



## Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	19A5.R2
True Name	Swine Influenza Vaccine, H1N1 & H3N2, Modified Live Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Ingelvac Provenza - Boehringer Ingelheim (Canada) Ltd. Ingelvac Provenza - Boehringer Ingelheim Vetmedica S.A. de C.V. Ingelvac Provenza - No distributor specified
Date of Compilation Summary	November 18, 2019

**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.**

<b>Study Type</b>	Efficacy																																								
<b>Pertaining to</b>	Swine Influenza Vaccine, H1N1																																								
<b>Study Purpose</b>	Demonstration of Efficacy against respiratory disease																																								
<b>Product Administration</b>	Single intranasal administration of vaccine																																								
<b>Study Animals</b>	84 newborn pigs, 2 – 5 days of age, divided into two groups																																								
<b>Challenge Description</b>	Influenza H1N1 challenge virus (A/Swine/Minnesota/64645/2007 H1N1) was administered to 36 vaccinated pigs and 48 control pigs, 24 days following vaccination																																								
<b>Interval observed after challenge</b>	Pigs were observed daily for up to 5 days after challenge. Tissues were examined day 5 post-challenge.																																								
<b>Results</b>	<p>An animal was considered affected with a lung lesion score of &gt;2%. Additional data to support the primary outcome of lung consolidation was the observance of one or more clinical signs for at least 2 days.</p> <p><b>Five-Number Summary for Lung Lesions by group (pig level):</b></p> <table border="1"> <thead> <tr> <th>Group</th> <th>No. of Pigs</th> <th>Min</th> <th>25th Pctl</th> <th>Median</th> <th>75th Pctl</th> <th>Max</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>48</td> <td>1.7</td> <td>12.7</td> <td>20.8</td> <td>25.8</td> <td>51.1</td> </tr> <tr> <td>Vaccine</td> <td>36</td> <td>1.5</td> <td>10.5</td> <td>14.2</td> <td>18.9</td> <td>27.4</td> </tr> </tbody> </table> <p><b>Summary of the Number of Affected Pigs in Each Group:</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Group</th> <th colspan="2">Lung Lesion<sup>1</sup></th> <th colspan="2">Clinical Signs<sup>2</sup></th> </tr> <tr> <th>Yes</th> <th>No</th> <th>Yes</th> <th>No</th> </tr> </thead> <tbody> <tr> <td>Control n=48</td> <td>47</td> <td>1</td> <td>27</td> <td>21</td> </tr> <tr> <td>Vaccine n=36</td> <td>35</td> <td>1</td> <td>5</td> <td>31</td> </tr> </tbody> </table> <p><sup>1</sup>Lung lesion score &gt;2% is considered affected  <sup>2</sup> Observation of any clinical signs indicative of influenza on at least 2 days is considered positive</p> <p><i>Raw data are provided on the following pages:</i></p>	Group	No. of Pigs	Min	25th Pctl	Median	75th Pctl	Max	Control	48	1.7	12.7	20.8	25.8	51.1	Vaccine	36	1.5	10.5	14.2	18.9	27.4	Group	Lung Lesion <sup>1</sup>		Clinical Signs <sup>2</sup>		Yes	No	Yes	No	Control n=48	47	1	27	21	Vaccine n=36	35	1	5	31
Group	No. of Pigs	Min	25th Pctl	Median	75th Pctl	Max																																			
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Group	Lung Lesion <sup>1</sup>		Clinical Signs <sup>2</sup>																																						
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Control n=48	47	1	27	21																																					
Vaccine n=36	35	1	5	31																																					
<b>USDA Approval Date</b>	April 25, 2018																																								

### Results of Control Pigs Following Challenge

A blank box= no clinical signs observed or no nasal virus shedding on that day. (Each line is a pig.)

S=Sneezing, D=Nasal/Ocular Discharge, B=Behavior (depression), C=Cough (1=mild, 2=moderate), R=Increased Respiration (1=mild, 2=moderate).

