥ 3) and/or tissues examined (fetal thymus, spleen, liver, lung, kidney, ear notch samples) were positive for BVD antigen (immunohistochemistry, virus isolation, and/or ELISA). Aborted fetuses were considered persistently infected. Number of BVD persistently infected calves: Controls: 10/10 Vaccinates (IM): 3/20
USDA Approval Date	03/07/2019

BVD Persistent Infection of Fetus Summary

Treatment Group	Animal Id.	Abortion	Fetal Serum NAb Titer		Fetal Tissue BVD	Fetal Tissue BVD Immunohistochemistry						Fetal Tissue BVD Viral Isolation						Persistent Infection
			BVD1	BVD2	Ear	Ear	Kidney	Liver	Lung	Spleen	Thymus	Serum	Kidney	Liver	Lung	Spleen	Thymus	
Con	15	No	<2	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
Con	25	No	<3	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
Con	34	No	<2	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
Con	37	No	<2	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
Con	47	No	<2	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
Con	53	Yes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Yes
Con	56	Yes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Yes
Con	94	No	<2	<3	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
Con	104	No	<2	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
Con	109	No	<2	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes

Con: Control; Nab: neutralizing antibody; +: fetal tissue positive for BVD; -: fetal tissue negative for BVD

Persistent Infection

Yes: positive for BVD persistent infection because at least one fetal tissue was positive for BVD by ELISA, immunohistochemistry, or viral isolation, or due to abortion of the dam
No: negative for BVD persistent infection because all fetal tissues were negative

Treatment Group	Animal Id.	Abortion	Fetal Serum NAb Titer		Fetal Tissue BVD	Fetal Tissue BVD Immunohistochemistry						Fetal Tissue BVD Viral Isolation						Persistent Infection
			BVD1	BVD2	Ear	Ear	Kidney	Liver	Lung	Spleen	Thymus	Serum	Kidney	Liver	Lung	Spleen	Thymus	
IM	10	No	<2	<3	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	14	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	19	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	29	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	36	No	<2	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
IM	41	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	43	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	44	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	45	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	51	No	<2	<2	+	+	+	+	+	+	+	+	+	+	+	+	+	Yes
IM	54	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	63	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	64	No	<2	<3	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	66	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	72	No	<2	<3	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	76	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	84	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	90	No	<2	<3	-	-	-	-	-	-	-	+	-	-	-	-	-	Yes
IM	99	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No
IM	106	No	<2	<2	-	-	-	-	-	-	-	-	-	-	-	-	-	No

Con: Control; Nab: neutralizing antibody; +: fetal tissue positive for BVD; -: fetal tissue negative for BVD

Persistent Infection

Yes: positive for BVD persistent infection because at least one fetal tissue was positive for BVD by ELISA, immunohistochemistry, or viral isolation, or due to abortion of the dam

No: negative for BVD persistent infection because all fetal tissues were negative

Study Type	Efficacy
Pertaining to	Bovine viral diarrhea virus, type 2 (BVDV2)
Study Purpose	Demonstrate efficacious against persistently infected calves caused by BVDV2
Product Administration	
Study Animals	
Challenge Description	Non-cytopathic BVDV2a strain 94B-5359a
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	08/06/2004

Study Type	Efficacy
Pertaining to	Bovine viral diarrhea virus, type 2 (BVDV2)
Study Purpose	Demonstrate efficacy against testicular infection by BVDV2.
Product Administration	
Study Animals	
Challenge Description	Non-cytopathic BVDV type 2a strain #24515
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	12/01/2003

Study Type	Efficacy
Pertaining to	Bovine viral diarrhea virus, type 2 (BVDV2)
Study Purpose	Demonstrate 1-year duration of immunity against persistently infected calves caused by BVDV2
Product Administration	
Study Animals	
Challenge Description	Non-cytopathic BVDV2a strain 94B-5359a
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	07/08/2005

Study Type	Efficacy
Pertaining to	Bovine viral diarrhea virus type 2 (BVDV2)
Study Purpose	Demonstrate efficacy against respiratory disease caused by BVDV2
Product Administration	
Study Animals	
Challenge Description	Non-cytopathic BVDV2a strain 24515
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	06/27/2005

Study Type	Efficacy
Pertaining to	Bovine Viral Diarrhea Virus, type 2 (BVDV2)
Study Purpose	Demonstrate efficacious against persistently infected calves caused by BVDV2
Product Administration	
Study Animals	Pre-breeding heifers seronegative to BVDV1 and BVDV2
Challenge Description	Non-cytopathic BVDV2a strain 94B-5359a
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	02/06/2002

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bovine viral diarrhea virus type 2 (BVDV2)</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against respiratory disease caused by BVDV2 in calves.</td></tr>
<tr><td>Product Administration</td><td>One dose was administered intramuscularly.</td></tr>
<tr><td>Study Animals</td><td>Twenty-nine, 3-4-month-old beef calves, 19 vaccinates and 10 controls. Seronegative (<1:2) to BVDV1 and BVDV2 at vaccination.</td></tr>
<tr><td>Challenge Description</td><td>BVDV2a Strain 24515 (non-cytopathic) administered 35 days following vaccination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Animals were clinically observed for 15 days following challenge. Blood samples were collected daily for 14 and 15 days for virus isolation, and white blood cell counts respectively.</td></tr>
<tr><td>Results</td><td>Viremia was defined as at least one occasion where virus was isolated post-challenge. Leukopenia was defined as ≥ 40% drop from baseline measurements at any time post-challenge. Duration of clinical signs, including nasal discharge, abnormal respiration, lethargy, gauntness, ocular discharge, hypersalivation, diarrhea, dehydration, lameness and/or reluctance to move, was evaluated.

<u>Leukopenia and Viremia Results:</u>

<table>
<tr><th rowspan="2">Treatment</th><th colspan="2">Ever Present</th></tr>
<tr><th>Leukopenia</th><th>Viremia</th></tr>
<tr><td>Controls</td><td>10/10 (100%)</td><td>10/10 (100%)</td></tr>
<tr><td>Vaccinates</td><td>0/19 (0%)</td><td>2/19 (10.5%)</td></tr>
</table>

<u>Duration of clinical signs:</u>

<table>
<tr><th>Group</th><th>Min.</th><th>Q1</th><th>Median</th><th>Q3</th><th>Max.</th></tr>
<tr><td>Controls</td><td>0</td><td>6</td><td>9</td><td>13</td><td>16</td></tr>
<tr><td>Vaccinates</td><td>0</td><td>0</td><td>1</td><td>4</td><td>12</td></tr>
</table>

See attached pages for individual animal data.</td></tr>
<tr><td>USDA Approval Date</td><td>7/17/2008</td></tr>
</table>

Clinical Disease:

Treatment	ID	Day 36	Day 37	Day 38	Day 39	Day 40	Day 41	Day 42	Day 43	Day 44	Day 45	Day 46	Day 47	Day 48	Day 49	Day 50	Day 51
Controls	14	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	0
	16	0	0	1	1	1	1	0	0	1	1	2	2	2	2	2	2
	21	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	27	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	0
	30	0	0	0	0	0	0	1	1	1	1	1	1	0	0	0	0
	35	0	0	0	1	1	0	1	1	1	1	1	2	2	2	2	2
	36	0	0	0	0	0	0	0	1	1	1	1	1	0	0	1	0
	37	0	0	0	0	0	0	1	1	1	0	1	2	2	2	2	2
	40	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0
	54	1	0	0	0	1	1	0	0	1	1	1	2	2	2	2	2
Vaccinates	02	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	03	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0
	04	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	05	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	06	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
	07	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	13	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
	25	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
	28	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
	29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	32	1	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0
	34	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	39	0	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0
	41	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0
	43	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	44	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	45	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	46	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
	53	0	0	0	0	1	0	0	0	0	1	1	1	0	0	0	0

0= Normal animal: no clinical signs. 1= Nonspecific clinical signs: clinical signs are not specific for acute BVDV infection. Clinical signs may include nasal discharge, abnormal respiration and mild lethargy. 2= Acute BVDV clinical disease: Clinical signs are moderate in degree and specific for acute BVDV infection. Clinical signs may include nasal discharge, abnormal respiration, lethargy, gauntness, ocular discharge, hypersalivation, diarrhea, dehydration, lameness and/or reluctance to move.

