Summary of Studies Supporting USDA Product Licensure

Establishment Name	Elanco US Inc.
USDA Vet Biologics Establishment Number	196
Product Code	19T1.20
True Name	Porcine Reproductive & Respiratory Syndrome Vaccine, Reproductive & Respiratory Forms, Modified Live Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Prevacent PRRS - Elanco US Inc.
Date of Compilation Summary	July 08, 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.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Porcine Reproductive and Respiratory Syndrome Virus (PRRSV)</td></tr>
<tr><td>Study Purpose</td><td>Efficacy against PRRSV associated reproductive disease</td></tr>
<tr><td>Product Administration</td><td>Approximately 6 weeks prior to breeding gilts were administered one dose intramuscularly.</td></tr>
<tr><td>Study Animals</td><td>6-8 month old pregnant gilts immunologically naive to PRRS. 14 vaccinated gilts and 10 placebo control gilts.</td></tr>
<tr><td>Challenge Description</td><td>At approximately 90 days of gestation, gilts were challenged with virulent PRRSV.</td></tr>
<tr><td>Interval observed after challenge</td><td>On the day of farrowing the number of viable piglets per litter were determined.
Viremia was evaluated in pregnant gilts at 3, 7, and 14 days post challenge.</td></tr>
<tr><td>Results</td><td>A piglet was considered affected (non-viable) if born dead or was under 1 kg at birth and/or could not move to eat.

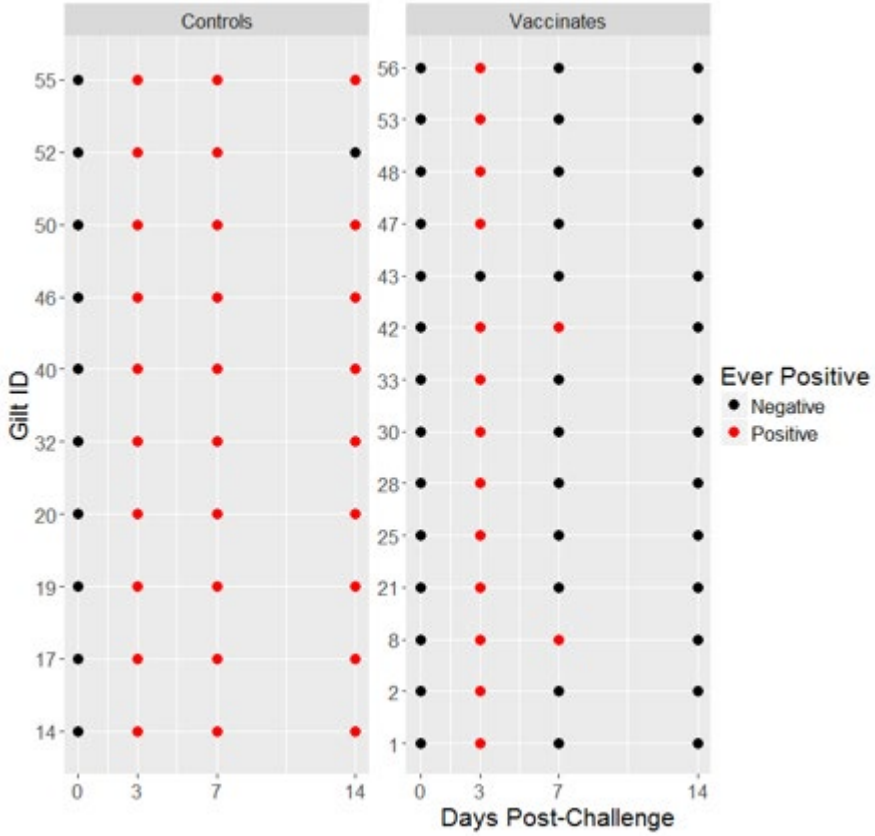
5 number summary of the percent (%) dead or non-viable piglets per litter
<table>
<tr><th>Group</th><th>Min</th><th>Q1</th><th>Median</th><th>Q3</th><th>Max</th></tr>
<tr><td>Control</td><td>61.1</td><td>84.7</td><td>93.3</td><td>98.7</td><td>100</td></tr>
<tr><td>Vaccinates</td><td>0.0</td><td>1.7</td><td>24.1</td><td>81.8</td><td>100</td></tr>
<tr><td>Sentinels</td><td>0.0</td><td>0.0</td><td>0.0</td><td>7.7</td><td>38.5</td></tr>
</table>