Lung Lesion (%)	Clinical Signs by Day				
	1	2	3	4	5
1.73					
8.30	C1,R1		C1	C1	
8.76					
9.46					C1
10.01					C1
10.55					
10.55					
11.74					C1,R1,B
11.95				C1,D	
12.15	C1	C1	C2	C1	D,S
12.30			C1	S,C2,R1,B	C2,R2,B
12.64					
12.75	R1				C1,R1
12.95					S,C1,R1
15.15					
15.80	C1,B			C1	C2,R2,D,B
16.25					R1,S
18.29		B	B	C1	S,C1,R1,D,B
18.40					
18.79				C2	C1
18.90	C1	C1,R1,B	C1	S,C2,R1,B	C2,R2,B
19.70					C2
20.60					C1,R1
20.65					C1
20.90				C1	C1
21.05					
21.30				C1	S
22.30		R1,B		C1,R1,B	C2,R2,B
23.00				C2	
23.05				R1	R1
24.35		C2		S,C2,D,B	C1,R1,B
24.65				C2	C1,R2
24.70			B1	B1	C1,R2,B
25.00					C1,R1,D
25.10				C1	C1,B
25.50			R1	C1	C1,R1
26.85				C2	C1
27.10					C1,R1
27.20				C2	C2,D,B
27.90		C2,D,B	C2,D,B	C1	C1,R2,B
30.00	C1		S,C1,D,B	C2,D1,B	C1,R2,D,B
30.70	C1	C1	D,B,S	B1	C1,R2,D,B
31.80			C1	C1	R1,D
32.20				C2	S,C2,R1,B
32.60	R1	R1,B	S	S,C2,R1,D,B	S,C2,R2,D,B
33.20				S,C1	
40.70	C1		C1,B	C1,R1,B	R2,D,B
51.10			C1	C2,B1	C2,R2,D,B

### Results of Vaccinated Pigs Following Challenge

A blank box= no clinical signs observed or no nasal virus shedding on that day. (Each line is a pig.)

S=Sneezing, D=Nasal/Ocular Discharge, B=Behavior (depression), C=Cough (1=mild, 2=moderate), R=Increased Respiration (1=mild, 2=moderate).

Lung Lesion (%)	Clinical Signs by Day				
	1	2	3	4	5
1.45					
2.20					
3.95					
4.35					
5.95					
8.15					D
8.30					
8.61	C1				
10.35					
10.49					
10.70					
10.99					
11.25	R1				
11.59					
11.79					
12.25					
13.30					
14.20					
14.30					
14.85					
14.99					
15.99			C2		
16.45					
16.60					C1
16.85					
18.05					
18.75	C1,R1			R1,B	
19.20					
19.40				C1	
19.85			C2	C1	C1
22.10	C1			C1	C1,R1,D,B,S
22.65				B	
23.50		C2		C1,R1	C1,R2
24.60					
25.40			C2	C1	C1,R2
27.40					

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<b>Study Purpose</b>	Demonstration of efficacy against respiratory disease and viral shedding																																																																																																						
<b>Product Administration</b>	Single intranasal administration of 1mL of vaccine																																																																																																						
<b>Study Animals</b>	56 newborn pigs, 1 – 5 days of age, divided into two groups																																																																																																						
<b>Challenge Description</b>	Influenza H1N2 challenge virus (A/Swine/North Carolina/001169/2006) was administered to 25 vaccinated pigs and 31 control pigs, 25 days following vaccination																																																																																																						
<b>Interval observed after challenge</b>	Pigs were observed daily for 5 days after challenge. Tissues were examined day 5 post challenge.																																																																																																						
<b>Results</b>	<p><b>Five-Number Summary for Lung Lesions:</b></p> <table border="1"> <thead> <tr> <th>Group</th> <th>No. of Pigs</th> <th>Minimum</th> <th>25th Percentile</th> <th>Median</th> <th>75th Percentile</th> <th>Maximum</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>31</td> <td>5.47</td> <td>12.02</td> <td>14.51</td> <td>21.09</td> <td>58.95</td> </tr> <tr> <td>Vaccine</td> <td>25</td> <td>0.44</td> <td>1.80</td> <td>3.38</td> <td>8.60</td> <td>23.92</td> </tr> </tbody> </table> <p><b>Frequency of Pigs considered Affected with Clinical Signs:</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Group</th> <th colspan="6">Number of Days Clinical Signs Observed</th> </tr> <tr> <th>0</th> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5</th> </tr> </thead> <tbody> <tr> <td><b>Control n=31</b></td> <td>9</td> <td>5</td> <td>12</td> <td>4</td> <td>1</td> <td>0</td> </tr> <tr> <td><b>Vaccine n=25</b></td> <td>15</td> <td>8</td> <td>2</td> <td>0</td> <td>0</td> <td>0</td> </tr> </tbody> </table> <p><b>Frequency of Pigs Shedding Virus from Nasal Swabs Following Challenge:</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Group</th> <th colspan="6">Number of Days Shedding Detected</th> </tr> <tr> <th>0</th> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5</th> </tr> </thead> <tbody> <tr> <td><b>Control n=31</b></td> <td>0</td> <td>2</td> <td>7</td> <td>9</td> <td>8</td> <td>5</td> </tr> <tr> <td><b>Vaccine n=25</b></td> <td>13</td> <td>7</td> <td>4</td> <td>1</td> <td>0</td> <td>0</td> </tr> </tbody> </table> <p><b>Summary of the Number of Affected Pigs in Each Group:</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Group</th> <th colspan="2">Lung Lesion<sup>1</sup></th> <th colspan="2">Clinical Signs<sup>2</sup></th> <th colspan="2">Virus Shedding<sup>3</sup></th> </tr> <tr> <th>Yes</th> <th>No</th> <th>Yes</th> <th>No</th> <th>Yes</th> <th>No</th> </tr> </thead> <tbody> <tr> <td><b>Control n=31</b></td> <td>31</td> <td>0</td> <td>17</td> <td>14</td> <td>31</td> <td>0</td> </tr> <tr> <td><b>Vaccine n=25</b></td> <td>18</td> <td>7</td> <td>2</td> <td>23</td> <td>12</td> <td>13</td> </tr> </tbody> </table> <p><sup>1</sup>Lung lesion score &gt;2% is considered affected  <sup>2</sup> Observation of any clinical signs indicative of influenza on at least 2 days is considered affected  <sup>3</sup> Any detection of viral shedding from nasal swabs is considered positive</p> <p><i>Raw data are provided in the following tables:</i></p>	Group	No. of Pigs	Minimum	25th Percentile	Median	75th Percentile	Maximum	Control	31	5.47	12.02	14.51	21.09	58.95	Vaccine	25	0.44	1.80	3.38	8.60	23.92	Group	Number of Days Clinical Signs Observed						0	1	2	3	4	5	<b>Control n=31</b>	9	5	12	4	1	0	<b>Vaccine n=25</b>	15	8	2	0	0	0	Group	Number of Days Shedding Detected						0	1	2	3	4	5	<b>Control n=31</b>	0	2	7	9	8	5	<b>Vaccine n=25</b>	13	7	4	1	0	0	Group	Lung Lesion <sup>1</sup>		Clinical Signs <sup>2</sup>		Virus Shedding <sup>3</sup>		Yes	No	Yes	No	Yes	No	<b>Control n=31</b>	31	0	17	14	31	0	<b>Vaccine n=25</b>	18	7	2	23	12	13
Group	No. of Pigs	Minimum	25th Percentile	Median	75th Percentile	Maximum																																																																																																	
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	Yes	No	Yes	No	Yes	No																																																																																																	
<b>Control n=31</b>	31	0	17	14	31	0																																																																																																	
<b>Vaccine n=25</b>	18	7	2	23	12	13																																																																																																	