Leukopenia:

Treatment	ID	Leukopenia (yes / no)														
		Day 36	Day 37	Day 38	Day 39	Day 40	Day 41	Day 42	Day 43	Day 44	Day 45	Day 46	Day 47	Day 48	Day 49	Day 50
Controls	14	N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	Y	Y
	16	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	21	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
	27	N	N	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N
	30	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N
	35	N	N	N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	N
	36	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
	37	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	40	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N
	54	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Vaccinates	02	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	03	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	04	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	05	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	06	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	07	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	13	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	25	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	28	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	29	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	32	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	34	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	39	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	41	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	43	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	44	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	45	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	46	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	53	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Y= Yes for a 40% or greater drop in white blood cell count. N= No for a 40% or greater drop in white blood cell count.

Trt	ID	Individual Animal White Blood Cell Counts (x 1000/uL)																	
		Day 33	Day 34	Day 35	Day 36	Day 37	Day 38	Day 39	Day 40	Day 41	Day 42	Day 43	Day 44	Day 45	Day 46	Day 47	Day 48	Day 49	Day 50
Ctrls	14	12.8	12.6	8.7	7.0	7.4	8.5	7.3	7.1	7.9	7.6	6.9	6.7	5.4	5.7	5.2	4.0	3.6	5.0
	16	16.5	16.3	16.0	15.7	14.1	9.1	7.8	6.4	5.8	5.4	4.8	4.6	4.2	4.1	4.2	4.2	3.9	4.2
	21	12.2	12.3	10.8	11.1	10.5	7.7	6.8	5.4	5.3	4.7	5.1	6.3	6.8	5.2	5.4	5.6	5.5	7.1
	27	14.5	14.2	15.6	16.0	13.2	6.1	6.0	6.3	5.4	5.9	5.6	8.5	9.1	7.7	6.4	7.3	8.4	9.7
	30	13.4	11.8	13.0	12.1	11.9	8.1	8.3	8.5	8.4	8.6	10.1	9.3	11.7	8.2	7.7	6.9	7.6	9.0
	35	10.2	11.4	10.5	9.4	8.7	9.2	8.6	7.1	7.4	6.4	5.7	4.0	4.2	4.7	5.3	4.6	4.3	6.9
	36	16.5	16.7	18.4	18.6	17.5	8.0	9.4	8.9	7.8	7.4	6.5	6.1	9.4	8.4	10.1	8.9	10.3	13.7
	37	14.4	14.7	15.1	13.3	11.7	6.6	6.7	5.1	5.9	6.4	4.9	4.7	3.9	3.5	3.6	3.2	2.8	3.2
	40	14.7	13.5	14.7	12.6	10.9	6.4	7.3	5.6	5.0	5.8	5.8	5.8	7.9	7.5	8.6	9.8	8.6	9.8
	54	13.1	12.5	13.9	13.4	12.3	7.5	7.5	7.1	6.0	5.4	4.4	4.3	3.4	2.0	1.5	1.9	1.6	2.3
Vactes	02	20.0	20.5	20.2	18.8	19.1	19.1	17.5	17.1	15.6	14.0	16.0	14.9	13.8	15.8	16.1	17.1	15.4	17.2
	03	12.2	10.1	9.1	8.0	9.2	9.6	7.5	7.3	6.7	8.2	11.1	14.7	17.4	12.3	11.7	9.7	9.0	10.1
	04	9.8	9.4	9.1	9.8	10.4	11.1	9.2	8.8	9.6	10.1	9.2	10.6	11.0	11.7	10.8	11.1	12.0	13.6
	05	13.9	14.3	14.0	13.2	13.8	11.0	9.7	9.3	9.3	9.0	11.0	11.7	11.8	10.1	11.0	10.5	10.1	11.6
	06	11.1	11.9	10.7	10.6	11.4	10.0	7.4	7.3	8.1	8.7	11.1	8.7	8.4	8.2	10.5	9.7	8.9	9.3
	07	12.7	13.5	13.1	11.4	12.3	12.1	12.1	11.5	10.7	10.8	11.4	11.1	10.9	10.8	11.1	11.3	10.6	11.0
	13	12.5	13.6	14.1	12.4	12.1	12.0	12.0	11.7	12.3	12.0	12.6	13.8	13.5	14.3	15.8	15.3	14.2	16.9
	25	19.7	18.3	16.4	14.4	14.9	16.2	15.4	16.1	16.6	14.8	15.6	17.0	16.5	16.7	15.3	16.8	15.5	17.1
	28	13.4	13.3	13.1	13.5	12.5	12.0	11.9	11.0	12.0	11.8	11.0	10.6	10.2	10.8	11.6	11.7	9.9	11.3
	29	13.8	13.1	13.0	12.2	12.2	12.9	11.8	12.0	11.3	11.2	10.9	11.6	12.4	12.1	13.0	12.9	11.4	12.0
	32	12.5	12.4	12.6	12.9	10.8	10.5	9.3	9.3	9.1	9.9	9.8	11.9	10.8	11.0	11.5	12.4	10.7	11.3
	34	11.7	9.5	10.5	11.7	12.2	11.5	10.3	11.4	9.3	8.8	9.4	8.9	9.0	9.1	9.9	10.6	11.8	12.3
	39	17.2	17.7	15.8	14.7	15.1	14.8	14.3	14.0	14.8	13.3	12.4	12.2	11.7	11.2	11.4	11.1	10.8	11.9
	41	10.7	11.1	11.6	12.3	11.1	11.8	11.3	10.1	11.3	11.5	12.3	12.4	12.0	11.4	11.7	12.4	11.6	12.7
	43	13.4	13.3	12.8	14.3	13.1	13.8	13.0	12.5	10.5	11.1	10.5	12.7	12.8	14.8	14.0	15.0	14.0	13.2
	44	12.3	11.3	11.3	9.9	10.3	10.0	7.5	8.7	7.6	7.5	8.7	8.8	9.4	9.7	10.2	10.3	10.9	11.6
	45	12.9	13.1	12.0	12.9	9.7	10.3	11.2	11.4	10.1	13.1	12.5	13.5	14.3	15.1	13.7	14.1	14.0	14.0
	46	14.1	15.9	12.8	12.5	11.8	13.3	12.1	13.3	13.4	15.6	16.3	14.1	13.2	13.0	12.3	13.5	11.7	11.1
	53	13.5	13.6	13.8	9.9	8.2	10.5	9.5	11.9	8.7	11.5	12.3	11.9	16.5	12.5	12.3	11.3	12.6	13.6

Trt: Treatment; Ctrls: Controls; Vactes: Vaccinates
Days 33, 34 and 35 were used to set the baseline for WBC counts

Viremia:

Treatment	ID	Virus Isolation (yes / no)													
		Day 36	Day 37	Day 38	Day 39	Day 40	Day 41	Day 42	Day 43	Day 44	Day 45	Day 46	Day 47	Day 48	Day 49
Controls	14	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	16	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
	21	N	N	N	N	Y	Y	Y	Y	Y	Y	N	N	N	N
	27	N	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N	N
	30	N	N	N	N	Y	Y	Y	Y	Y	Y	Y	N	N	N
	35	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N
	36	N	N	N	Y	Y	Y	Y	Y	Y	Y	N	N	N	N
	37	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N
	40	N	N	N	N	Y	Y	Y	Y	Y	Y	Y	N	N	N
	54	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Vaccinates	02	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	03	N	N	N	N	N	Y	N	N	N	N	N	N	N	N
	04	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	05	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	06	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
	07	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	13	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	25	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	28	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	29	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	32	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	34	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	39	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	41	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	43	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	44	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	45	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	46	N	-*	N	N	N	N	N	N	N	N	N	N	N	N
	53	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Y= Yes for virus isolation from sample. N= No for virus isolation from sample. * Virus isolation data was not obtained due to loss of sample and it was excluded from data analysis.

