



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	2799.21
True Name	Lawsonia Intracellularis Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Porcilis Ileitis - Merck Animal Health Porcilis Ileitis - No distributor specified
Date of Compilation Summary	June 08, 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.

Study Type	Efficacy																							
Pertaining to	<i>Lawsonia intracellularis</i>																							
Study Purpose	Demonstrate efficacy against ileitis																							
Product Administration	A single 2 mL dose administered intramuscularly																							
Study Animals	37 vaccinate and 37 control pigs, 3-4 weeks of age Group A: 23 vaccinates and 23 placebo controls Group B: 14 vaccinates and 14 placebo controls																							
Challenge Description	<i>Lawsonia intracellularis</i> administered 4 weeks following vaccination																							
Interval observed after challenge	Group A: For Ileitis and Colonization, tissues were evaluated 21 days post-challenge Group B: For Shedding, feces were evaluated three times a week for up to 60 days post-challenge																							
Results	<p><u>Ileitis</u> Group A animals were considered affected by the challenge if they presented with a gross lesion score > 1 or a microscopic histopathological lesion score > 0.</p> <table border="1"> <thead> <tr> <th rowspan="2">Treatment Group</th> <th colspan="2">Gross Lesion Score >1</th> <th rowspan="2">Histopathological Lesion Score >0</th> <th rowspan="2">Affected</th> </tr> <tr> <th>Scorer #1</th> <th>Scorer #2</th> </tr> </thead> <tbody> <tr> <td>Vaccinate</td> <td>12/23</td> <td>11/23</td> <td>8/23</td> <td>14/23</td> </tr> <tr> <td>Control</td> <td>13/23</td> <td>14/23</td> <td>22/23</td> <td>23/23</td> </tr> </tbody> </table> <p><u>Colonization</u> Group A animals were considered affected if they presented with a microscopic immunohistochemistry (IHC) score of > 0 or a qPCR value \geq limit of detection (LOD) for <i>Lawsonia</i> in mucosal scrapings.</p> <table border="1"> <thead> <tr> <th>Treatment Group</th> <th>Affected</th> </tr> </thead> <tbody> <tr> <td>Vaccinate</td> <td>10/23</td> </tr> <tr> <td>Control</td> <td>23/23</td> </tr> </tbody> </table> <p><u>Fecal Shedding</u> Group B animals were considered affected if they presented with a qPCR value \geq LOD for <i>Lawsonia</i> in fecal samples for one or more of the post-challenge testing time points. Summary for duration of shedding in days is as follows:</p>	Treatment Group	Gross Lesion Score >1		Histopathological Lesion Score >0	Affected	Scorer #1	Scorer #2	Vaccinate	12/23	11/23	8/23	14/23	Control	13/23	14/23	22/23	23/23	Treatment Group	Affected	Vaccinate	10/23	Control	23/23
Treatment Group	Gross Lesion Score >1		Histopathological Lesion Score >0	Affected																				
	Scorer #1	Scorer #2																						
Vaccinate	12/23	11/23	8/23	14/23																				
Control	13/23	14/23	22/23	23/23																				
Treatment Group	Affected																							
Vaccinate	10/23																							
Control	23/23																							

	Treatment	Min	Q ₁	Median	Q ₃	Max	
	Controls	8	19	22	29	31	
	Vaccinates	0	8	12	19	29	
	Raw data are shown below.						
USDA Approval Date	March 5, 2014						

SCORING GUIDE

Ileitis

Gross Lesion Score

- 0 – Normal mucosa
- 1 – Slight mucosal edema or slight hyperemia
- 2 – Moderate ileitis
- 3 – Severe ileitis
- 4 – Severe ileitis plus additionally hemorrhaging and/or necrosis, blood clots or yellowish pseudomembrane

Microscopic Histopathological Lesion Score

- 0 No diagnostic lesions
- 1 Mild individual crypt proliferative change
- 2 Marked proliferative enterocolitis

Colonization

IHC Score

- 0 Negative, no staining
- 1 Positive, rare positive staining in fewer than 10 crypts per section
- 2 Positive, moderate positive staining in 10-20 crypts per section
- 3 Positive, abundant positive staining in more than 20 crypts per section

qPCR of Mucosal Scrapings

Results shown are Log₁₀ DNA copies/reaction

BLD: Below Limit of Detection

Fecal Shedding

qPCR of Fecal Samples

Results shown are Log₁₀ DNA copies/reaction

B: Below Limit of Detection

ns: No Sample

RAW DATA TABLES

Vaccinate Group A					
ID	Gross Lesion Scores		Histopathological Score	IHC Score	qPCR of Mucosal Scrapings
	Scorer #1	Scorer #2			
86	0	0	0	0	BLD
90	2	2	0	0	1.5
91	1	1	0	0	BLD
92	2	3	0	0	BLD
96	1	1	1	1	2.5
102	0	0	0	0	BLD
103	2	1	0	0	BLD
104	2	2	0	0	BLD
105	1	1	0	0	BLD
108	2	2	2	3	2.0
110	2	2	1	2	2.8
118	1	1	0	0	0.8
127	2	2	1	2	2.2
132	1	1	2	3	1.6
133	2	2	1	2	2.9
136	1	1	0	0	BLD
140	2	2	0	0	BLD
141	2	2	0	0	BLD
149	1	1	0	0	BLD
151	2	2	2	3	3.9
155	1	1	0	0	BLD
156	1	1	0	0	BLD
161	2	2	1	1	2.2

Control Group A					
ID	Gross Lesion Scores		Histopathological Score	IHC Score	qPCR of Mucosal Scrapings
	Scorer #1	Scorer #2			
85	1	1	1	2	3.3
87	1	1	1	1	2.3
89	2	2	0	0	0.9
95	1	2	1	1	2.2
98	1	1	2	3	4.1
99	2	2	1	2	3.1
100	3	3	2	3	3.7
107	2	2	2	3	3.0
112	1	1	2	3	2.6
113	3	3	2	3	3.5
114	3	3	2	3	3.3
120	0	0	2	3	2.1
122	4	4	2	3	2.0
124	2	2	1	1	1.2
128	1	1	1	1	2.2
134	0	0	1	1	2.6
137	1	1	1	1	2.1
143	1	1	1	1	2.2
145	2	2	2	3	4.5
152	2	2	1	1	2.8
157	3	3	2	3	3.8
160	2	2	1	1	3.1
163	4	4	2	3	4.1