S=Sneeze, C=Cough, D=Ocular/Nasal Discharge, R=Increased Respiration, B=Depression/Lethargy  
 A blank box= no clinical signs observed, depression/lethargy not observed, or no nasal virus shedding on that day. Lung lesion is percent affected lung.

**Results of Control Pigs Following Challenge**

Lung Lesion	Clinical Signs by Day					Nasal Shedding by Day				
	1	2	3	4	5	1	2	3	4	5
5.47								Yes	Yes	Yes
7.07						Yes	Yes	Yes	Yes	Yes
7.81									Yes	
9.23					C				Yes	
9.73						Yes	Yes	Yes	Yes	Yes
11.06					C				Yes	Yes
11.28	C		D					Yes	Yes	
12.02								Yes	Yes	Yes
12.82	C					Yes	Yes	Yes	Yes	Yes
12.92	C			S,C			Yes	Yes	Yes	Yes
13.40						Yes	Yes	Yes	Yes	
13.74	C				D		Yes	Yes	Yes	Yes
14.12			D	C	C			Yes	Yes	
14.22			C	C	C			Yes	Yes	
14.32						Yes	Yes	Yes	Yes	Yes
14.51								Yes	Yes	Yes
14.55					C	Yes	Yes	Yes	Yes	
15.03	C		C	D	C			Yes	Yes	
15.83				D	D		Yes	Yes	Yes	
18.56				C	C,B	Yes	Yes	Yes	Yes	Yes
19.44		C			R		Yes	Yes	Yes	Yes
19.55	C			C				Yes	Yes	Yes
20.09				C				Yes	Yes	
21.09	C				C,R		Yes	Yes	Yes	
23.15			C,D		D,B		Yes	Yes	Yes	Yes
23.37								Yes	Yes	
24.39				C	C,B		Yes	Yes	Yes	Yes
25.60			D	D		Yes	Yes	Yes	Yes	
37.98				D,R	C,D		Yes	Yes	Yes	
45.90			C	C	C,D		Yes	Yes	Yes	
58.95			R	D	C,R		Yes	Yes	Yes	

S=Sneeze, C=Cough, D=Ocular/Nasal Discharge, R=Increased Respiration, B=Depression/Lethargy  
 A blank box= no clinical signs observed or no nasal virus shedding on that day. Lung lesion is percent affected lung.