Study Type	Efficacy
Pertaining to	*Campylobacter fetus* (*C. fetus*)
Study Purpose	Demonstrate efficacy against campylobacteriosis caused by *C. fetus*
Product Administration	
Study Animals	
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	2/21/1980

Study Type	Efficacy
Pertaining to	Infectious bovine rhinotracheitis (IBR)
Study Purpose	Demonstrate efficacy against abortion caused by infectious bovine rhinotracheitis
Product Administration	One dose administered intramuscularly (IM)
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	February 6, 2002

Study Type	Efficacy
Pertaining to	Herpesvirus, bovine (IBR)
Study Purpose	Demonstrate efficacy against respiratory disease caused by infectious bovine rhinotracheitis
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	01/08/2001

Study Type	Efficacy
Pertaining to	Herpesvirus, bovine (IBR)
Study Purpose	Demonstrate a 1 year duration of immunity against abortion caused by infectious bovine rhinotracheitis
Product Administration	
Study Animals	Pre-breeding heifers
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	07/08/2005

Study Type	Efficacy
Pertaining to	Herpesvirus, bovine (IBR)
Study Purpose	Demonstrate efficacy against respiratory disease caused by infectious bovine rhinotracheitis
Product Administration	One dose administered intramuscularly (IM)
Study Animals	20 IM vaccinates and 10 control calves, 6–8 months of age and seronegative to IBR (serum neutralizing antibody titer < 1:2). The study was conducted per 9 CFR 113.310.
Challenge Description	IBR virus administered on day 35
Interval observed after challenge	Animals were observed daily for 14 days
Results	Animals were considered to have IBR disease if a clinical sign was observed/detected on at least one day post-challenge to include depression, nasal discharge, rectal temperature, or increased respiratory effort. Number of animals affected (IBR disease): Controls: 10/10 (100%) IM vaccinates: 4/20 (20%)
USDA Approval Date	01/23/2008

IBR Disease: Depression

Treatment Group	Animal Id	Study Day														
		35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
Controls	2119	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2123	0	0	0	0	0	1	1	1	1	1	1	1	0	0	0
	2145	0	0	0	0	0	1	1	1	1	0	1	1	0	0	0
	2148	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0
	2153	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2161	0	0	0	0	0	1	1	1	1	1	1	1	1	0	0
	2171	0	0	0	0	0	1	0	1	1	1	1	0	0	0	0
	2178	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0
	2197	0	0	0	0	0	0	1	1	1	1	1	1	0	1	0
	2200	0	0	0	0	0	0	1	1	1	1	1	1	0	0	0
IM Vaccinates	2122	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2126	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2127	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2131	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2140	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2150	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2151	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2155	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2163	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2164	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2168	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2174	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2176	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2181	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2183	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2185	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2188	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2189	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2198	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2199	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

0 = Normal. Alert, active, stands, moves and responds to stimuli quickly and steadily, shows continuous interest in surroundings.
1 = Mild. Tends to lie down frequently, lethargic and somnolent, stands, moves and responds to stimuli reluctantly and unsteadily, holds head low, staggers, shows little interest in surroundings.
2 = Severe. Recumbent or shows little or no response to stimuli or stands/moves with difficulty.

IBR Disease: Nasal Discharge

Treatment Group	Animal Id	Study Day														
		35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
Controls	2119	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	2123	0	0	0	0	0	1	0	0	0	1	0	1	1	0	0
	2145	0	0	0	1	1	1	1	1	1	1	0	1	0	1	0
	2148	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0
	2153	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0
	2161	0	0	0	0	0	1	1	1	1	1	1	0	1	1	0
	2171	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	2178	0	0	0	0	1	1	0	0	0	1	1	1	0	0	0
	2197	0	0	0	0	0	1	0	1	1	1	1	1	1	0	1
	2200	0	0	0	0	0	0	1	1	1	1	1	0	1	0	0
IM Vaccinates	2121	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2124	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2125	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2128	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2129	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2130	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	2132	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2133	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2139	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2147	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2149	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2156	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0
	2162	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2166	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2167	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2169	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2172	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	2175	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2177	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2193	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

0 = No discharge/small amount of discharge (approx. 1 mL or less) of clear, mucoid or whitish discharge.
1 = Mild. Notable amount (approx. 2–3 mL or more) of clear mucoid discharge streaked with mucopurulent discharge running down the nostrils.
2 = Severe. Notable amount (approx. 2–3 mL or more) of mucopurulent discharge running down the nostrils.

IBR Disease: Respiratory Effort

Treatment Group	Animal Id	Study Day														
		35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
Controls	2119	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2123	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2145	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2148	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2153	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2161	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	2171	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	2178	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2197	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2200	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IM Vaccinates	2121	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2124	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2125	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2128	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2129	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2130	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2132	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2133	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2139	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2147	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2149	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2156	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2162	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2166	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2167	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2169	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2172	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2175	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2177	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2193	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

0 = Normal. Respirations are shallow and mostly thoracic (difficult to see at a distance of approximately 10 feet).
1 = Mild. Respirations are rapid, labored and mostly abdominal.
2 = Severe. Respirations are very labored or animal grunts during breathing.

Rectal Temperatures (°C)

Treatment Group	Animal Id	Study Day														
		35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
Controls	2119	39.1	38.9	38.9	40.9	40.4	40.4	40.5	39.9	39.5	39	38.7	38.5	38.7	38.7	38.7
	2123	39.2	39.1	40.4	41.6	41.5	41.4	40.4	40.5	40.7	40.6	39.9	39	38.9	38.8	38.6
	2145	39.4	39	39.2	41.7	41.3	41.1	40.6	39.7	40	40	38.9	38.8	39.2	39.2	39
	2148	39.1	39.3	39.3	40.8	41.3	40.4	40.4	40	39.5	39.1	39	39.1	38.7	38.7	38.6
	2153	39.4	39.2	39.3	39.9	40.7	40.4	40	39	39.6	39.2	39.2	38.9	39.3	39.3	39.1
	2161	39.2	39.6	41	42.3	41.7	41.5	40.9	40.4	40.1	39.9	39.3	39.3	38.9	39	38.7
	2171	39.3	39.2	39.3	41.8	40.7	40.9	40.7	40.6	40.6	40.6	39.6	39.3	38.8	39.2	38.6
	2178	39.2	39.2	38.8	41.2	41.7	41.2	41.1	40.7	40.1	39.4	39.2	39.1	38.9	39.1	39.1
	2197	39.1	39	39.4	41.6	41.4	40.4	40.4	40.5	39.6	39.7	39	39.1	38.6	38.9	38.8
	2200	39.5	39.3	39.3	41.1	40.6	40.9	40.3	40.2	39.7	39.8	38.9	39.1	38.8	38.9	39.1
IM Vaccinates	2121	38.9	39.1	38.9	38.7	39	39	38.8	38.9	39.2	38.7	39.1	38	38.7	38.9	38.9
	2124	39	38.9	39.1	39.2	39	39	39.1	38.9	39.1	38.8	39.2	38.9	39	38.7	38.9
	2125	39	38.8	38.8	38.8	38.9	38.8	38.8	38.9	38.9	38.9	39.1	39.1	38.9	39	39.1
	2128	39.2	39	39.1	38.9	38.9	39.1	38.7	39.2	39.1	38.9	38.9	38.9	38.9	38.9	38.8
	2129	39	39.2	39.2	39.3	39.3	39.2	38.9	39.4	39.1	39.1	39.4	38.7	38.9	38.8	39.1
	2130	39	39.2	39	39.3	38.9	38.9	38.9	39.1	39.2	39	39	39.1	38.7	38.6	38.8
	2132	39.6	39.9	39.4	39.2	39.5	39.4	39.2	39	39.2	39	39.3	39.1	39.2	39	39.1
	2133	38.9	38.8	38.8	38.9	38.8	38.8	38.9	38.7	38.8	38.6	39.1	38.8	38.8	38.6	38.7
	2139	39	39.2	39.4	38.7	38.9	38.8	39	39.1	38.7	38.9	38.7	38.9	38.9	39	38.8
	2147	39	39	38.9	38.8	39	38.9	38.8	38.8	38.7	38.7	38.6	38.8	39.2	38.7	38.8
	2149	39.2	39.2	38.9	39.1	39	38.8	38.8	38.9	38.7	38.7	39.2	38.7	38.7	38.7	38.9
	2156	39	38.9	38.9	39.1	39.2	39.3	39.2	38.8	38.6	38.8	38.9	38.7	38.9	38.8	39.1
	2162	38.9	39.3	39.3	38.9	39.2	39.4	38.9	39	39	38.9	39.4	38.9	38.8	38.7	39.1
	2166	39.2	39.1	38.9	39.3	39.1	39.1	38.8	39	38.9	39.2	39.3	39.1	38.9	38.9	38.8
	2167	38.9	38.6	38.7	38.7	38.7	38.7	38.9	38.6	38.7	38.8	38.6	38.8	38.7	38.9	38.7
	2169	39.3	39.1	38.9	39	39	39.3	38.9	39	39.2	38.9	39.1	39.1	38.8	39	39
	2172	39.9	39	38.8	39.2	38.8	38.9	39.1	39.1	38.9	38.9	38.9	39	38.9	38.8	38.6
	2175	39.1	38.8	38.6	38.6	38.9	39	38.7	38.7	38.8	38.6	38.9	39	38.7	38.9	38.6
	2177	39.1	39.5	39.3	39.3	39	39	38.9	39.1	38.7	39	39.6	38.9	39.1	38.9	39
	2193	39	39.3	39	39.1	39.3	38.9	38.8	39.5	39.1	39	38.8	38.8	38.6	38.7	39