Fecal Shedding Group B

ID	Treatment	Day Post-Challenge																											
		-3	4	6	8	11	13	15	18	20	22	25	27	29	32	34	36	39	41	43	46	48	50	53	55	57	60		
84	Vaccinate	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
88	Vaccinate	B	B	B	B	B	B	1.4	3.0	ns	3.3	3.2	2.8	1.7	1.2	B	B	B	B	0.7	B	B	B	B	B	B	B	B	
94	Vaccinate	B	B	B	B	B	B	B	B	B	0.8	1.1	1.1	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
106	Vaccinate	B	B	B	B	B	B	0.7	0.6	1.7	1.1	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
111	Vaccinate	B	B	B	B	B	B	B	B	B	0.6	1.0	1.1	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
121	Vaccinate	B	B	B	B	B	B	0.6	0.5	0.9	2.0	3.1	2.7	1.3	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
123	Vaccinate	B	B	B	B	B	B	B	B	B	1.8	1.8	1.0	B	0.7	B	B	B	B	B	B	B	B	B	B	B	B	B	
130	Vaccinate	B	B	B	B	B	B	B	B	B	1.6	2.4	2.5	2.8	3.2	3.7	3.5	3.6	3.3	3.6	3.3	3.3	2.9	3.4	3.5	3.1	2.5	1.5	
131	Vaccinate	B	B	B	B	B	B	1.1	1.2	2.1	2.6	2.8	2.2	2.5	2.5	2.7	2.1	1.5	0.7	B	B	B	B	B	B	B	B		
138	Vaccinate	B	B	B	B	B	B	B	B	B	B	0.9	B	B	0.9	0.5	0.5	1.0	B	B	B	B	B	B	B	B	B		
150	Vaccinate	B	B	B	B	B	B	B	B	B	2.3	2.9	1.0	3.4	2.1	1.2	B	B	B	B	B	B	B	B	B	B	B		
153	Vaccinate	B	B	B	B	B	B	B	B	B	1.2	2.1	1.5	1.5	B	0.9	B	B	B	B	B	B	B	B	B	B	B		
162	Vaccinate	B	B	B	B	B	B	0.6	0.6	1.0	4.4	3.3	2.8	1.5	B	0.5	B	B	B	B	B	B	B	B	B	B	B		
165	Vaccinate	B	B	B	B	B	B	0.7	0.6	1.1	2.4	1.5	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B		
82	Control	B	B	B	B	B	B	B	1.4	1.8	1.8	1.5	0.9	B	B	B	B	B	B	0.9	0.9	B	B	B	B	B	B		
83	Control	B	B	B	B	B	B	0.8	2.0	3.5	3.1	1.4	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B		
93	Control	B	B	B	B	B	B	1.0	2.7	3.4	4.6																		
109	Control	B	B	B	B	B	B	2.0	3.1	3.5	4.5	4.1	2.8	2.1	2.1	1.7	B	B	B	B	B	B	B	B	B	B	B		
115	Control	B	B	B	B	B	B	0.6	2.0	2.0	4.0	4.2	3.7	2.0	1.2	0.5	B	B	B	B	B	B	B	B	B	B	B		
116	Control	B	B	B	B	B	B	B	B	B	1.3	2.2	1.9	1.3	B	B	B	B	B	B	B	B	B	B	B	B	B		
119	Control	B	B	B	B	B	B	1.4	2.6	3.8	3.8	3.7	3.7	1.5	1.4	0.8	B	B	B	B	B	B	B	B	B	B	B		
125	Control	B	B	B	B	B	B	1.5	1.7	2.7	4.6	5.1	4.6	4.4	4.0	2.5	3.7	B	B	B	B	B	B	B	B	B	B		
126	Control	B	B	B	B	B	B	0.9	2.2	2.6	2.8	4.5	5.1	5.5	5.0	3.6	3.7	4.1	1.1	3.1	1.9	B	B	B	B	B	B		
129	Control	B	B	B	B	B	B	1.4	1.7	2.5	5.2	5.5	5.0	4.5	4.0	2.1	2.4	4.2	4.3	2.0	B	B	B	B	B	B	B		
144	Control	B	B	B	B	B	B	1.0	1.5	2.6	4.1	4.0	3.4	3.1	3.1	2.7	2.3	1.8	B	B	B	B	B	B	B	B	B		
146	Control	B	B	B	B	B	B	0.5	B	1.0	1.6	2.5	2.7	1.4	1.5	0.8	B	B	B	B	B	B	B	B	B	B	B		
148	Control	B	B	B	B	B	B	ns	B	1.6	B	1.0	2.3	2.1	0.8	B	B	B	B	B	B	B	B	B	B	B	B		
154	Control	B	B	B	B	B	B	0.9	1.7	2.9	3.6	2.2	4.9	4.3	3.5	3.0	1.5	B	B	B	B	B	B	B	B	B	B		

The firm affirmed that ID 93 died as a result of the challenge.