**Results of Vaccinated Pigs Following Challenge**

Lung Lesion	Clinical Signs by Day					Nasal Shedding by Day				
	1	2	3	4	5	1	2	3	4	5
0.44										
0.74	C							Yes		
0.91								Yes		
0.98								Yes	Yes	
1.18										
1.54	R									
1.80	R									
2.40	R							Yes		
2.60					R					
2.70								Yes		
2.95										
3.14										
3.38	C				D					
3.40							Yes			
5.42							Yes	Yes	Yes	
5.50								Yes		
6.18			C							
6.38										
8.60										
8.73	C,R									
9.81										
11.29				D			Yes	Yes		
12.40						Yes			Yes	
18.95				C	C			Yes		
23.92									Yes	Yes

**USDA Approval Date**

January 22, 2015

<b>Study Type</b>	Efficacy																					
<b>Pertaining to</b>	Swine Influenza Vaccine, H1N1 & H3N2, Modified Live Virus																					
<b>Study Purpose</b>	Demonstration of efficacy against disease caused by swine influenza H3N2 virus 12 weeks following vaccination																					
<b>Product Administration</b>	1 dose Intranasal																					
<b>Study Animals</b>	Newborn pigs, 2 to 5 days of age: 36 vaccinated 46 controls																					
<b>Challenge Description</b>	Swine influenza virus strain H3N2 A/Swine/Utah/14-03037-1/2014 administered 12.5 weeks following vaccination																					
<b>Interval observed after challenge</b>	Pigs were evaluated for clinical signs and viral nasal shedding daily for 5 days post challenge. Lung lesions were evaluated at 5 days post challenge.																					
<b>Results</b>	<p>A pig was considered positive for lung lesions if the percent of the lung with gross lesions was <math>\geq 2\%</math>.</p> <p>5 number summary for litter median lung lesions:</p> <table border="1"> <thead> <tr> <th>Group</th> <th>#</th> <th>Min.</th> <th>25<sup>th</sup> p.</th> <th>Med.</th> <th>75<sup>th</sup> p.</th> <th>Max.</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>12</td> <td>1.6</td> <td>4.1</td> <td>9.9</td> <td>11.7</td> <td>15.6</td> </tr> <tr> <td>Vaccine</td> <td>10</td> <td>0.5</td> <td>0.9</td> <td>3.3</td> <td>6.5</td> <td>10.0</td> </tr> </tbody> </table> <p>p.=percentile</p> <p>A pig was considered positive if viral nasal shedding was detected on one or more days.</p> <p>Pigs positive for virus shedding:  Vaccinates 30/36 positive  Controls 46/46 positive</p> <p>Raw data is found in the following tables.</p>	Group	#	Min.	25 <sup>th</sup> p.	Med.	75 <sup>th</sup> p.	Max.	Control	12	1.6	4.1	9.9	11.7	15.6	Vaccine	10	0.5	0.9	3.3	6.5	10.0
Group	#	Min.	25 <sup>th</sup> p.	Med.	75 <sup>th</sup> p.	Max.																
Control	12	1.6	4.1	9.9	11.7	15.6																
Vaccine	10	0.5	0.9	3.3	6.5	10.0																
<b>USDA Approval Date</b>	November 8, 2018																					

**Individual pig clinical signs and lung lesions: Control Group**

Pig ID	Clinical Signs by Study Day (SD), Challenge = SD 87					% lung lesions
	SD 88	SD 89	SD 90	SD 91	SD 92	
178		R	R			3.21
179					C	11.35
180						1.40
186						1.21
191				D		9.29
192			X	C		15.35
193		R	R	R		13.10
195		R		R		2.94
200						2.76
201					C	4.15
205			S,R,X		C	7.54
207	X					12.80
210		R				5.64
213		R				0.41
214						2.40
216			R		R	0.72
220					R	7.05
221		C,D	R	C,R	C,R,B	26.90
222	R	R			C	10.65
225	R,X					4.09
329	R,X	R	X			8.34
330	X	D,R,B	R	C		14.95
331	R,X	R	R			13.70
333		R		C		2.40
340		C				18.65
341		R	R	C		16.55
346		R	R	R		3.34
347			X		C	9.49
351					C,R,B	15.35
352						10.04
355						12.95
356						6.45
359		R	R	R	C,R,B	16.90
360					C	14.20
366		R	C	C,R		13.10
367			C	S,C,R,B	C	7.29
369			R			4.65
370						2.11
379						0.91
380	R,X	C,R		C	C,R,B	6.20
383						2.50
384						1.50
408	R,X	R	R		C2	12.25
410	X	X				10.63
411	X	C	X	C	C2	11.55
417		X	X			17.95