Raw data on the next page.</td></tr>
<tr><td>USDA Approval Date</td><td>August 24, 2018</td></tr>
</table>

Table 1. Non-viable piglets/total piglets in each litter

Vaccinates	Controls
0/9	1/6
0/18	7/10
0/7	11/18
0/12	12/12
1/15	13/14
2/16	14/14
2/18	14/15
4/11	14/14
5/14	16/18
8/17	18/19
12/12	
14/15	
14/14	

Figure 1. Viremia results for each gilt post-challenge study days



<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Porcine Reproductive and Respiratory Syndrome Virus (PRRSV)</td></tr>
<tr><td>Study Purpose</td><td>Efficacy against respiratory form of PRRSV disease</td></tr>
<tr><td>Product Administration</td><td>One dose administered intramuscularly.</td></tr>
<tr><td>Study Animals</td><td>Crossbred pigs, 14-15 days old, seronegative to PRRSV. Twenty placebo controls and one group of 20 vaccinates.</td></tr>
<tr><td>Challenge Description</td><td>28 Days after vaccination, pigs were challenged with virulent PRRSV Type 2.</td></tr>
<tr><td>Interval observed after challenge</td><td>Lungs were evaluated 14 days after challenge.</td></tr>
<tr><td>Results</td><td>The percent of the lung mass that was abnormal was calculated for every animal. A pig was considered affected if the lung lesion score was ≥2%.

5-number summary for lung consolidation (%)

<table>
<tr><th>Treatment Group</th><th>Min</th><th>Q1</th><th>Med</th><th>Q3</th><th>Max</th></tr>
<tr><td>Placebo Control</td><td>8.2</td><td>47.2</td><td>56.0</td><td>68.5</td><td>76.5</td></tr>
<tr><td>Vaccinate</td><td>0.0</td><td>0.4</td><td>1.2</td><td>3.7</td><td>56.5</td></tr>
</table>

Raw data shown on attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>August 16, 2016</td></tr>
</table>

Lung Consolidation scores (%), in order of rank	
Placebo Control Group	**Vaccinate Group**
8.2	0.0
32.5	0.1
42.5	0.1
45.0	0.2
46.0	0.3
48.5	0.4
49.5	0.4
50.5	0.5
52.5	0.5
55.0	1.0
57.0	1.5
57.5	1.7
58.5	2.2
59.5	2.4
67.0	3.6
70.0	3.8
70.0	4.3
71.5	4.5
74.5	21.8
76.5	56.5

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Porcine Reproductive and Respiratory Syndrome Virus (PRRSV)</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate 26 week Duration of Immunity against PRRSV-associated respiratory disease.</td></tr>
<tr><td>Product Administration</td><td>One dose administered intramuscularly</td></tr>
<tr><td>Study Animals</td><td>Sixty-eight (68) Crossbred pigs, 14 days old, seronegative to PRRSV were randomized into 2 treatment groups. Thirty-two (32) placebo controls and 36 vaccinates were used for the study analysis.</td></tr>
<tr><td>Challenge Description</td><td>Twenty-six weeks (182 days) after vaccination pigs were challenged with PRRSV.</td></tr>
<tr><td>Interval observed after challenge</td><td>Lungs were evaluated 14 days after challenge.</td></tr>
<tr><td>Results</td><td>Primary outcome of the study was the reduction in lung lesion score. The percent of the lung mass that was abnormal was calculated for every animal.

5-number summary for lung consolidation (%)

<table>
<tr><th>Treatment Group</th><th>Min</th><th>Q1</th><th>Med</th><th>Q3</th><th>Max</th></tr>
<tr><td>Placebo</td><td>0</td><td>2.9</td><td>18.6</td><td>35.5</td><td>66</td></tr>
<tr><td>Vaccinate - low dose</td><td>0</td><td>0</td><td>0.2</td><td>0.4</td><td>34</td></tr>
</table>

Raw data shown on attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>April 30, 2018</td></tr>
</table>