Study Type	Efficacy																							
Pertaining to	<i>Lawsonia intracellularis</i>																							
Study Purpose	Demonstrate 20-week duration of immunity against ileitis																							
Product Administration	A single 2 mL dose administered intramuscularly																							
Study Animals	38 vaccinate and 40 control pigs, 3-4 weeks of age Group A: 24 vaccinates and 25 placebo controls Group B: 14 vaccinates and 15 placebo controls																							
Challenge Description	<i>Lawsonia intracellularis</i> administered 20 weeks after vaccination																							
Interval observed after challenge	Group A: For Ileitis and Colonization, tissues were evaluated 21 days post-challenge Group B: For Shedding, feces were evaluated three times a week for up to 49 days post-challenge																							
Results	<p><u>Ileitis</u> Group A animals were considered affected by the challenge if they presented with a gross lesion score > 1 or a microscopic histopathological lesion score > 0.</p> <table border="1"> <thead> <tr> <th rowspan="2">Treatment Group</th> <th colspan="2">Gross Lesion Score >1</th> <th rowspan="2">Histopathological Lesion Score >0</th> <th rowspan="2">Affected</th> </tr> <tr> <th>Scorer #1</th> <th>Scorer #2</th> </tr> </thead> <tbody> <tr> <td>Vaccinate</td> <td>5/24</td> <td>5/24</td> <td>5/24</td> <td>5/24</td> </tr> <tr> <td>Control</td> <td>15/25</td> <td>16/25</td> <td>19/25</td> <td>19/25</td> </tr> </tbody> </table> <p><u>Colonization</u> Group A animals were considered affected if they presented with a microscopic immunohistochemistry (IHC) score of > 0 or a qPCR value ≥ limit of detection (LOD) for <i>Lawsonia</i> in mucosal scrapings.</p> <table border="1"> <thead> <tr> <th>Treatment Group</th> <th>Affected</th> </tr> </thead> <tbody> <tr> <td>Vaccinate</td> <td>13/24</td> </tr> <tr> <td>Control</td> <td>23/25</td> </tr> </tbody> </table> <p><u>Fecal Shedding</u> Group B animals were considered affected if they presented a qPCR value ≥ LOD for <i>Lawsonia</i> in fecal samples for one or more of the post challenge testing time points. Samples were collected every 2-3 days. Summary for duration of shedding in days is as follows:</p>	Treatment Group	Gross Lesion Score >1		Histopathological Lesion Score >0	Affected	Scorer #1	Scorer #2	Vaccinate	5/24	5/24	5/24	5/24	Control	15/25	16/25	19/25	19/25	Treatment Group	Affected	Vaccinate	13/24	Control	23/25
Treatment Group	Gross Lesion Score >1		Histopathological Lesion Score >0	Affected																				
	Scorer #1	Scorer #2																						
Vaccinate	5/24	5/24	5/24	5/24																				
Control	15/25	16/25	19/25	19/25																				
Treatment Group	Affected																							
Vaccinate	13/24																							
Control	23/25																							

	Treatment	Min	Q ₁	Median	Q ₃	Max
	Controls	10	17	19	21	36
	Vaccinates	0	5	7	12	25
Raw data shown below						
USDA Approval Date	March 6, 2014					

SCORING GUIDE

Ileitis

Gross Lesion Score

- 0 – Normal mucosa
- 1 – Slight mucosal edema or slight hyperemia
- 2 – Moderate ileitis
- 3 – Severe ileitis
- 4 – Severe ileitis plus additionally hemorrhaging and/or necrosis, blood clots or yellowish pseudomembrane

Microscopic Histopathological Lesion Score

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qPCR of Mucosal Scrapings

Results shown are Log₁₀ DNA copies/reaction
 BLD: Below Limit Of Detection

Fecal Shedding

qPCR of Fecal Samples

Results shown are Log₁₀ DNA copies/reaction
 B: Below Limit Of Detection

RAW DATA TABLES

Vaccinate Group A					
ID	Gross Lesion Scores		Histopathological Score	IHC Score	qPCR of Mucosal Scrapings
	Scorer #1	Scorer #2			
629	1	1	0	0	0.5
634	1	1	0	0	1.2
638	1	1	0	0	BLD
639	1	1	0	0	BLD
641	1	1	0	0	BLD
645	0	0	0	0	1.0
648	0	0	0	0	1.0
653	0	1	0	0	1.7
655	1	1	0	0	BLD
659	1	1	0	0	BLD
663	0	0	0	0	BLD
665	2	2	0	0	0.7
670	0	0	0	0	1.8
673	1	1	0	0	BLD
674	0	0	0	0	BLD
675	1	0	0	0	BLD
676	1	1	0	0	0.7
681	2	2	2	2	3.5
683	2	2	0	0	0.7
684	2	3	2	3	3.5
691	1	1	0	0	0.7
698	2	3	0	0	BLD
699	1	1	0	0	BLD
707	1	1	0	0	1.4

Control Group A					
ID	Gross Lesion Scores		Histopathological Score	IHC Score	qPCR of Mucosal Scrapings
	Scorer #1	Scorer #2			
631	2	2	2	3	3.9
632	4	4	2	3	5.0
633	3	3	2	3	4.1
637	1	2	2	3	4.0
643	3	3	2	3	2.1
649	2	3	2	3	4.0
651	2	2	2	2	3.3
652	1	0	2	2	1.0
654	3	3	2	2	2.2
661	0	0	0	0	1.1
662	1	1	0	0	0.5
668	4	4	2	2	3.6
669	3	3	2	3	3.7
671	0	0	0	0	1.5
678	3	3	2	2	3.9
679	1	1	2	3	1.1
685	2	2	2	3	2.8
686	1	1	0	0	BLD
687	0	0	0	0	0.7
689	4	4	2	2	3.2
694	1	1	1	1	1.1
696	3	3	2	3	3.0
701	1	1	0	0	BLD
706	2	2	1	1	2.8
709	2	2	1	1	2.1