S=Sneezing, C=Cough (2=moderate), D=Nasal/Ocular Discharge, R=Increased Respiration, B=Behavior (depression)  
X=pyrexia (≥1.5°C increase over baseline which was the average of SD 85, SD 86, and SD 87 body temperatures)

### Individual pig clinical signs and lung lesions: Vaccine Group

Pig ID	Clinical Signs by Study Day (SD), Challenge = SD 87					% lung lesions
	SD 88	SD 89	SD 90	SD 91	SD 92	
230					R	2.3
236						3.49
238		R			R	2.35
240			R			1.4
241	R	R	R			7.18
244						5.04
246	B	B				1.09
251						2.54
256		C				4.6
258	R					9.55
260						10.45
261	C	C				12.75
265						4.55
266						3.74
269						1.7
270						1.26
274						2.19
275					R	3.85
277						3.14
280						9.89
281			R,B			9.9
283						4.3
284	C,R				R	0.91
290					C	12.25
292	R	R	R		R	0.41
293			R	R	R	4.15
296					R,B	0.16
299	R	R	R	R	R	1.19
300						0.11
302						0.66
304						3.43
306						0.27
311						0.4
312						1.3
402	R					4.85
403						3.93

S=Sneezing, C=Cough (2=moderate), D=Nasal/Ocular Discharge, R=Increased Respiration, B=Behavior (depression)  
X=pyrexia ( $\geq 1.5^{\circ}\text{C}$  increase over baseline which was the average of SD 85, SD 86, and SD 87 body temperatures)

**Individual pig data for nasal swab virus isolation by Study Day (SD): Control Group**

<b>Pig ID</b>	<b>SD 87</b>	<b>SD 88</b>	<b>SD 89</b>	<b>SD 90</b>	<b>SD 91</b>	<b>SD 92</b>
178	Neg	Positive	Positive	Positive	Positive	Positive
179	Neg	Positive	Positive	Positive	Positive	Positive
180	Neg	Positive	Positive	Positive	Positive	Positive
186	Neg	Positive	Positive	Positive	Positive	Positive
191	Neg	Positive	Positive	Positive	Positive	Neg
192	Neg	Positive	Positive	Positive	Positive	Positive
193	Neg	Positive	Positive	Positive	Positive	Positive
195	Neg	Positive	Positive	Positive	Positive	Positive
200	Neg	Positive	Positive	Positive	Positive	Positive
201	Neg	Positive	Positive	Positive	Positive	Positive
205	Neg	Neg	Positive	Positive	Positive	Positive
207	Neg	Positive	Positive	Positive	Positive	Positive
210	Neg	Positive	Positive	Positive	Positive	Positive
213	Neg	Positive	Positive	Positive	Positive	Positive
214	Neg	Positive	Positive	Positive	Positive	Neg
216	Neg	Positive	Positive	Positive	Positive	Positive
220	Neg	Neg	Positive	Positive	Positive	Positive
221	Neg	Positive	Positive	Positive	Positive	Positive
222	Neg	Positive	Positive	Positive	Positive	Positive
225	Neg	Positive	Positive	Positive	Positive	Positive
329	Neg	Positive	Positive	Positive	Positive	Positive
330	Neg	Positive	Positive	Positive	Positive	Neg
331	Neg	Positive	Positive	Positive	Positive	Positive
333	Neg	Positive	Positive	Positive	Positive	Positive
340	Neg	Positive	Positive	Positive	Positive	Positive
341	Neg	Positive	Positive	Positive	Positive	Positive
346	Neg	Positive	Positive	Positive	Positive	Positive
347	Neg	Positive	Positive	Positive	Positive	Positive
351	Neg	Neg	Positive	Positive	Positive	Positive
352	Neg	Neg	Positive	Positive	Positive	Positive
355	Neg	Neg	Positive	Positive	Positive	Neg
356	Neg	Neg	Neg	Positive	Positive	Positive
359	Neg	Positive	Positive	Positive	Positive	Positive
360	Neg	Positive	Positive	Positive	Positive	Positive
366	Neg	Positive	Positive	Positive	Positive	Positive
367	Neg	Neg	Positive	Positive	Positive	Positive
369	Neg	Neg	Positive	Positive	Positive	Positive
370	Neg	Neg	Positive	Positive	Positive	Positive
379	Neg	Neg	Positive	Positive	Positive	Positive
380	Neg	Neg	Positive	Positive	Positive	Positive
383	Neg	Positive	Positive	Positive	Positive	Neg
384	Neg	Positive	Positive	Positive	Positive	Positive
408	Neg	Positive	Positive	Positive	Positive	Positive
410	Neg	Positive	Positive	Positive	Positive	Positive
411	Neg	Positive	Positive	Positive	Positive	Positive
417	Neg	Positive	Positive	Positive	Positive	Positive