IBR Serum Neutralization

Treatment Group	Animal Id	Study Day			
		0	27	34	49
Controls	2119	<2	<2	<2	38
	2123	<2	<2	<2	23
	2145	<2	<2	<2	76
	2148	<2	<2	<2	54
	2153	<2	<2	<2	38
	2161	<2	<2	<2	54
	2171	<2	<2	<2	76
	2178	<2	<2	<2	27
	2197	<2	<2	<2	76
	2200	<2	<2	<2	76
IM Vaccinates	2121	<2	23	27	128
	2124	<2	16	16	256
	2125	<2	16	19	45
	2128	<2	19	19	362
	2129	<2	16	16	54
	2130	<2	27	23	256
	2132	<2	13	16	304
	2133	<2	38	45	304
	2139	<2	32	45	76
	2147	<2	13	16	256
	2149	<2	45	38	181
	2156	<2	13	13	91
	2162	<2	13	10	609
	2166	<2	11	13	431
	2167	<2	27	23	108
	2169	<2	11	13	152
	2172	<2	19	23	152
	2175	<2	13	16	152
	2177	<2	6	6	256
	2193	<2	45	45	181

Titers are expressed as the greatest neutralizing dilution.

Study Type	Efficacy
Pertaining to	Herpesvirus, bovine [Infectious Bovine Rhinotracheitis (IBR)]
Study Purpose	Demonstrate efficacy against respiratory disease caused by IBR
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	01/08/2001

Study Type	Efficacy
Pertaining to	*Leptospira interrogans* serovar c*anicola* (*L canicola*)
Study Purpose	Demonstration of efficacy against leptospirosis caused by *L. canicola*
Product Administration	One dose administered intramuscularly
Study Animals	15 Calves approximately 6 months of age; 10 vaccinates and 5 controls. All animals were seronegative for *Leptospira canicola, icterohaemorrhagiae, hardjo, grippotyphosa, pomona*.
Challenge Description	Animals were challenged 3 weeks following vaccination.
Interval observed after challenge	Animals were observed post challenge for 8 days. Body temperatures and blood samples were collected daily.
Results	Leptospira Isolation Results in Blood: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive Temperature Results: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive See the following tables for individual raw data
USDA Approval Date	09/13/1977

Blood culture for isolation of Leptospires:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)							
		1	2	3	4	5	6	7	8
CONTROLS	45	+	+	+	-	-	-	-	-
	68	+	+	-	-	-	-	-	-
	75	+	+	+	-	-	-	-	-
	86	+	+	-	-	-	-	-	-
	106	+	+	+	-	-	-	-	-
VACCINATES	39	-	-	-	-	-	-	-	-
	57	-	-	-	-	-	-	-	-
	63	-	-	-	-	-	-	-	-
	67	-	-	-	-	-	-	-	-
	82	-	-	-	-	-	-	-	-
	85	-	-	-	-	-	-	-	-
	92	-	-	-	-	-	-	-	-
	99	-	-	-	-	-	-	-	-
	103	-	-	-	-	-	-	-	-
	104	-	-	-	-	-	-	-	-

+: Leptopires detected; -: Leptopires not detected

Temperature in ºF:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)								
		0	1	2	3	4	5	6	7	8
CONTROLS	45	102.4	101.0	104.4	107.2	106.2	103.6	103.8	101.6	100.8
	68	102.2	102.0	106.6	106.8	103.6	101.2	102.8	101.0	100.6
	75	102.0	102.0	102.0	106.6	106.4	101.4	101.6	101.6	101.8
	86	102.4	103.4	105.6	106.4	105.2	101.8	102.4	102.0	102.0
	106	102.0	102.0	104.0	104.8	104.4	102.8	101.6	101.4	101.0
VACCINATES	39	102.2	101.6	102.0	102.0	102.0	102.0	102.6	103.0	102.2
	57	101.2	102.0	101.4	101.0	101.0	100.2	100.8	100.8	100.2
	63	101.6	101.0	101.0	100.8	100.6	100.4	101.0	101.0	101.4
	67	102.0	102.0	101.6	101.0	101.4	101.8	101.8	101.6	102.0
	82	102.4	102.4	101.6	100.8	101.4	101.0	101.8	102.2	100.2
	85	100.8	102.8	101.4	100.4	100.6	100.2	100.6	101.0	100.8
	92	102.0	101.6	101.0	100.6	100.8	100.0	101.4	101.6	101.2
	99	102.0	102.0	101.4	101.8	102.0	101.4	101.6	101.6	100.6
	103	102.8	102.0	102.0	101.4	100.8	100.0	101.0	101.0	100.8
	104	101.8	101.6	102.0	101.2	101.2	101.2	101.4	101.4	100.6

Temperature >103 ºF was considered as pyrexia

Study Type	Efficacy
Pertaining to	*Leptospira interrogans* serovar *grippotyphosa* (*L Grippotyphosa*)
Study Purpose	Demonstration of efficacy against leptospirosis caused by *L. Grippotyphosa*
Product Administration	One dose
Study Animals	15 Calves; 10 vaccinates and 5 controls. All animals were seronegative for *Leptospira Grippotyphosa, hardjo, pomona*.
Challenge Description	Animals were challenged 8 weeks following vaccination.
Interval observed after challenge	Animals were observed for 8 days post challenge. Body temperatures and blood samples were collected daily.
Results	Leptospira Isolation Results in Blood: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive Temperature Results: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive See the following tables for individual raw data
USDA Approval Date	12/09/1975

Blood culture for isolation of Leptospires:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)							
		1	2	3	4	5	6	7	8
CONTROLS	161	+	+	+	+	+	-	-	-
	164	+	+	+	+	-	-	-	-
	165	+	+	+	+	-	-	-	-
	241	+	+	-	-	-	-	-	-
	248	+	+	+	-	-	-	-	-
VACCINATES	130	-	-	-	-	-	-	-	-
	137	-	-	-	-	-	-	-	-
	143	-	-	-	-	-	-	-	-
	145	-	-	-	-	-	-	-	-
	155	-	-	-	-	-	-	-	-
	247	-	-	-	-	-	-	-	-
	250	-	-	-	-	-	-	-	-
	255	-	-	-	-	-	-	-	-
	260	-	-	-	-	-	-	-	-
	261	-	-	-	-	-	-	-	-