Fecal Shedding Group B

ID	Treatment	Day Post-Challenge																					
		-3	2	4	7	9	11	14	16	18	21	23	25	28	30	32	35	37	39	42	44	46	49
630	Vaccinate	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
640	Vaccinate	B	B	B	2.4	B	B	2.5	2.6	2.1	3.3	2.6	0.6	B	B	B	B	B	B	B	B	B	B
644	Vaccinate	B	B	B	B	B	B	1.4	1.7	0.8	B	B	B	B	B	B	B	B	B	B	B	B	B
646	Vaccinate	B	B	B	B	B	B	1.9	2.4	0.9	B	B	B	B	B	B	B	B	B	B	B	B	B
656	Vaccinate	B	B	B	B	B	B	1.3	2.3	2.9	2.3	1.4	B	B	B	B	B	B	B	B	B	B	B
664	Vaccinate	B	B	B	B	B	B	1.2	2.0	2.6	0.9	B	B	B	B	B	B	B	B	B	B	B	B
672	Vaccinate	B	B	0.9	1.9	2.2	1.8	1.2	B	B	B	0.6	1.0	B	B	B	B	B	B	B	B	B	B
677	Vaccinate	B	B	1.3	2.7	3.4	3.9	4.5	4.3	4.1	3.0	B	B	B	B	B	B	B	B	B	B	B	B
688	Vaccinate	B	B	B	0.7	0.9	1.1	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
692	Vaccinate	B	B	B	0.9	1.1	1.0	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
700	Vaccinate	B	B	B	B	B	B	B	1.9	B	B	B	B	B	B	B	B	B	B	B	B	B	B
703	Vaccinate	B	B	B	B	B	B	B	B	0.7	B	B	B	B	B	B	B	B	B	B	B	B	B
704	Vaccinate	B	B	B	1.9	1.8	2.0	3.1	3.2	1.4	B	B	B	B	B	B	B	B	B	B	B	B	B
708	Vaccinate	B	B	B	0.9	2.1	3.1	1.9	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B
628	Control	B	B	B	B	1.5	1.5	1.9	2.1	2.5	2.6	1.9	1.8	B	B	B	B	B	B	B	B	B	B
642	Control	B	B	B	0.7	2.0	3.0	3.5	3.6	3.2	2.4	1.8	B	B	B	B	B	B	B	B	B	B	B
647	Control	B	B	B	B	1.0	1.5	2.5	3.2	3.3	3.3	2.9	2.6	1.2	B	B	B	B	B	B	B	B	B
650	Control	B	B	B	B	B	1.6	2.2	2.7	2.7	3.2	2.4	2.2	2.3	1.4	B	B	B	B	B	B	B	B
657	Control	B	B	B	0.5	0.9	1.8	1.8	1.7	0.6	B	B	B	B	B	B	B	B	B	B	B	B	B
660	Control	B	B	B	0.7	1.8	2.7	3.6	3.5	3.6	2.9	1.1	B	B	B	B	B	B	B	B	B	B	B
667	Control	B	B	B	1.9	2.3	3.9	5.0	5.2	4.3	5.7	4.8	5.0	3.7	3.8	3.6	3.2	3.8	2.6	0.5	B	B	B
680	Control	B	B	B	1.4	1.2	3.3	4.2	4.1	4.2	4.7	4.5	4.7	4.0	3.0	B	B	B	B	B	B	B	B
682	Control	B	B	1.1	1.4	2.6	2.8	3.1	2.7	2.5	2.1	1.8	1.4	B	B	B	B	B	B	B	B	B	B
693	Control	B	B	B	B	1.2	1.7	1.9	2.2	1.0	B	B	B	B	B	B	B	B	B	B	B	B	B
695	Control	B	B	B	1.9	2.3	3.3	4.8	5.2	4.3	2.7	3.0	1.5	B	B	B	B	B	B	B	B	B	B
697	Control	B	B	B	1.2	2.8	3.1	4.8	4.5	4.5	4.5	3.6	0.6	B	B	B	B	B	B	B	B	B	B
702	Control	B	B	1.2	1.9	2.2	3.7	3.7	2.9	2.2	1.7	B	B	B	B	B	B	B	B	B	B	B	B
705	Control	B	B	0.7	2.3	2.9	4.0	5.7	5.4	5.2	4.9	3.2	0.6	B	B	B	B	B	B	B	B	B	B
711	Control	B	B	B	1.5	2.0	2.7	3.7	3.7	3.3	3.3	1.8	1.6	B	B	B	B	B	B	B	B	B	B

Study Type	Efficacy																							
Pertaining to	<i>Lawsonia intracellularis</i>																							
Study Purpose	Demonstrate efficacy against ileitis																							
Product Administration	Two 1 mL doses administered intramuscularly at a 3-4 week interval																							
Study Animals	40 vaccinate and 38 control pigs, 3-6 days of age Group A: 25 vaccinates and 23 placebo controls Group B: 15 vaccinates and 15 placebo controls																							
Challenge Description	<i>Lawsonia intracellularis</i> administered 4 weeks following the second vaccination																							
Interval observed after challenge	Group A: For Ileitis and Colonization, tissues were evaluated 21 days post-challenge. Group B: For Shedding, feces were evaluated three times a week for up to 51 days post-challenge.																							
Results	<p><u>Ileitis</u> Group A animals were considered affected by the challenge if they presented with a gross lesion score > 1 or a microscopic histopathological lesion score > 0.</p> <table border="1"> <thead> <tr> <th rowspan="2">Treatment Group</th> <th colspan="2">Gross Lesion Score >1</th> <th rowspan="2">Histopathological Lesion Score >0</th> <th rowspan="2">Affected</th> </tr> <tr> <th>Scorer #1</th> <th>Scorer #2</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>6/25</td> <td>6/25</td> <td>1/25</td> <td>14/25</td> </tr> <tr> <td>Control</td> <td>19/23</td> <td>18/23</td> <td>22/23</td> <td>23/23</td> </tr> </tbody> </table> <p><u>Colonization</u> Group A animals were considered affected if they presented with a microscopic IHC score of > 0 or a qPCR value \geq LOD for <i>Lawsonia</i> in mucosal scrapings.</p> <table border="1"> <thead> <tr> <th>Treatment Group</th> <th>Affected</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>4/25</td> </tr> <tr> <td>Control</td> <td>22/23</td> </tr> </tbody> </table> <p><u>Fecal Shedding</u> Group B animals were considered affected if they presented a qPCR value \geq LOD for <i>Lawsonia</i> in fecal samples for one or more of the post challenge testing time points. A summary of duration of shedding in days is as follows:</p>	Treatment Group	Gross Lesion Score >1		Histopathological Lesion Score >0	Affected	Scorer #1	Scorer #2	Vaccinates	6/25	6/25	1/25	14/25	Control	19/23	18/23	22/23	23/23	Treatment Group	Affected	Vaccinates	4/25	Control	22/23
Treatment Group	Gross Lesion Score >1		Histopathological Lesion Score >0	Affected																				
	Scorer #1	Scorer #2																						
Vaccinates	6/25	6/25	1/25	14/25																				
Control	19/23	18/23	22/23	23/23																				
Treatment Group	Affected																							
Vaccinates	4/25																							
Control	22/23																							