Challenge = SD 87

Neg = negative

**Individual pig data for nasal swab virus isolation by Study Day (SD): Vaccine Group**

<b>Pig ID</b>	<b>SD 87</b>	<b>SD 88</b>	<b>SD 89</b>	<b>SD 90</b>	<b>SD 91</b>	<b>SD 92</b>
230	Neg	Neg	Neg	Neg	Neg	Neg
236	Neg	Neg	<b>Positive</b>	<b>Positive</b>	Neg	Neg
238	Neg	Neg	Neg	Neg	Neg	Neg
240	Neg	Neg	Neg	<b>Positive</b>	Neg	Neg
241	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg	Neg
244	Neg	Neg	Neg	<b>Positive</b>	<b>Positive</b>	Neg
246	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
251	Neg	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>
256	Neg	Neg	<b>Positive</b>	Neg	Neg	Neg
258	Neg	Neg	Neg	Neg	<b>Positive</b>	Neg
260	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
261	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
265	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
266	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
269	Neg	Neg	Neg	<b>Positive</b>	<b>Positive</b>	Neg
270	Neg	Neg	<b>Positive</b>	<b>Positive</b>	Neg	Neg
274	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
275	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>
277	Neg	Neg	<b>Positive</b>	Neg	<b>Positive</b>	<b>Positive</b>
280	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
281	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
283	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
284	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
290	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>
292	Neg	Neg	Neg	Neg	Neg	Neg
293	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>
296	Neg	Neg	Neg	Neg	Neg	Neg
299	Neg	Neg	<b>Positive</b>	Neg	<b>Positive</b>	Neg
300	Neg	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
302	Neg	Neg	Neg	Neg	Neg	Neg
304	Neg	Neg	Neg	Neg	Neg	Neg
306	Neg	Neg	Neg	Neg	<b>Positive</b>	Neg
311	Neg	Neg	Neg	Neg	<b>Positive</b>	Neg
312	Neg	Neg	<b>Positive</b>	Neg	Neg	Neg
402	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg
403	Neg	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	Neg