+: Leptospires detected; -: Leptospires not detected

Temperature in ºF:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)								
		0	1	2	3	4	5	6	7	8
CONTROLS	161	101.6	102.4	102.2	105.4	104.8	104.4	99.4	100.6	102.8
	164	101.4	101.8	105.8	104.6	106.4	103.6	101.4	101.4	101.4
	165	102.0	102.6	102.2	104.0	104.4	104.8	101.8	102.2	102.0
	241	102.2	101.8	101.2	105.4	103.8	104.2	100.4	101.0	101.2
	248	101.6	100.4	101.8	106.0	104.4	103.6	101.0	101.2	101.6
101.4VACCINATES	130	102.0	102.0	102.0	102.4	101.6	101.4	100.2	101.4	101.8
	137	101.6	101.8	101.8	102.0	101.8	101.4	100.6	100.8	101.0
	143	102.0	101.8	101.8	101.8	102.4	101.8	100.4	99.8	101.2
	145	102.0	101.4	101.4	101.8	102.4	101.6	99.6	101.2	101.4
	155	102.2	102.0	102.0	102.4	102.2	101.2	100.0	100.4	100.8
	247	101.4	100.8	101.6	101.6	101.6	101.8	100.0	100.6	100.8
	250	101.8	102.0	102.2	101.4	101.6	101.6	101.2	101.4	101.8
	255	102.4	101.8	101.8	102.6	102.2	102.4	101.8	102.0	101.4
	260	102.0	102.6	102.8	102.4	102.0	101.6	100.0	101.2	101.2
	261	102.2	100.6	101.2	101.4	101.4	101.0	100.2	100.4	100.6

Temperature >103.5 ºF was considered as pyrexia

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Leptospira hardjo (L. hardjo)</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against leptospirosis caused by L. hardjo</td></tr>
<tr><td>Product Administration</td><td>One dose</td></tr>
<tr><td>Study Animals</td><td>Sera (pre-vaccination and 3 weeks post-vaccination, 1:4 diluted and undiluted) from 20 vaccinated cattle were obtained and were administered intraperitoneally to hamsters. Four hamsters were used for each sera..</td></tr>
<tr><td>Challenge Description</td><td>Hamsters were challenged with a virulent L. hardjo inoculate one day post administration of cattle sera.</td></tr>
<tr><td>Interval observed after challenge</td><td>Hamsters were humanely euthanized 14 days post challenge and kidneys examined for L. hardjo culture.</td></tr>
<tr><td>Results</td><td><u>L. hardjo Isolation in Hamster Kidneys Summary:</u>

<table>
<tr><th>Cattle Sera</th><th>Hamsters Positive for L. hardjo / Tested (%)</th></tr>
<tr><td>Pre vaccination</td><td>76/80 (95%)</td></tr>
<tr><td>1:4 dilution Post-vaccination</td><td>50/80 (62.5%)</td></tr>
<tr><td>Undiluted Post-vaccination</td><td>25/80 (31.25%)</td></tr>
</table>

See table for individual data</td></tr>
<tr><td>USDA Approval Date</td><td>08/22/1978</td></tr>
</table>

Bovine Serological Titers and Hamster Passive protection testing:

Cattle ID	Bovine Serological Titers		Hamster Kidney Isolations Positive / Total
354	Pre vaccination	-	4/4
	1:4 dilution		1/4
	Undiluted	64	0/4
355	Pre vaccination	-	4/4
	1:4 dilution		4/4
	Undiluted	4	1/4
358	Pre vaccination	-	3/4
	1:4 dilution		4/4
	Undiluted	16	2/4
359	Pre vaccination	-	4/4
	1:4 dilution		4/4
	Undiluted	32	0/4
390	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	8	3/4
361	Pre vaccination	-	4/4
	1:4 dilution		1/4
	Undiluted	64	1/4
375	Pre vaccination	-	3/4
	1:4 dilution		1/4
	Undiluted	128	1/4
376	Pre vaccination	-	4/4
	1:4 dilution		2/4
	Undiluted	128	0/4
381	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	16	3/4
382	Pre vaccination	-	4/4
	1:4 dilution		2/4
	Undiluted	32	0/4
357	Pre vaccination	4	4/4
	1:4 dilution		3/4
	Undiluted	32	3/4
386	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	32	2/4
389	Pre vaccination	-	4/4
	1:4 dilution		0/4
	Undiluted	32	0/4

394	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	16	1/4
No Ears	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	64	0/4
424	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	32	1/4
426	Pre vaccination	-	4/4
	1:4 dilution		3/4
	Undiluted	16	2/4
427	Pre vaccination	-	4/4
	1:4 dilution		4/4
	Undiluted	16	2/4
435	Pre vaccination	-	3/4
	1:4 dilution		0/4
	Undiluted	256	1/4
438	Pre vaccination	-	3/4
	1:4 dilution		3/4
	Undiluted	32	2/4

1:4 dilution Post-vaccination
Undiluted Post-vaccination
- is Negative

Study Type	Efficacy
Pertaining to	*Leptospira interrogans* serovar icterohaemorrhagiae (*L. icterohaemorrhagiae*)
Study Purpose	Demonstration of efficacy against leptospirosis caused by *L. icterohaemorrhagiae*
Product Administration	One dose administered intramuscularly
Study Animals	15 Calves approximately 6 months of age; 10 vaccinates and 5 controls. All animals were seronegative for *Leptospira canicola, icterohaemorrhagiae, hardjo, grippotyphosa, pomona*.
Challenge Description	Animals were challenged 7 weeks following vaccination.
Interval observed after challenge	Animals were observed for 8 days post challenge. Body temperatures and blood samples were collected daily.
Results	Leptospira Isolation Results in Blood: Controls: 4/5 (80 %) positive Vaccinates: 0/10 (0 %) positive Temperature Results: Controls: 5/5 (100 %) positive Vaccinates: 0/10 (0 %) positive See the following tables for individual raw data
USDA Approval Date	09/13/1977

Blood culture for isolation of Leptospires:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)							
		1	2	3	4	5	6	7	8
CONTROLS	66	+	+	-	-	-	-	-	-
	71	+	+	-	-	-	-	-	-
	79	+	+	+	-	-	-	-	-
	113	+	+	-	-	-	-	-	-
	120	-	-	-	-	-	-	-	-
VACCINATES	58	-	-	-	-	-	-	-	-
	69	-	-	-	-	-	-	-	-
	80	-	-	-	-	-	-	-	-
	102	-	-	-	-	-	-	-	-
	107	-	-	-	-	-	-	-	-
	114	-	-	-	-	-	-	-	-
	121	-	-	-	-	-	-	-	-
	122	-	-	-	-	-	-	-	-
	124	-	-	-	-	-	-	-	-
	128	-	-	-	-	-	-	-	-

+: Leptopires detected; -: Leptopires not detected

Temperature in ºF:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)								
		0	1	2	3	4	5	6	7	8
CONTROLS	66	101.0	103.6	104.8	101.0	100.8	101.2	100.0	100.4	101.0
	71	101.0	104.0	102.0	102.2	101.8	101.4	100.4	102.0	101.4
	79	101.6	103.0	104.8	103.0	102.4	102.0	102.0	101.8	102.4
	113	101.4	104.4	104.2	102.8	100.8	100.2	101.0	101.2	101.4
	120	100.0	105.4	103.0	102.6	102.0	101.2	100.6	101.0	100.8
VACCINATES	58	99.8	101.6	101.4	101.4	101.8	101.6	101.0	101.2	102.4
	69	101.0	100.2	102.4	102.4	102.0	101.2	101.2	101.2	101.6
	80	101.4	101.8	101.4	101.0	102.0	101.6	100.6	101.0	101.6
	102	101.2	101.6	101.4	102.0	102.0	100.6	101.4	101.0	102.0
	107	101.2	102.0	101.8	99.8	101.8	101.0	100.8	101.6	101.4
	114	101.0	101.8	101.6	101.6	101.6	102.0	101.0	101.4	101.4
	121	101.4	101.8	102.0	101.8	101.8	101.4	102.0	101.2	102.2
	122	101.2	100.4	101.8	102.0	101.6	101.6	101.8	101.8	101.4
	124	101.4	101.4	101.4	101.0	101.6	100.8	101.0	101.2	101.8
	128	101.2	101.4	101.2	101.4	102.4	101.4	100.8	102.2	101.2