	Treatment	Min	Q₁	Median	Q₃	Max
	Controls	15	22	24	26	36
	Vaccinates	1	10	13	17	22
	Raw data shown below					
USDA Approval Date	March 6, 2014					

SCORING GUIDE

Ileitis

Gross Lesion Score

- 0 – Normal mucosa
- 1 – Slight mucosal edema or slight hyperemia
- 2 – Moderate ileitis
- 3 – Severe ileitis
- 4 – Severe ileitis plus additionally hemorrhaging and/or necrosis, blood clots or yellowish pseudomembrane

Microscopic Histopathological Lesion Score

- 0 No diagnostic lesions
- 1 Mild individual crypt proliferative change
- 2 Marked proliferative enterocolitis

Colonization

IHC Score

- 0 Negative, no staining
- 1 Positive, rare positive staining in fewer than 10 crypts per section
- 2 Positive, moderate positive staining in 10-20 crypts per section
- 3 Positive, abundant positive staining in more than 20 crypts per section

qPCR of Mucosal Scrapings

Results shown are Log₁₀ DNA copies/reaction
 BLD: Below Limit Of Detection

Fecal Shedding

qPCR of Fecal Samples

Results shown are Log₁₀ DNA copies/reaction

B: Below Limit Of Detection

ns: No Sample

RAW DATA TABLES

Vaccination Group A					
ID	Gross Lesion Scores		Histopathological Score	IHC Score	qPCR of Mucosal Scrapings
	Scorer #1	Scorer #2			
117	1	1	0	0	BLD
118	0	0	0	0	BLD
121	1	1	0	0	BLD
130	0	1	0	0	BLD
138	2	2	0	0	BLD
147	1	1	0	0	BLD
149	1	1	0	0	1.8
153	1	1	0	0	BLD
155	1	1	0	0	1.0
167	0	0	0	0	BLD
169	1	1	0	0	BLD
172	1	1	0	0	BLD
174	1	1	0	0	BLD
180	1	1	0	0	BLD
185	1	1	0	0	0.5
191	2	2	0	0	BLD
193	0	1	0	0	BLD
203	2	2	0	0	BLD
206	2	2	0	0	BLD
211	2	2	0	0	BLD
219	1	1	0	0	BLD
235	1	1	0	0	BLD
237	1	1	0	0	BLD
239	1	1	0	0	BLD
242	3	3	2	3	3.9

Control Group A					
ID	Gross Lesion Scores		Histopathological Score	IHC Score	qPCR of Mucosal Scrapings
	Scorer #1	Scorer #2			
119	4	4	2	3	4.6
123	4	4	2	3	3.5
127	3	3	2	3	3.6
132	2	2	2	3	3.4
144	2	1	2	3	3.4
148	1	1	1	2	2.7
151	4	3	2	3	4.2
152	2	2	2	3	3.6
163	1	1	1	1	1.4
170	1	1	2	3	4.1
176	2	2	2	3	3.3
178	2	2	1	2	2.9
183	4	4	2	3	4.6
186	3	3	2	3	4.1
187	3	3	2	3	3.8
195	3	3	2	3	4.4
204	1	1	1	1	2.0
208	2	2	2	3	2.4
227	3	3	2	3	BLD
233	2	2	0	0	BLD
236	2	2	2	3	3.1
243	4	4	2	3	4.0
249	3	3	2	3	4.4