Challenge = SD 87

Neg = negative

<b>Study Type</b>	Efficacy																																																																																																						
<b>Pertaining to</b>	Swine Influenza Vaccine, H3N2																																																																																																						
<b>Study Purpose</b>	Demonstration of efficacy against respiratory disease and viral shedding																																																																																																						
<b>Product Administration</b>	Single intranasal administration of 1mL of vaccine																																																																																																						
<b>Study Animals</b>	56 newborn pigs, 1 – 4 days of age, divided into two groups																																																																																																						
<b>Challenge Description</b>	Influenza H3N2 challenge virus (A/Swine/Nebraska/97901-10/2008) was administered to 30 vaccinated pigs and 26 control pigs, 30 days following vaccination																																																																																																						
<b>Interval observed after challenge</b>	Pigs were observed daily for 5 days after challenge. Tissues were examined day 5 post challenge.																																																																																																						
<b>Results</b>	<p><b>Five-Number Summary for Lung Lesions:</b></p> <table border="1"> <thead> <tr> <th>Group</th> <th>No. of Pigs</th> <th>Minimum</th> <th>25th Pctl</th> <th>Median</th> <th>75th Pctl</th> <th>Maximum</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>26</td> <td>0.66</td> <td>2.75</td> <td>9.51</td> <td>14.40</td> <td>29.09</td> </tr> <tr> <td>Vaccine</td> <td>30</td> <td>0.26</td> <td>1.41</td> <td>1.94</td> <td>4.77</td> <td>12.79</td> </tr> </tbody> </table> <p><b>Frequency of Pigs considered Affected with Clinical Signs:</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Group</th> <th colspan="6">Number of Days Clinical Signs Observed</th> </tr> <tr> <th>0 days</th> <th>1 day</th> <th>2 days</th> <th>3 days</th> <th>4 days</th> <th>5 days</th> </tr> </thead> <tbody> <tr> <td><b>Control n=26</b></td> <td>3</td> <td>8</td> <td>9</td> <td>3</td> <td>1</td> <td>2</td> </tr> <tr> <td><b>Vaccine n=30</b></td> <td>15</td> <td>7</td> <td>5</td> <td>3</td> <td>0</td> <td>0</td> </tr> </tbody> </table> <p><b>Frequency of Pigs Shedding Virus from Nasal Swabs Following Challenge:</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Group</th> <th colspan="6">Number of Days Shedding Detected</th> </tr> <tr> <th>0 days</th> <th>1 day</th> <th>2 days</th> <th>3 days</th> <th>4 days</th> <th>5 days</th> </tr> </thead> <tbody> <tr> <td><b>Control n=26</b></td> <td>1</td> <td>2</td> <td>3</td> <td>8</td> <td>8</td> <td>4</td> </tr> <tr> <td><b>Vaccine n=30</b></td> <td>17</td> <td>4</td> <td>9</td> <td>0</td> <td>0</td> <td>0</td> </tr> </tbody> </table> <p><b>Summary of the Number of Affected Pigs in Each Group:</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Group</th> <th colspan="2">Lung Lesion<sup>1</sup></th> <th colspan="2">Clinical Signs<sup>2</sup></th> <th colspan="2">Virus Shedding<sup>3</sup></th> </tr> <tr> <th>Yes</th> <th>No</th> <th>Yes</th> <th>No</th> <th>Yes</th> <th>No</th> </tr> </thead> <tbody> <tr> <td><b>Control n=26</b></td> <td>22</td> <td>4</td> <td>15</td> <td>11</td> <td>25</td> <td>1</td> </tr> <tr> <td><b>Vaccine n=30</b></td> <td>15</td> <td>15</td> <td>8</td> <td>22</td> <td>13</td> <td>17</td> </tr> </tbody> </table> <p><sup>1</sup>Lung lesion score &gt;2% is considered affected  <sup>2</sup> Observation of any clinical signs indicative of influenza on at least 2 days is considered positive  <sup>3</sup> Any detection of viral shedding from nasal swabs is considered positive</p> <p><i>Raw data are provided in the following tables:</i></p>	Group	No. of Pigs	Minimum	25th Pctl	Median	75th Pctl	Maximum	Control	26	0.66	2.75	9.51	14.40	29.09	Vaccine	30	0.26	1.41	1.94	4.77	12.79	Group	Number of Days Clinical Signs Observed						0 days	1 day	2 days	3 days	4 days	5 days	<b>Control n=26</b>	3	8	9	3	1	2	<b>Vaccine n=30</b>	15	7	5	3	0	0	Group	Number of Days Shedding Detected						0 days	1 day	2 days	3 days	4 days	5 days	<b>Control n=26</b>	1	2	3	8	8	4	<b>Vaccine n=30</b>	17	4	9	0	0	0	Group	Lung Lesion <sup>1</sup>		Clinical Signs <sup>2</sup>		Virus Shedding <sup>3</sup>		Yes	No	Yes	No	Yes	No	<b>Control n=26</b>	22	4	15	11	25	1	<b>Vaccine n=30</b>	15	15	8	22	13	17
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S=Sneeze, C=Cough, D=Ocular/Nasal Discharge, R=Increased Respiration, B=Depression/Lethargy  
 A blank box= no clinical signs observed, depression/lethargy not observed, or no nasal virus shedding on that day. Lung lesion is percent affected lung.

**Results of Control Pigs Following Challenge**

Lung Lesion	Clinical Signs by Day					Nasal Shedding by Day				
	1	2	3	4	5	1	2	3	4	5
0.66			R							
1.09		C		C				Yes	Yes	Yes
1.16	C	C	C,R	R		Yes	Yes	Yes	Yes	Yes
1.43					C		Yes	Yes	Yes	Yes
2.01								Yes	Yes	Yes
2.60			C	R		Yes	Yes	Yes	Yes	
2.75			B					Yes	Yes	
2.98			C				Yes	Yes	Yes	Yes
3.44			R	R					Yes	
5.32			R	R				Yes	Yes	Yes
5.60				R		Yes	Yes	Yes	Yes	Yes
5.77			D					Yes	Yes	Yes
9.28			C					Yes	Yes	Yes
9.73	C		C		C	Yes	Yes	Yes	Yes	Yes
11.10	R		R		C			Yes	Yes	Yes
11.62					R	Yes	Yes	Yes	Yes	Yes
12.90				C	C					Yes
13.66							Yes	Yes	Yes	Yes
13.98				C,B	C		Yes	Yes	Yes	Yes
14.40			R,B	R,B					Yes	Yes
14.43	C			R			Yes	Yes	Yes	
14.80	C	R	C	C,R	C			Yes	Yes	Yes
17.05							Yes	Yes	Yes	Yes
19.68			C,R	R				Yes	Yes	
23.24			C	R,B	C		Yes	Yes	Yes	Yes
29.09	C	R	C	R	C,R	Yes		Yes	Yes	Yes

S=Sneeze, C=Cough, D=Ocular/Nasal Discharge, R=Increased Respiration, B=Depression/Lethargy  
 A blank box= no clinical signs observed or no nasal virus shedding on that day.  
 Lung lesion is percent affected lung.