Temperature >103 ºF was considered as pyrexia

Study Type	Efficacy
Pertaining to	*Leptospira interrogans* serovar p*omona* (*L pomona*)
Study Purpose	Demonstration of efficacy against leptospirosis caused by *L. Pomona*
Product Administration	One dose
Study Animals	15 Calves; 10 vaccinates and 5 controls. All animals were seronegative for *Leptospira grippotyphosa, hardjo, pomona*.
Challenge Description	Animals were challenged 5 weeks following vaccination.
Interval observed after challenge	Animals were observed for 8 days post challenge. Body temperatures and blood samples were collected daily.
Results	Leptospira Isolation Results in Blood: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive Temperature Results: Controls: 5/5 (100%) positive Vaccinates: 0/10 (0%) positive See the following tables for individual raw data
USDA Approval Date	12/09/1975

Blood culture for isolation of Leptospires:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)							
		1	2	3	4	5	6	7	8
CONTROLS	159	+	+	+	+	-	-	-	-
	163	+	+	+	-	-	-	-	-
	244	+	+	+	-	-	-	-	-
	252	+	+	+	-	-	-	-	-
	265	+	+	+	-	-	-	-	-
VACCINATES	134	-	-	-	-	-	-	-	-
	135	-	-	-	-	-	-	-	-
	142	-	-	-	-	-	-	-	-
	149	-	-	-	-	-	-	-	-
	151	-	-	-	-	-	-	-	-
	242	-	-	-	-	-	-	-	-
	245	-	-	-	-	-	-	-	-
	246	-	-	-	-	-	-	-	-
	257	-	-	-	-	-	-	-	-
	262	-	-	-	-	-	-	-	-

+: Leptospires detected; -: Leptospires not detected

Temperature in ºF:

Treatment Group	Animal ID	Study Day (Challenge was on Day 0)								
		0	1	2	3	4	5	6	7	8
CONTROLS	159	102.6	102.2	104.6	105.8	106.2	103.4	100.8	102.0	102.8
	163	102.6	102.2	105.6	106.0	106.6	103.2	101.0	103.0	102.6
	244	101.6	102.2	103.2	104.6	103.8	102.4	101.8	101.8	102.4
	252	102.6	102.4	103.0	107.4	104.6	103.0	102.2	103.0	103.0
	265	101.8	102.8	103.6	106.4	105.6	103.0	102.0	103.8	102.0
101.4VACCINATES	134	102.2	101.4	101.6	101.6	102.0	102.2	101.4	102.0	103.0
	135	102.6	102.6	102.6	102.4	103.2	102.8	102.0	102.8	102.4
	142	102.6	102.6	101.6	102.0	102.0	102.8	99.8	102.2	102.6
	149	102.4	102.0	102.6	102.0	101.6	102.0	101.6	102.0	102.4
	151	101.6	101.4	102.0	101.4	101.4	101.6	101.4	102.2	101.8
	242	101.6	101.2	101.6	102.0	101.6	102.0	100.8	101.4	101.0
	245	102.8	102.6	102.4	102.0	101.8	102.6	101.0	102.6	102.8
	246	102.4	101.6	102.0	102.0	102.2	102.6	101.0	102.0	102.6
	257	102.2	101.6	101.0	101.6	102.0	101.6	101.2	101.6	101.0
	262	102.6	102.0	101.0	102.0	101.6	101.8	101.0	102.6	101.4

Temperature >103.5 ºF was considered as pyrexia

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bovine Parainfluenza type 3 Virus</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against virulent bovine parainfluenza type 3 virus (PI3) when challenged 28 days post-vaccination.</td></tr>
<tr><td>Product Administration</td><td>One dose administered intramuscularly</td></tr>
<tr><td>Study Animals</td><td>Six- to 8-month-old Holstein calves and seronegative to PI3 (SN antibody titer ≤ 2). Twelve placebo controls and 24 vaccinates.</td></tr>
<tr><td>Challenge Description</td><td>PI3 challenge on day 28.</td></tr>
<tr><td>Interval observed after challenge</td><td>Virus isolation from nasal swabs, serum neutralizing antibody titers, and clinical signs up to 14 days post-challenge. The study was conducted according to 9 CFR 113.309.</td></tr>
<tr><td>Results</td><td>Virus isolation at any occasion during the 2 week post-challenge observation period:
12/12 (100%) controls
17/24 (71%) vaccinates
<table>
<tr><th rowspan="2">Treatment</th><th colspan="5">Post-Challenge Duration of Virus Shedding (Days)</th></tr>
<tr><th>Min.</th><th>Q1</th><th>Median</th><th>Q3</th><th>Max.</th></tr>
<tr><td>Controls</td><td>3</td><td>5</td><td>5</td><td>6.0</td><td>6</td></tr>
<tr><td>Vaccinates</td><td>0</td><td>0</td><td>1</td><td>1.5</td><td>6</td></tr>
</table>
Serology outcome
Vaccinates: 22/25 (88%) had SN antibody titers ≥1:4 on day 28.
Controls: 11/11 (100%) were seronegative on day 28.

Individual animal data are attached.</td></tr>
<tr><td>USDA Approval Date</td><td>01/23/2008</td></tr>
</table>

PI3 virus isolation (log_{10} $TCID_{50}$) post-challenge :

animal	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
Controls														
8515	1.50[1]	2.30	4.60	5.10	2.80	5.60	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8520	1.80	1.80	5.30	5.10	5.10	5.30	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8524	1.50	1.50	1.80	3.30	2.80	3.60	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8535	1.50	2.60	5.30	4.80	4.60	5.10	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8561	2.60	1.80	1.80	2.30	1.80	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8562	1.50	1.80	3.10	3.80	3.60	3.60	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8566	1.80	4.30	5.10	4.80	5.80	3.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8691	1.50	1.50	4.80	4.60	5.60	4.10	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8701	1.50	3.10	4.10	5.60	5.30	3.30	1.50	1.80	1.50	1.50	1.50	1.50	1.50	1.50
8715	1.50	2.30	2.30	3.30	4.10	3.80	2.30	1.50	1.80	1.50	1.50	1.50	1.50	1.50
8722	2.60	3.60	4.80	5.30	4.80	4.10	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8731	3.10	3.80	5.60	5.30	5.60	4.30	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50
Vaccinates														
8491	1.50	1.50	1.50	3.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8494	1.50	1.50	1.80	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8505	1.50	1.50	1.50	1.50	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8510	1.50	2.80	1.50	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8511	1.50	1.50	2.60	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8516	1.50	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8522	1.50	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8523	1.50	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8525	1.50	2.60	3.80	3.60	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8540	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8547	1.80	2.60	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8549	1.50	1.50	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8555	1.80	1.80	1.80	1.50	1.50	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8558	1.50	3.10	2.30	2.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50

animal	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
8559	1.80	1.80	3.30	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8567	1.50	1.50	1.80	2.60	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8611	1.50	1.80	3.60	3.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8617	1.50	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8694	1.50	1.50	1.50	2.30	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8702	1.50	1.50	1.80	3.10	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8703	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8719	2.60	1.50	1.50	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8723	1.50	2.30	1.50	1.80	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
8729	2.30	1.50	3.10	3.80	3.30	2.30	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50

[1]A virus titer of $\leq$1.8 $\log_{10}$ $TCID_{50}$ is considered negative.
Red cells indicate a virus titer positive for PI3 virus

PI3 Serum Neutralizing Antibody Titers, Study Day
Challenge performed on Day 28. Day 35 is 7 days post-challenge. Day 42 is 14 days post-challenge.