Lung Consolidation Scores (%) in order of rank	
Vaccinates	Controls
0	0
0	0.1
0	0.1
0	0.1
0	0.4
0	0.55
0	0.8
0	1.2
0	3.45
0	4.15
0	4.95
0	8.65
0	11.45
0	11.8
0.1	12.9
0.1	18
0.1	19.35
0.1	21.75
0.2	26.25
0.2	27
0.2	28.7
0.2	32.5
0.2	33.6
0.2	35.5
0.2	35.5
0.3	38.5
0.35	46
0.45	51.5
0.5	52.2
0.6	55.5
1.75	64
1.95	66
2.5	
3.6	
7.9	
34	

Study Type	Safety
Pertaining to	All
Study Purpose	Demonstrate safety of product under typical use conditions
Product Administration	1 Dose administered by the IM route
Study Animals	1717 gilts/sows were enrolled in the study and received either one of 2 serials or sterile diluent. The animals were separated into groups and were vaccinated at one of four gestational stages, pre-breeding, 1st trimester, 2nd trimester, and 3rd trimester. Some of the sows from Site 1 and Site 2 were also allowed to have a second litter and for that second litter they were considered as being vaccinated pre-breeding. The study was conducted at three independent study sites.
Challenge Description	NA
Interval observed after challenge	Gilts/Sows were observed for 21 days post-vaccination. Gilts/Sows were also observed at the time of farrowing and their piglets were observed for 7 days post farrowing.
Results	Sows/Gilts Adverse Events after Vaccination:

Adverse Event	**Site1**		**Site 2**		**Site 3**	
	Vaccinates N=459	Controls N=230	Vaccinates N=400	Controls N=200	Vaccinates N=288	Controls N=140
Normal	443	226	378	190	281	138
Abnormal Breathing	1	0	1	0	0	0
Abortion	1	0	2	0	4	0
Anorexia	0	2	0	0	0	0
Death*	3	2	2	1	2	2
Decreased Appetite	4	2	5	3	0	0
Depression	0	0	2	0	0	0
Hypersalivation	0	0	5	4	0	0
Injection Site Swelling**	1	0	4	0	0	0
Intrauterine Death	1	0	0	0	0	0
Lameness	5	0	1	0	0	0
Loss of Appetite	0	0	1	0	0	0
Vaginal Prolapse	0	0	0	0	0	1
Agalactia	0	0	0	0	1	0
Uterine Prolapse	1	1	0	0	1	0
Rectal Prolapse	0	0	0	0	1	0
Pale	1	0	0	0	0	0
Ulcer	1	0	0	0	0	0
Bleeding Injection Site	0	0	5	2	0	0
Vaginal Discharge	0	0	2	0	0	0
Stillbirth	0	0	1	0	0	0
Weakness	0	0	1	0	0	0

*Deaths not attributable to vaccine as affirmed by licensee

**Injection site reaction included swellings or hemorrhage which resolved within 21 days following vaccination.

Summary of Litter Size by Serial					
Serial	**Min**	**Q1**	**Median**	**Q4**	**Max**
Serial 1	3	12	15	17	26
Serial 2	1	12	15	17	27
Placebo	0	12	15	17	26

Summary of Litter Size by Pregnancy Status at Vaccination						
Status	Group	Min	Q1	Median	Q3	Max
Pre-breeding	Control	0	13	16	18	26
Pre-breeding	Vaccinate	4	13	15	18	24
1st Trimester	Control	3	12	15	17	23
1st Trimester	Vaccinate	1	12	15	17	24
2nd Trimester	Control	2	12	14.5	17	24
2nd Trimester	Vaccinate	3	12	15	17	23
3rd Trimester	Control	2	12	15	16	23
3rd Trimester	Vaccinate	3	12	15	17	27
3rd trimester/Pre-breeding	Control	4	12	14	16	21
3rd trimester/Pre-breeding	Vaccinate	2	12	13.5	15	26

Birth Events by Serial						
Serial	**Total number of piglets**	**Stillborns**	**Aborted**	**Mummified**	**Post Farrowing Mortality**	**Weak**
Serial 1	8406	732	0	222	76	103
Serial 2	8667	782	0	195	92	110
Placebo	8640	778	0	240	92	100

