Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	49R8.21
True Name	Porcine Reproductive & Respiratory Syndrome Vaccine, Modified Live Virus, Mycoplasma Hyopneumoniae Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	FlexMycoPRRS - No distributor specified
Date of Compilation Summary	August 14, 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>Mycoplasma Hyponeumoniae</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate efficacy of the Mycoplasma Hyponeumoniae component of the combination package product</td></tr>
<tr><td>Product Administration</td><td>Administration of one dose intramuscularly</td></tr>
<tr><td>Study Animals</td><td>40 pigs, 24-25 days old divided into 20 vaccinates and 20 controls</td></tr>
<tr><td>Challenge Description</td><td>Challenged with virulent Mycoplasma Hyponeumoniae 35 days after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Pigs were observed for 28 days after challenge, and then tissues were examined for lung lesions</td></tr>
<tr><td>Results</td><td>Summary of Results:

Lungs were examined and scored for percent lung pathology.

<table>
<tr><th>Group</th><th>Minimum</th><th>25th percentile</th><th>Median</th><th>75th percentile</th><th>Maximum</th></tr>
<tr><td>Vaccinates</td><td><1</td><td>1</td><td>4</td><td>11</td><td>35</td></tr>
<tr><td>Controls</td><td><1</td><td>7</td><td>15</td><td>20</td><td>30</td></tr>
</table>

See tables on the following pages for data.</td></tr>
<tr><td>USDA Approval Date</td><td>August 10, 2006</td></tr>
</table>

Individual Pig Lung Lesion Scoes (%) in Vaccinates

ID#	R. Apical	R. Cardiac	R. Diaphragmatic	L. Apical	L. Cardiac	L. Diaphragmatic	Intermediate	Total
184	0.0	0.2	0.0	0.0	0.2	0.0	0.0	0.4
187	0.0	0.5	0.25	0.0	1.0	0.25	0.1	2.1
188	0.0	1.0	0.25	0.0	2.0	0.0	0.0	3.25
189	0.0	5.0	0.25	0.0	2.0	0.5	0.5	8.25
193	4.0	7.0	2.5	4.0	7.0	1.25	9.0	34.75
194	0.0	0.1	0.25	0.0	0.2	0.25	0.0	0.8
195	0.5	2.0	1.25	0.1	4.0	0.0	5.0	12.85
200	0.1	0.2	0.0	0.0	0.1	0.0	0.0	0.4
201	1.0	3.0	0.5	0.0	3.0	0.5	8.0	16.0
202	0.5	3.0	0.0	0.0	2.0	0.0	0.0	5.5
217	0.5	3.0	0.5	0.0	3.0	0.0	3.0	10.0
218	.	.	.	.	.	.	.	.
219	0.0	3.0	1.25	0.0	2.0	0.5	0.2	6.95
220	0.0	3.0	1.25	0.0	2.0	0.5	0.2	14.95
222	0.2	2.0	0.25	0.0	1.0	0.25	0.5	4.2
223	0.1	0.5	0.0	0.0	0.0	0.0	1.0	1.6
224	0.1	0.2	0.5	0.1	1.0	0.25	1.0	3.15
226	0.0	0.2	0.0	0.0	1.0	0.0	0.0	1.2
227	0.5	5.0	0.0	1.0	7.0	0.0	0.0	13.5
228	0.0	0.2	0.0	0.0	1.0	0.0	0.0	1.2

. = no data

Individual Pig Lung Lesion Scoes (%) in Controls

ID#	R. Apical	R. Cardiac	R. Diaphragmatic	L. Apical	L. Cardiac	L. Diaphragmatic	Intermediate	Total
181	2.0	6.0	2.5	0.5	5.0	2.5	7.0	25.5
182	0.0	1.0	0.0	0.2	0.5	0.0	5.0	6.7
183	0.1	0.5	0.5	0.1	2.0	0.5	0.2	3.9
185	0.5	4.0	1.25	0.5	5.0	2.5	6.0	19.75
186	0.1	1.0	0.25	0.0	6.0	0.25	0.5	8.1
191	0.0	0.1	0.0	0.0	0.5	0.0	0.0	0.6
192	1.0	7.0	1.25	0.2	7.0	0.0	4.0	20.45
196	.	.	.	.	.	.	.	.
198	0.0	1.0	1.25	0.1	7.0	0.25	8.0	17.6
204	0.2	2.0	0.25	0.2	2.0	0.0	1.0	5.65
205	0.2	3.0	0.0	0.1	1.0	0.0	3.0	7.3
207	0.2	5.0	0.5	0.2	5.0	0.5	3.0	14.4
211	1.0	5.0	1.25	1.0	6.0	0.5	4.0	18.75
212	0.2	6.0	1.25	0.1	5.0	0.25	7.0	19.8
215	1.0	3.0	1.25	0.1	4.0	0.5	5.0	14.85
225	0.1	1.0	0.25	0.0	2.0	0.5	0.1	3.95
230	0.2	4.0	0.5	0.1	3.0	0.25	2.0	10.05
231	0.0	3.0	0.5	3.0	6.0	1.25	1.0	14.75
232	1.0	8.0	1.25	1.0	8.0	1.25	9.0	29.5
233	2.0	6.0	1.25	2.0	7.0	0.25	3.0	21.5