Treatment	animal	Day 0	Day 7	Day 21	Day 28	Day 35	Day 42
Control Group	8515	<2	2	<2	<2	<2	144
	8520	<2	<2	<2	<2	<2	362
	8524	<2	<2	<2	<2	<2	287
	8535	<2	<2	<2	<2	3	304
	8561	<2	<2	<2	<2	6	512
	8562	<2	<2	<2	<2	<2	181
	8566	<2	<2	<2	<2	<2	362
	8691	<2	<2	<2	<2	<2	304
	8701	<2	<2	<2	<2	2	304
	8715	<2	<2	<2	<2	10	91
	8722	<2	<2	<2	<2	<2	304
	8731	<2	<2	<2	<2	2	512
Vaccinated Group	8491	<2	<2	4	10	1722	2435
	8494	<2	<2	23	38	3444	≥5793
	8505	<2	<2	6	16	431	2896
	8510	<2	<2	38	45	2048	4096
	8511	<2	<2	152	215	4096	≥4871
	8516	<2	<2	5	23	152	1722

	8522	<2	<2	64	91	362	≥4871
	8523	<2	<2	32	64	2048	≥4871
	8525	<2	<2	27	38	≥4871	≥4598
	8540	<2	2	13	64	1448	3649
	8547	<2	<2	54	108	2435	4096
	8549	<2	<2	23	54	2435	≥4871
	8555	<2	2	<2	3	215	724
	8558	<2	<2	23	45	1722	2299
	8559	<2	<2	54	45	3444	≥4598
	8567	<2	<2	10	8	1448	2896
	8611	<2	<2	16	38	1024	2435
	8617	<2	<2	23	27	64	2435
	8694	<2	<2	7	32	1024	4096
	8702	<2	<2	76	54	2048	≥5793
	8703	<2	<2	45	54	2048	3444
	8719	<2	<2	256	152	3444	≥5793
	8723	<2	<2	13	27	2896	≥4598
	8729	<2	<2	<2	<2	<2	362

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bovine Respiratory Syncytial Virus (BRSV)</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate effectiveness against respiratory disease caused by BRSV.</td></tr>
<tr><td>Product Administration</td><td>One dose administered intramuscularly (IM)</td></tr>
<tr><td>Study Animals</td><td>Sixteen- to 40-day-old Holstein calves and seronegative to BRSV. 14 controls and 20 vaccinates.</td></tr>
<tr><td>Challenge Description</td><td>BRSV challenge 25 days after vaccination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Mortality and lungs (at the time of mortality or at 8 days post-challenge) were evaluated.</td></tr>
<tr><td>Results</td><td>The percent of lung that was abnormal (consolidated/lesion) was calculated for every animal.

<u>Percent of Lung Lesions (5-number summary)</u>:

<table>
<tr><th rowspan="2">Treatment</th><th colspan="5">Percent (%) Total Lung with Lesions</th></tr>
<tr><th>Min.</th><th>Q1</th><th>Median</th><th>Q3</th><th>Max.</th></tr>
<tr><td>Controls</td><td>14.7</td><td>25</td><td>50.3</td><td>66.5</td><td>81.2</td></tr>
<tr><td>Vaccinates</td><td>3.8</td><td>11.9</td><td>18.2</td><td>23.2</td><td>57.3</td></tr>
</table>

<u>Post-Challenge Mortality Rates</u>:

<table>
<tr><th>Treatment</th><th>Mortality</th><th>Percent</th></tr>
<tr><td>Controls</td><td>9/14</td><td>64.3 %</td></tr>
<tr><td>Vaccinates</td><td>1/19</td><td>5.3 %</td></tr>
</table>

Please see attached page for individual raw data.</td></tr>
<tr><td>USDA Approval Date</td><td>07/17/2008</td></tr>
</table>

Individual Mortality and Lung Lesion Results:

Treatment	Animal ID	Mortality	Percent of Lung Lesions
Controls	03	Yes	66.53
	09	Yes	70.48
	13	Yes	81.18
	14	No	14.65
	15	Yes	66.25
	16	Yes	74.41
	40	Yes	31.75
	42	No	61.33
	43	No	46.45
	44	No	25.00
	53	Yes	54.10
	56	No	22.10
	59	Yes	16.30
	61	Yes	39.84
Vaccinates	01	No	20.08
	04	No	16.28
	05	No	22.85
	07	No	6.15
	12	No	15.22
	19	No	4.63
	21	No	10.33
	35	No	16.24
	36	No	57.25
	38	No	13.375
	41	No	23.60
	45	No	20.08
	46	-*	3.76
	48	No	47.80
	50	No	9.43
	55	No	20.18
	58	No	24.90
	60	No	14.04
	63	No	54.70
	64	No	21.19

*: Animal died from severe diarrhea and was removed from the mortality analysis.

Study Type	Efficacy
Pertaining to	Bovine Viral Diarrhea Virus, type 1 (BVDV1)
Study Purpose	Demonstrate efficacy against respiratory disease caused by BVDV1
Product Administration	
Study Animals	
Challenge Description	Non-cytopathic BVDV1b 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	09/19/1996

<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>To demonstrate safety under field conditions</td></tr>
<tr><td>Product Administration</td><td>IBR-BVD-PI3-BRSV-VL5 or IBR-BVD-PI3-BRSV-L5 was administered intramuscularly (IM), followed by a second vaccination 28 days later with BRSV-VL5 or BRSV-L5, respectively</td></tr>
<tr><td>Study Animals</td><td>The study was conducted at 3 locations with 660 head of cattle (331 vaccinates and 329 controls). The animals were allotted to non-vaccinated control (329), intramuscular (IM) vaccination with IBR-BVD-PI3-BRSV-VL5 (211) and IM vaccination with IBR-BVD-PI3-BRSV-L5 (120) treatment groups.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after administration</td><td>Animals were observed for 1 to 3 hours after each vaccination, then once weekly for injection site reactions for at least 49 days after first injection or until resolution. Animals were also observed daily for general health observations for 49 days after the first injection.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><th>Cattle Enrolled by Age</th><th>Vaccinate</th><th>Control</th></tr>
<tr><td>17-43 days</td><td>98</td><td>101</td></tr>
<tr><td>10-11 months</td><td>20</td><td>20</td></tr>
<tr><td>13 months</td><td>31</td><td>30</td></tr>
<tr><td>Pregnant 14-26months</td><td>100</td><td>98</td></tr>
<tr><td>Pregnant 1-6 years</td><td>82</td><td>80</td></tr>
</table>
<table>
<tr><th colspan="2">Number of animals</th><th>Animal with no AE (%)</th><th>Animals with AE (%)</th></tr>
<tr><td>Enrolled</td><td>660</td><td></td><td></td></tr>
<tr><td>Completed the study</td><td>659</td><td>638 (96.8)</td><td>21 (3.2)</td></tr>
<tr><td>Did not Complete the study</td><td>1*</td><td>0</td><td>1</td></tr>
</table>
* Died from punctured abomasum before second vaccination.

Frequency of Adverse Event observations per category of calves:
<table>
<tr><th rowspan="3">Observations</th><th colspan="3">Minimum age calves (17 to 43 days of age) Number of animals</th></tr>
<tr><td>Controls</td><td colspan="2">Vaccinates</td></tr>
<tr><td>IM (1)</td><td>IM (2)</td></tr>
<tr><td>Bloat</td><td>1**</td><td>0</td><td>1</td></tr>
<tr><td>Ear drop</td><td>0</td><td>0</td><td>1</td></tr>
<tr><td>Depression</td><td>1</td><td>0</td><td>0</td></tr>
<tr><td>Diarrhea</td><td>1</td><td>0</td><td>0</td></tr>
</table>
</td></tr>
</table>

Death*	0	0	1
Depression with ear drop	0	0	1
Lameness	2	0	0
Enterotoxemia/Diarrhea	1	0	0
Draining ear	1	0	0

* Animal died from complications from bloat.
** Animal also was diagnosed with Enterotoxemia
(1) Vaccination with IBR-BVD-PI3-BRSV-L5 and BRSV-L5
(2) Vaccination with IBR-BVD-PI3-BRSV-VL5 and BRSV-VL5

These Adverse Events were considered by the Regional Investigator not to be related to the use of the vaccine.