Fecal Shedding Group B

Pig ID #	Treatment	Day Post-Challenge																							
		1	5	7	9	12	14	16	19	21	23	26	28	30	33	35	37	40	42	44	47	49	51		
114	Vaccine	B	B	B	B	B	B	B	B	1.7	B	B	B	B	B	B	B	B	B	B	B	B	B		
128	Vaccine	B	B	B	B	1.0	1.3	0.6	1.1	1.7	B	B	B	B	B	B	B	B	B	B	B	B	B		
136	Vaccine	B	B	B	B	B	B	B	B	B	0.6	B	B	B	B	B	B	B	B	B	B	0.9	0.6		
141	Vaccine	B	B	B	B	B	0.6	0.9	1.2	B	B	B	B	B	B	B	B	B	B	B	B	B	B		
142	Vaccine	B	B	B	B	B	B	B	B	B	B	B	B	B	0.8	B	B	B	B	B	B	B	B		
157	Vaccine	B	0.8	0.5	1.4	2.5	3.2	3.0	3.5	3.0	3.3	1.6	B	B	B	B	B	B	B	B	B	B	B		
162	Vaccine	B	B	B	0.6	2.0	2.2	2.4	2.0	2.0	1.4	0.7	B	B	B	B	B	B	B	B	B	B	B		
177	Vaccine	B	B	B	B	B	B	1.0	0.9	1.1	1.2	0.8	B	B	B	B	B	B	B	B	B	B	B		
182	Vaccine	B	1.3	2.5	2.7	2.5	3.7	3.7	1.8	1.1	B	B	B	B	B	B	B	B	B	B	B	B	B		
189	Vaccine	B	B	B	B	B	B	1.4	0.6	B	B	1.4	1.5	B	B	B	B	B	B	B	B	B	B		
192	Vaccine	B	B	B	B	B	B	1.2	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B		
207	Vaccine	B	B	B	B	B	B	B	B	B	0.5	1.0	1.1	1.4	1.1	1.2	0.9	B	B	B	B	B	B		
214	Vaccine	B	B	B	B	B	B	0.7	B	B	B	1.5	B	B	B	B	B	B	B	B	B	B	B		
232	Vaccine	B	B	B	B	B	B	1.0	0.8	1.2	2.2	2.6	2.4	1.3	1.9	B	B	B	B	B	B	B	B		
246	Vaccine	B	B	B	B	B	B	1.8	2.1	2.9	1.7	1.2	B	B	B	B	B	B	B	B	B	B	B		
115	Placebo	B	B	B	B	2.0	2.3	3.5	4.2	4.1	3.5	3.1	2.0	2.2	B	B	B	B	B	B	B	B	B		
131	Placebo	B	B	1.3	2.2	3.7	4.2	5.4	4.4	3.7	3.4	2.7	2.4	2.2	B	B	B	B	B	B	B	B	B		
135	Placebo	B	B	B	B	B	B	1.4	2.4	2.8	2.9	3.1	2.1	2.7	B	B	B	B	B	B	B	ns	B		
140	Placebo	B	B	B	B	B	B	0.7	1.8	2.7	2.7	2.9	2.1	2.6	1.6	1.4	1.2	B	B	B	B	B	B		
143	Placebo	B	B	B	B	B	B	1.3	3.3	3.8	4.2	3.8	3.3	2.8	2.1	1.9	B	B	B	B	B	B	B		
156	Placebo	B	1.6	2.2	2.2	4.4	4.8	4.6	4.3	3.8	3.7	3.1	2.1	1.6	B	B	B	B	B	B	B	B	B		
171	Placebo	B	B	1.2	1.7	3.0	4.0	4.6	5.4																
173	Placebo	B	B	0.7	2.2	2.8	3.8	4.5	3.9	4.2	4.5	3.6	2.1	0.9	B	B	B	B	B	B	B	B	ns		
184	Placebo	B	1.6	3.2	3.7	5.2	5.6	5.1	3.5	4.8	5.0	4.8	5.0												
194	Placebo	B	B	B	0.9	1.8	2.4	3.2	4.0	4.0	3.7	3.2	1.4	0.9	B	B	B	B	B	B	B	B	B		
200	Placebo	B	B	B	0.9	1.2	1.9	2.0	2.9	3.5	3.6	3.7	2.1	2.2	B	B	B	B	B	B	B	B	B		
210	Placebo	B	B	B	0.6	1.1	1.9	2.2	2.8	3.1	3.8	2.9	1.3	1.9	1.0	1.2	B	B	B	B	B	B	B		
222	Placebo	B	B	B	B	B	0.9	1.7	1.9	2.7	1.5	3.4	3.6	4.2	3.6	3.8	3.8	3.1	3.0	2.6	2.1	0.6	B		
238	Placebo	B	B	B	1.3	2.4	3.2	4.2	5.3	5.4	4.9	4.7	4.3	3.4	0.8	B	B	B	B	B	B	B	B		
241	Placebo	B	B	B	0.8	2.1	2.8	3.3	4.4	4.0	4.4	4.4	3.8	3.6	3.6	3.7	2.6	B	B	B	B	B	B		

The firm affirmed that ID 114 and 171 were removed due to causes unrelated to the vaccination or challenge. ID 184 was removed due to severe ileitis.

Study Type	Efficacy																																			
Pertaining to	<i>Lawsonia intracellularis</i>																																			
Study Purpose	Demonstrate 20-week duration of immunity against ileitis due to <i>L. intracellularis</i> .																																			
Product Administration	Two doses, administered intramuscularly to pigs 3-5 days of age and repeated at 3 weeks of age																																			
Study Animals	40 vaccinated and 38 control pigs Group A: 25 vaccinates and 23 placebo controls Group B: 15 vaccinates and 15 placebo controls																																			
Challenge Description	<i>Lawsonia intracellularis</i> administered 20 weeks after the second vaccination																																			
Interval observed after challenge	Group A: To evaluate for ileitis, ileal tissues were evaluated 21 days post-challenge Group B: To evaluate for fecal shedding, feces and rectal swabs were evaluated three times a week for up to 59 days post-challenge.																																			
Results	<p>A. Ileitis Group A animals were considered affected by the challenge if ileal tissue presented with a gross lesion score > 1 or a microscopic histopathological lesion score > 0.</p> <table border="1"> <thead> <tr> <th rowspan="2">Treatment Group</th> <th colspan="2">Gross Lesion Score >1</th> <th rowspan="2">Histopathological Lesion Score >0</th> <th rowspan="2">Affected</th> </tr> <tr> <th>Scorer #1</th> <th>Scorer #2</th> </tr> </thead> <tbody> <tr> <td>Vaccinate</td> <td>4/25</td> <td>4/25</td> <td>4/25</td> <td>5/25</td> </tr> <tr> <td>Control</td> <td>12/23</td> <td>13/23</td> <td>20/23</td> <td>23/23</td> </tr> </tbody> </table> <p>B. Fecal Shedding Group B animals were considered affected if they presented with a quantitative Polymerase Chain Reaction (qPCR) value log₁₀ DNA copies/mL > 0 in fecal samples for one or more of the post challenge testing time points. The duration of shedding was evaluated by qPCR of the fecal samples. The duration of shedding was calculated as time (in days) between the first positive PCR sample and the last positive PCR sample.</p> <p>Summary for duration of shedding in days is as follows:</p> <table border="1"> <thead> <tr> <th>Group</th> <th>Minimum</th> <th>Q1</th> <th>Median</th> <th>Q3</th> <th>Maximum</th> </tr> </thead> <tbody> <tr> <td>Vaccinate</td> <td>9</td> <td>15</td> <td>18</td> <td>22</td> <td>49</td> </tr> <tr> <td>Control</td> <td>18</td> <td>24</td> <td>30</td> <td>40</td> <td>50</td> </tr> </tbody> </table> <p>Q = quartile</p> <p>Raw data tables are shown below.</p>	Treatment Group	Gross Lesion Score >1		Histopathological Lesion Score >0	Affected	Scorer #1	Scorer #2	Vaccinate	4/25	4/25	4/25	5/25	Control	12/23	13/23	20/23	23/23	Group	Minimum	Q1	Median	Q3	Maximum	Vaccinate	9	15	18	22	49	Control	18	24	30	40	50
Treatment Group	Gross Lesion Score >1		Histopathological Lesion Score >0	Affected																																
	Scorer #1	Scorer #2																																		
Vaccinate	4/25	4/25	4/25	5/25																																
Control	12/23	13/23	20/23	23/23																																
Group	Minimum	Q1	Median	Q3	Maximum																															
Vaccinate	9	15	18	22	49																															
Control	18	24	30	40	50																															
USDA Approval Date	February 22, 2021																																			