. = no data

Study Type	Efficacy
Pertaining to	*Mycoplasma Hyponeumoniae*
Study Purpose	Demonstration of a 26 week Duration of Immunity
Product Administration	Administration of one dose intramuscularly
Study Animals	Pigs approximately 3 weeks of age, divided into 20 vaccinates and 20 controls
Challenge Description	Challenged with *Mycoplasma hyopneumoniae* 184 days post vaccination
Interval observed after challenge	Pigs were observed for 33 days post-challenge for clinical signs of *Mycoplasma hyopneumoniae* infection and then tissues were examined for lung lesions consistent with *Mycoplasma hyopneumoniae* infection.
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	August 7, 2006

<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>To demonstrate efficacy of the PRRSV, respiratory form</td></tr>
<tr><td>Product Administration</td><td>Administration of one dose intramuscularly</td></tr>
<tr><td>Study Animals</td><td>Forty pigs, 22-24 days old, divided into 20 vaccinates and 20 controls</td></tr>
<tr><td>Challenge Description</td><td>Challenged with virulent PRRS virus 28 days after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Pigs were observed for 14 days after challenge, and tissues were examined for lung lesions</td></tr>
<tr><td>Results</td><td>The percentage of lung consolidation was evaluated.

Summary of Results:
<table><tr><th>Treatment Group</th><th>Minimum</th><th>25th Percentile</th><th>Median</th><th>75th Percentile</th><th>Maximum</th></tr><tr><td>Vaccinates</td><td>0</td><td>1</td><td>1</td><td>4</td><td>27</td></tr><tr><td>Controls</td><td>2</td><td>13</td><td>28</td><td>55</td><td>81</td></tr></table>
See tables on the following pages for data. The total percent lung lesion score was defined as the sum of the % lung pathology for the right and left apical, right and left cardiac, right and left diaphragmatic and intermediate lobes.</td></tr>
<tr><td>USDA Approval Date</td><td>June 18, 2009</td></tr>
</table>

Lung Lesions Percent Pathology for Vaccinates

ID#	R. Apical	R. Cardiac	R. Diaphragmatic	L. Apical	L. Cardiac	L. Diaphragmatic	Intermediate	Total
477	0.2	0.5	0	0	0.2	0	0	0.9
482	0	0.2	0	0.2	0	0	0	0.4
485	0	0.2	0	0	0	0	0	0.2
486	0	0.5	0	0	1	0	0	1.5
487	0.2	0.5	0	0.1	0.5	0	0	1.3
488	0.1	0.2	0	0	0.5	0	0.1	0.9
489	0.5	3	0	1	3	0	0.5	8
490	0.2	1	0.5	2	1	1.25	0.5	6.45
491	0	0	0	0	0	0	0	0
492	0	0.5	0	0	0.2	0	0	0.7
505	0	0.2	0	0	0.5	0	0.5	1.2
507	0	0.5	0	0	0.2	0.25	0	0.95
516	0.2	0.1	0.25	0	0	0.25	0	0.8
517	0	0.5	0	0	0.2	0	0	0.7
518	0	1	1.25	0	0.1	0	0.5	2.85
524	0	0.5	0.5	0	0.2	0	0.2	1.4
525	0.2	1.5	0	5	8	12.5	0.2	27.4
526	4	5	2.5	3	3	5	3	25.5
528	0.5	5	2.5	0.2	0.5	0.5	0.5	9.7
529	0	0	0	0	0	0	0	0