Summary of Birth Events by Pregnancy Status at Vaccination						
Status	Group	% Stillborn	%Aborted	%Mummified	% Post Farrowing Mortality	%Weak
Pre-breeding	Control	8.4	0	3.4	0.7	1.6
Pre-breeding	Vaccinate	10.6	0	2.8	1.1	1.4
1st Trimester	Control	8.0	0	2.4	1.5	1.0
1st Trimester	Vaccinate	7.7	0	2.8	1.3	1.4
2nd Trimester	Control	9.9	0	2.9	1.3	1.1
2nd Trimester	Vaccinate	8.6	0	2.5	0.6	1.5
3rd Trimester	Control	9.0	0	3.0	1.7	1.7
3rd Trimester	Vaccinate	8.1	0	2.6	1.7	1.4
3rd trimester/Pre-breeding	Control	10.4	0	1.4	0	0
3rd trimester/Pre-breeding	Vaccinate	9.0	0	1.0	0	0

Summary of Adverse Events by Pregnancy Status at Vaccination				
Status	**Group**	**Number**	**Number Affected**	**Percent Affected**
Pre-breeding	Control	130.0	7	5
Pre-breeding	Vaccinate	260.0	17	7
1st Trimester	Control	136.0	3	2
1st Trimester	Vaccinate	280.0	5	2
2nd Trimester	Control	149.0	1	1
2nd Trimester	Vaccinate	295.0	9	3
3rd Trimester	Control	110.0	4	4
3rd Trimester	Vaccinate	217.0	11	5
3rd trimester/Pre-breeding	Control	46.0	1	2
3rd trimester/Pre-breeding	Vaccinate	95.0	3	3

USDA Approval Date	June 11, 2020

<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 of product under typical use conditions</td></tr>
<tr><td>Product Administration</td><td>1 Dose administered by the IM route</td></tr>
<tr><td>Study Animals</td><td>920 crossbred/ mixed pigs 14-24 days of age were enrolled in the study into 3 groups: one group was administered Serial 1 of the vaccine; another group was administered Serial 2 of the vaccine; and the Control Product group was administered sterile diluent. The Serial 1 group and the Control Product group each consisted of 132 pigs receiving a dose at 14 days of age and 175 pigs receiving a dose at 15-24 days of age. The Serial 2 group consisted of 131 pigs receiving a dose at 14 days of age and 175 pigs receiving a dose at 15-24 days of age. Pigs were located in three distinct geographical areas.</td></tr>
<tr><td>Challenge Description</td><td>NA</td></tr>
<tr><td>Interval observed after challenge</td><td>Pigs were observed 1-2 hours post vaccination. Daily pen-side observations were conducted from day 1 through 21 days post vaccination. Palpation of injection site was performed on day 7 post vaccination.</td></tr>
<tr><td>Results</td><td>Palpable injection site reactions were not observed.

Frequency of Events:
<table>
<tr><th>Reaction Type</th><th>Control Product (Sterile Diluent) No. of Pigs</th><th>Serial 1 No. of Pigs</th><th>Serial 2 No. of Pigs</th></tr>
<tr><td>Injection Site Scab post-vaccination</td><td>0</td><td>1</td><td>1</td></tr>
<tr><td>Loss of Condition</td><td>10</td><td>17</td><td>9</td></tr>
<tr><td>Decreased Appetite</td><td>1</td><td>2</td><td>1</td></tr>
<tr><td>Anorexia</td><td>0</td><td>2</td><td>2</td></tr>
<tr><td>Diarrhea</td><td>2</td><td>1</td><td>1</td></tr>
<tr><td>Ataxia</td><td>0</td><td>1</td><td>1</td></tr>
<tr><td>Tremor</td><td>0</td><td>1</td><td>0</td></tr>
<tr><td>Lameness</td><td>4</td><td>2</td><td>1</td></tr>
<tr><td>Depression</td><td>2</td><td>2</td><td>3</td></tr>
<tr><td>Dyspnea</td><td>0</td><td>2</td><td>1</td></tr>
<tr><td>Inguinal hernia</td><td>0</td><td>1</td><td>0</td></tr>
<tr><td>Death*</td><td>3</td><td>5</td><td>3</td></tr>
<tr><td>No Reaction</td><td>285</td><td>270</td><td>283</td></tr>
</table>
* Deaths not attributable to vaccine affirmed by licensee</td></tr>
</table>

USDA Approval Date	April 10, 2018