GROSS and HISTOPATHOLOGICAL SCORE OF ILEAL TISSUE

Vaccination Group A				Control Group A			
ID	Gross Lesion Score Scorer #1	Gross Lesion Score Scorer #2	Histo-pathological Score	ID	Gross Lesion Score Scorer #1	Gross Lesion Score Scorer #2	Histo-pathological Score
12	0	0	0	17	2	2	0
18	1	1	0	21	1	1	1
24	0	0	0	27	2	2	2
31	0	0	0	29	0	0	2
39	1	1	1	33	1	2	0
41	0	0	0	35	1	1	2
48	2	2	2	37	1	1	2
52	0	0	0	44	0	0	2
53	2	2	2	46	3	2	2
54	0	0	0	55	2	2	2
57	1	0	0	59	2	2	2
66	1	0	0	60	0	0	2
71	1	1	0	64	2	2	2
74	0	0	0	67	3	3	2
76	0	1	0	70	2	2	2
78	0	0	0	84	1	1	2
79	2	2	0	87	0	1	2
88	0	0	0	93	3	3	2
95	1	1	0	94	4	4	2
111	1	1	0	113	2	2	2
117	0	0	0	115	1	1	1
118	0	0	0	138	0	1	2
131	1	1	0	140	4	4	0
132	1	1	0				
133	2	2	2				

Scoring Guide

Gross Lesion Score

- 0 – Normal mucosa
- 1 – Slight mucosal edema or slight hyperemia
- 2 – Moderate ileitis
- 3 – Severe ileitis
- 4 – Severe ileitis plus addition of hemorrhaging and/or necrosis, blood clots or yellowish pseudomembrane

Microscopic Histopathological Lesion Score

- 0 No diagnostic lesions
- 1 Mild individual crypt proliferative change
- 2 Marked proliferative enterocolitis

FECAL SHEDDING QUANTITATIVE PCR RESULTS

Pig ID	Treatment	Number of Days after Challenge																											
		-3	3	5	7	10	12	14	17	19	21	24	26	28	31	33	35	38	40	42	45	47	49	52	54	56	59		
16	Vaccinate	B	B	B	3.0	3.7	4.9	5.0	3.5	2.3	2.4	2.2	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
19	Vaccinate	B	B	B	B	4.7	4.4	3.9	3.4	3.2	2.5	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
23	Vaccinate	B	B	2.3	2.6	4.3	4.3	4.8	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
26	Vaccinate	B	B	B	B	B	2.6	B	2.6	2.5	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
43	Vaccinate	B	B	2.2	B	4.0	5.0	5.9	B	3.9	3.0	6.1	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B		
49	Vaccinate	B	B	B	B	3.2	2.9	2.6	B	B	3.2	2.1	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
62	Vaccinate	B	B	B	B	B	2.6	B	2.6	2.9	2.7	4.0	3.6	3.7	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
65	Vaccinate	B	B	2.3	3.0	4.7	4.9	5.0	4.2	2.3	2.3	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
68	Vaccinate	B	B	B	B	B	2.7	3.8	2.7	B	B	3.9	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
82	Vaccinate	B	B	B	B	2.9	3.2	3.3	B	2.5	2.1	3.0	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
89	Vaccinate	B	B	B	B	2.3	3.3	7.1	5.9	2.6	3.6	3.7	3.3	2.4	2.9	B	B	B	B	B	B	B	B	B	B	B	B	B	
96	Vaccinate	B	B	2.6	B	4.3	4.4	3.3	2.3	3.3	3.9	B	B	B	B	2.1	B	B	B	B	B	B	B	B	B	B	B	B	
112	Vaccinate	B	B	B	B	B	2.1	B	B	B	B	B	2.3	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
116	Vaccinate	B	B	B	B	5.1	3.8	4.3	B	2.4	2.7	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
137	Vaccinate	B	B	B	B	3.3	5.9	3.4	B	5.6	2.9	B	B	B	B	B	B	B	B	B	B	2.7	B	2.4	B	B	B	B	
15	Placebo	B	B	B	B	4.1	4.9	5.2	4.9	6.0	5.2	4.5	2.5	B	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
22	Placebo	B	B	3.0	4.1	6.2	7.4	6.5	5.1	6.2	5.5	6.5	6.5	4.7	Died														
32	Placebo	B	B	B	2.6	6.0	6.1	7.1	6.4	6.0	6.9	5.9	5.1	5.7	6.4	4.3	4.5	3.1	B	B	B	B	B	B	B	B	B	B	
36	Placebo	B	B	B	B	2.7	4.9	4.2	2.6	4.2	3.8	3.9	4.1	3.9	3.6	B	B	B	B	B	B	B	B	B	B	B	B	B	
45	Placebo	B	B	B	B	4.7	4.7	5.5	6.0	6.6	7.0	6.8	6.0	6.3	6.1	4.3	3.3	3.1	B	B	B	B	B	B	B	B	B	B	
63	Placebo	B	B	B	2.1	3.5	4.9	5.7	6.1	6.1	7.2	7.1	6.6	6.7	5.8	B	B	B	B	B	B	B	B	B	B	B	B	B	
72	Placebo	B	B	B	B	2.5	3.3	3.2	2.6	4.1	4.1	4.1	3.5	3.2	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
75	Placebo	B	B	B	B	2.2	4.9	5.6	4.6	3.8	3.7	4.7	4.2	3.9	3.7	2.9	B	B	B	B	B	B	B	B	B	B	B	B	
80	Placebo	B	B	B	2.3	5.4	5.9	7.0	6.1	5.1	6.4	B	5.1	4.6	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
85	Placebo	B	B	B	B	4.9	5.8	6.5	4.7	5.7	6.4	5.6	4.8	4.5	5.5	3.6	4.1	4.3	B	B	B	B	B	B	B	B	B	B	
90	Placebo	B	B	2.3	4.2	6.8	5.6	3.1	4.4	7.0	5.6	5.8	5.5	6.0	7.5	4.9	5.9	6.4	5.5	6.8	5.1	4.5	B	B	B	B	B	B	
108	Placebo	B	B	B	B	4.1	4.8	4.5	4.1	4.2	4.6	4.0	3.6	3.4	B	B	B	B	B	B	B	B	B	B	B	B	B	B	
114	Placebo	B	B	B	B	4.9	3.8	5.3	5.1	5.8	6.4	6.5	5.0	5.9	5.8	B	B	B	B	B	B	B	B	B	B	B	B	B	
134	Placebo	B	B	B	2.1	5.7	6.0	6.3	6.5	8.0	7.1	6.0	6.3	5.6	6.4	5.9	6.3	6.8	6.5	7.2	4.6	4.0	3.7	B	B	B	B	B	
136	Placebo	B	B	2.7	2.1	6.3	6.0	6.4	5.9	6.1	6.8	5.3	5.5	6.2	6.4	4.8	3.3	B	4.4	2.8	B	2.3	B	B	B	B	B	B	