Lung Lesions Percent Pathology for Controls

ID#	R. Apical	R. Cardiac	R. Diaphragmatic	L. Apical	L. Cardiac	L. Diaphragmatic	Intermediate	Total
476	0	3	1.25	0	0.5	0.5	1	6.25
478	7	8	15	9	9	15	7	70
483	8	9	17.5	8	9	20	8	79.5
484	9	9	7.5	3	6	5	5	44.5
493	2	5	1.25	1	2	1.25	1	13.5
494	3	6	5	2	6	7.5	5	34.5
495	1	5	0.5	0	1	2.5	5	15
497	0.5	7	1.25	2	3	1.25	6	21
499	7	7	7.5	5	8	12.5	7	54
500	3	6	15	8	8	12.5	6	58.5
503	2.5	6	1.25	3	6	2.5	8	29.25
508	0.5	5	1.25	9.5	10	2.5	0.5	29.25
509	8	8	22.5	9	8	17.5	8	81
513	2	6	2.5	1	3	2.5	5	22
514	0.2	1	0.5	0	2	0.25	0.5	4.45
515	4	8	1.25	5	7	1.25	1	27.5
519	0	0.2	0.5	0.1	0.2	0.5	0.5	2
520	0.2	1	0.5	0.2	0.5	0.5	1.5	4.4
521	6	8	12.5	5	8	15	5	59.5
522	0.2	1.5	0.5	0.2	1.5	0.25	0	4.15

Study Type	Efficacy
Pertaining to	Porcine Reproductive and Respiratory Syndrome Virus (PRRS)
Study Purpose	Demonstration of a Duration of Immunity of at least 4 months against the respiratory form of PRRS disease
Product Administration	Administration of one dose intramuscularly to 1 month old pigs
Study Animals	
Challenge Description	Challenged with PRRS 110 days after vaccination
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	March 11, 1994

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>All fractions</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate safety of the product under field conditions</td></tr>
<tr><td>Product Administration</td><td>Adminstration of one dose intramuscularly</td></tr>
<tr><td>Study Animals</td><td>1349 pigs, 18-25 days of age, at three different geographical locations divided into 672 vaccinates and 677 controls</td></tr>
<tr><td>Challenge Description</td><td>Not Applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>Animals were observed for at least 2 hours after vaccination and then daily for 14 days after vaccination</td></tr>
<tr><td>Results</td><td>Results Summary:

No injection site reactions were observed.

The number of pigs by site with specific clinical observations post-vaccination are presented in the following table:

<table>
<tr><th>Clinical Observation</th><th colspan="2">Site 1</th><th colspan="2">Site 2</th><th colspan="2">Site 3</th></tr>
<tr><th></th><th>Vac.</th><th>Cont.</th><th>Vac.</th><th>Cont.</th><th>Vac.</th><th>Cont.</th></tr>
<tr><td>Cough</td><td>1</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Gaunt</td><td>4</td><td>1</td><td>0</td><td>0</td><td>2</td><td>0</td></tr>
<tr><td>Lacking vigor / growth</td><td>1</td><td>2</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Red anus</td><td>0</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Red ears</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Swollen joint/foot /leg</td><td>0</td><td>1</td><td>2</td><td>0</td><td>2</td><td>2</td></tr>
<tr><td>Inflamed umbilicus</td><td>3</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Greasy pig disease</td><td>0</td><td>0</td><td>0</td><td>0</td><td>8</td><td>14</td></tr>
<tr><td>Pneumonia</td><td>0</td><td>0</td><td>0</td><td>0</td><td>3</td><td>0</td></tr>
<tr><td>Scours</td><td>0</td><td>0</td><td>0</td><td>0</td><td>18</td><td>15</td></tr>
<tr><td>Streptococcus infection</td><td>0</td><td>0</td><td>0</td><td>0</td><td>1</td><td>0</td></tr>
<tr><td>Lame</td><td>0</td><td>0</td><td>1</td><td>0</td><td>2</td><td>5</td></tr>
</table>
Additional observations were affirmed by licensee to be due to causes other than vaccination.
Vac. is vaccinate; Cont. is control.

The total number of animals exhibiting clinical signs for at least one day at all three sites are as follows:
<table>
<tr><th></th><th>Clinical Signs Present</th><th>Clinical Signs Absent</th><th>Percent with Clincal Signs</th></tr>
<tr><td>Vaccinates</td><td>48</td><td>624</td><td>7%</td></tr>
<tr><td>Controls</td><td>43</td><td>634</td><td>6%</td></tr>
</table></td></tr>
<tr><td>USDA Approval Date</td><td>June 18, 2009</td></tr>
</table>