Observations	**Older calves (10-13 months of age) Number of animals**		
	Controls	Vaccinates	
		IM (1)	IM (2)
Foot Rot	0	1	0

(1) Vaccination with IBR-BVD-PI3-BRSV-L5 and BRSV-L5
(2) Vaccination with IBR-BVD-PI3-BRSV-VL5 and BRSV-VL5

These Adverse Events were considered by the Regional Investigator not to be related to the use of the vaccine.

Frequency of Adverse Event observations per category of pregnant heifers and cows:
Cattle were confirmed pregnant on day of first vaccination.

Cattle Enrolled by Trimester	**Vaccinate**	**Control**
1	54	53
2	78	77
3	50	48

Observations	**Pregnant cattle Number of animals**		
	Controls	Vaccinates	
		IM (1)	IM (2)
Abortion	4*	1	0

* Cause of abortions was undetermined.
(1) Vaccination with IBR-BVD-PI3-BRSV-L5 and BRSV-L5
(2) Vaccination with IBR-BVD-PI3-BRSV-VL5 and BRSV-VL5

Observations	**Pregnant cattle Number of animals**		
	Controls	Vaccinates	
		IM (1)	IM (2)
Foot Rot	2	0	0
Keratitis	1	0	0
Cracked hoof	1	0	0
Lameness/edema	0	0	1

Frequency of Injection Site Reaction Scores per Category of Age:

Pregnant Cattle							
Controls*		Vaccinates					
		IM (1)			IM (2)		
1st injection							
0.5-2 cm	2-5 cm	0.5-2 cm	2-5 cm	>5 cm	0.5-2 cm	2-5 cm	>5 cm
1	1	1	0	0	3**	0	0
2nd injection							
2	0	0	0	0	4	2	0

Minimum Age Calves							
Controls*		Vaccinates					
		IM (1)			IM (2)		
1st injection							
0.5-2 cm	2-5 cm	0.5-2 cm	>5 cm	0.5-2 cm	0.5-2 cm	2-5 cm	>5 cm
0	0	n/a	n/a	n/a	0	0	0
2nd injection							
3	0	n/a	n/a	n/a	5	0	0

Older Calves							
Controls*		Vaccinates					
		IM (1)			IM (2)		
1st injection							
0.5-2 cm	2-5 cm	0.5-2 cm	2-5 cm	>5 cm	0.5-2 cm	2-5 cm	>5 cm
1	0	5**	5**	0	0	0	0
2nd injection							
0	0	0	0	0	0	0	0

* Controls did not have Injection Site Reactions greater than 2-5 cm
** In the case where an individual animal had an injection site reaction present on multiple weekly observations, only the largest reaction score is represented in the Table.
n/a: Minimum age calves were vaccinated only with IBR-BVD-PI3-BRSV-VL5 and BRSV-VL5
(1): Vaccination with IBR-BVD-PI3-BRSV-L5 and BRSV-L5
(2): Vaccination with IBR-BVD-PI3-BRSV-VL5 and BRSV-VL5

The Injection Sites Reactions resolved without incident within 30 days following each vaccination with the exception of one pregnant cow, vaccinated IM with IBR-BVD-PI3-BRSV-VL5 and BRSV-VL5, which was completely resolved on day 58.

USDA Approval Date	05/14/2008

<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>To demonstrate safety under field conditions.</td></tr>
<tr><td>Product Administration</td><td>Two doses administered intramuscularly (IM) 28 days apart. Second dose of vaccine consisted of Bacterin only.</td></tr>
<tr><td>Study Animals</td><td>205 beef calves, approximately 7 weeks (69 calves) or 9 months of age (136 calves), at each of 3 sites: Control (103 calves) and IM administration of product (102 calves) treatment groups.</td></tr>
<tr><td>Challenge Description</td><td>Not Applicable</td></tr>
<tr><td>Interval observed after administration</td><td>Calves were observed daily for 48 days.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><th colspan="2">Animals Total</th><th>Animals with no Adverse Event Observations (%)</th><th>Animals with Adverse Event Observations (%)</th></tr>
<tr><td>Completed the study</td><td>204</td><td>201 (98.5)</td><td>3 (1.5)</td></tr>
<tr><td>Did not Complete the study</td><td>1</td><td>0 (0)</td><td>1 (100)</td></tr>
<tr><td>Total</td><td>205</td><td>201 (98.0)</td><td>4 (2.0)</td></tr>
</table>
<table>
<tr><th rowspan="2">Abnormal Health Events (VeDDRA Code)</th><th colspan="2">Number of Adverse Event Observations</th></tr>
<tr><td>Controls</td><td>Vaccinates</td></tr>
<tr><td>Lameness</td><td>0</td><td>1*</td></tr>
<tr><td>Depression</td><td>1**</td><td>0</td></tr>
<tr><td>Dyspnea</td><td>1**</td><td>0</td></tr>
<tr><td>Death</td><td>1**</td><td>0</td></tr>
<tr><td>Anorexia</td><td>0</td><td>1</td></tr>
<tr><td>Cough</td><td>0</td><td>1</td></tr>
</table>
*: Same calve observed on 2 different days. This calf had a lame right hind (physical injury). After appearing to resolve, the lameness was observed again and did not resolve by the end of the study.
**: Same calf observed on 3 different days (diagnosed post necropsy with a fibronecrotizing bronchopneumonia).
<table>
<tr><th rowspan="2">Adverse Event Observations</th><th colspan="2">Number of Animals (%)</th></tr>
<tr><td>Controls</td><td>Vaccinates</td></tr>
<tr><td>Normal</td><td>102 (99.03)</td><td>99 (97.0)</td></tr>
<tr><td>Abnormal</td><td>1 (0.97)</td><td>3 (3.0)</td></tr>
</table>
None of the Adverse Events were considered by the study Investigator to be related to vaccination.
</td></tr>
</table>

<table>
<tr><td></td><td>
<table>
<tr><th rowspan="3">Treatment Group</th><th rowspan="3">Total Number of Animals</th><th colspan="3">Number of Animals with Injection Site Reactions (%)</th></tr>
<tr><th rowspan="2">7-week-old calves</th><th rowspan="2">9-month-old calves</th><th colspan="2">Injection Site Reactions in cm</th></tr>
<tr><th>< 1.5</th><th>1.5 to 5</th></tr>
<tr><td>Controls</td><td>103</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>IM</td><td>102</td><td>1 (0.98)</td><td>0 (0)</td><td>1</td><td>0</td></tr>
</table>

All injections site reactions were resolved by Day 48.
</td></tr>
<tr><td>USDA Approval Date</td><td>06/17/2009</td></tr>
</table>

Study Type	Safety
Pertaining to	All fractions
Study Purpose	Demonstrate safety in pregnant cattle and calves nursing pregnant cattle under field condition
Product Administration	
Study Animals	Bovine
Challenge Description	NA
Interval observed after administration	
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	07/16/2003

Study Type	Safety
Pertaining to	All fractions
Study Purpose	Demonstrate safety in pregnant cattle and calves nursing pregnant cattle under field condition
Product Administration	
Study Animals	Bovine
Challenge Description	NA
Interval observed after administration	
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	07/16/2003

Study Type	Safety
Pertaining to	All fractions
Study Purpose	Demonstrate safety in pregnant cattle and calves nursing pregnant cattle under field condition
Product Administration	
Study Animals	Bovine
Challenge Description	NA
Interval observed after administration	
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	07/16/2003