All values in log₁₀ c/mL
 B : below limit of detection in qPCR assay

Pig #22 died due to severe ileitis

Study Type	Safety																																																		
Pertaining to	All																																																		
Study Purpose	Demonstrate safety of product under typical use conditions																																																		
Product Administration	Two doses administered intramuscularly 3 weeks apart																																																		
Study Animals	665 pigs, 3-5 days of age at first administration, three study sites in three geographically distinct locations.																																																		
Challenge Description	NA																																																		
Interval observed after challenge	Animals were observed for at least 1 hour following completion of all vaccinations, and then daily for 21 days, or until resolution of any adverse events.																																																		
Results	<table border="1"> <thead> <tr> <th>Adverse Events (AE) (Total 665 pigs)</th> <th>Number</th> </tr> </thead> <tbody> <tr> <td>Injection Site Swelling¹ *</td> <td>441</td> </tr> <tr> <td> <u>First Vaccination</u></td> <td></td> </tr> <tr> <td> S (<1.5 cm)</td> <td>35</td> </tr> <tr> <td> M (1.5 to 5 cm)</td> <td>76</td> </tr> <tr> <td> L (>5 to 10 cm)</td> <td>1</td> </tr> <tr> <td> <u>Second Vaccination</u></td> <td></td> </tr> <tr> <td> S (<1.5 cm)</td> <td>246</td> </tr> <tr> <td> M (1.5 to 5 cm)</td> <td>82</td> </tr> <tr> <td> L (>5 to 10 cm)</td> <td>1</td> </tr> <tr> <td>Respiratory tract infection NOS</td> <td>220</td> </tr> <tr> <td>Death²</td> <td>27</td> </tr> <tr> <td>Diarrhoea</td> <td>27</td> </tr> <tr> <td>Dyspnoea</td> <td>14</td> </tr> <tr> <td>Respiratory tract disorder NOS</td> <td>13</td> </tr> <tr> <td>Lameness</td> <td>9</td> </tr> <tr> <td>Unthrifty</td> <td>9</td> </tr> <tr> <td>Ataxia</td> <td>2</td> </tr> <tr> <td>Anaphylaxis³ *</td> <td>1</td> </tr> <tr> <td>Abscess NOS</td> <td>1</td> </tr> <tr> <td>Lethargy</td> <td>1</td> </tr> <tr> <td>Rectal prolapse</td> <td>1</td> </tr> <tr> <td>Trauma NOS</td> <td>1</td> </tr> <tr> <td>Cellulitis</td> <td>1</td> </tr> <tr> <td>No adverse events</td> <td>163</td> </tr> </tbody> </table> <p>Subjects may have had AE's in more than one VeDDRA Preferred Term and are counted once in each appropriate class.</p> <p>¹ Injection site swellings resolved within 1- 25 days.</p>	Adverse Events (AE) (Total 665 pigs)	Number	Injection Site Swelling ¹ *	441	<u>First Vaccination</u>		S (<1.5 cm)	35	M (1.5 to 5 cm)	76	L (>5 to 10 cm)	1	<u>Second Vaccination</u>		S (<1.5 cm)	246	M (1.5 to 5 cm)	82	L (>5 to 10 cm)	1	Respiratory tract infection NOS	220	Death ²	27	Diarrhoea	27	Dyspnoea	14	Respiratory tract disorder NOS	13	Lameness	9	Unthrifty	9	Ataxia	2	Anaphylaxis ³ *	1	Abscess NOS	1	Lethargy	1	Rectal prolapse	1	Trauma NOS	1	Cellulitis	1	No adverse events	163
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	<p>² Deaths affirmed by licensee to have a cause other than vaccination.</p> <p>³ Animal recovered within 10 minutes after vaccination.</p> <p>*Vaccine related AE.</p> <p>NOS = Not otherwise specified</p>
USDA Approval Date	February 8, 2019

Study Type	Safety																																							
Pertaining to	All																																							
Study Purpose	Demonstrate safety of product under typical use conditions.																																							
Product Administration	One dose administered intramuscularly																																							
Study Animals	1,220 pigs, 17-31 days of age, at five study sites in three geographically distinct locations.																																							
Challenge Description	NA																																							
Interval observed after challenge	Animals were observed once between one and four hours after vaccination, and then daily for 14 days, or until resolution of any adverse events.																																							
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