**Results of Vaccinated Pigs Following Challenge**

Lung Lesion	Clinical Signs by Day					Nasal Shedding by Day				
	1	2	3	4	5	1	2	3	4	5
0.26										
0.55								Yes	Yes	
0.60									Yes	
0.62										
1.01										
1.20				R					Yes	
1.22				R						
1.41				R				Yes	Yes	
1.41										
1.41									Yes	
1.41	R									
1.45										
1.46	R		R	R						
1.49	C		R					Yes	Yes	
1.55										
2.33										
2.58	R			R						
2.76								Yes	Yes	
2.94										
3.68								Yes	Yes	
3.87			R		C			Yes	Yes	
4.27										
4.77		R		R,B				Yes	Yes	
5.01	R		C		C			Yes	Yes	
5.13	C									
6.17			R						Yes	
6.43										
9.25	C,R		R	C,R				Yes	Yes	
11.70		R		S						
12.79			R							

**USDA Approval Date**

January 22, 2015

<b>Study Type</b>	Safety																																																																																																				
<b>Pertaining to</b>	All fractions																																																																																																				
<b>Study Purpose</b>	To demonstrate safety under field conditions																																																																																																				
<b>Product Administration</b>	Single intranasal administration of 1mL of vaccine																																																																																																				
<b>Study Animals</b>	997 newborn pigs, 1 – 5 days of age, at three different geographical locations																																																																																																				
<b>Challenge Description</b>	Not Applicable																																																																																																				
<b>Interval observed after vaccination</b>	Pigs were observed daily for 14 days following vaccination																																																																																																				
<b>Results</b>	<p>Numbers of pigs by site with specific clinical observation post-vaccination:</p> <table border="1"> <thead> <tr> <th><b>Clinical Observation</b></th> <th><b>MO Site N=499</b></th> <th><b>NC Site N=250</b></th> <th><b>IA Site N=248</b></th> </tr> </thead> <tbody> <tr> <td><b>None*</b></td> <td><b>470</b></td> <td><b>42</b></td> <td><b>229</b></td> </tr> <tr> <td>Depression</td> <td>0</td> <td>174</td> <td>0</td> </tr> <tr> <td>Loss of condition</td> <td>5</td> <td>82</td> <td>5</td> </tr> <tr> <td>Conjunctivitis</td> <td>0</td> <td>47</td> <td>0</td> </tr> <tr> <td>Panting</td> <td>0</td> <td>46</td> <td>0</td> </tr> <tr> <td>Lameness</td> <td>1</td> <td>22</td> <td>2</td> </tr> <tr> <td>Laceration/trauma</td> <td>0</td> <td>21</td> <td>0</td> </tr> <tr> <td>Ataxia</td> <td>1</td> <td>15</td> <td>0</td> </tr> <tr> <td>Anorexia</td> <td>0</td> <td>15</td> <td>0</td> </tr> <tr> <td>Mortality</td> <td>15</td> <td>14</td> <td>6</td> </tr> <tr> <td>Unthrifty</td> <td>0</td> <td>9</td> <td>0</td> </tr> <tr> <td>Aggression</td> <td>0</td> <td>6</td> <td>0</td> </tr> <tr> <td>Decreased appetite</td> <td>0</td> <td>6</td> <td>0</td> </tr> <tr> <td>Reddening of the skin</td> <td>0</td> <td>6</td> <td>0</td> </tr> <tr> <td>Dehydrated</td> <td>0</td> <td>5</td> <td>0</td> </tr> <tr> <td>Sneezing</td> <td>0</td> <td>4</td> <td>0</td> </tr> <tr> <td>Localized swelling (not at the injection site)</td> <td>0</td> <td>3</td> <td>0</td> </tr> <tr> <td>Hernia</td> <td>0</td> <td>2</td> <td>0</td> </tr> <tr> <td>Ocular discharge</td> <td>0</td> <td>2</td> <td>0</td> </tr> <tr> <td>Bursitis</td> <td>0</td> <td>2</td> <td>0</td> </tr> <tr> <td>Abnormal breathing</td> <td>1</td> <td>1</td> <td>11</td> </tr> <tr> <td>Cough</td> <td>0</td> <td>1</td> <td>1</td> </tr> <tr> <td>Nasal discharge</td> <td>0</td> <td>1</td> <td>0</td> </tr> <tr> <td>Diarrhea</td> <td>23</td> <td>0</td> <td>0</td> </tr> </tbody> </table> <p>*For “none”, a pig had to be observed without clinical observations for the entire 14 days of the study. Observations at the NC Site were generally attributed to study pigs unexpectedly being weaned early and to adverse environmental conditions (high temperature and high humidity) during the study.</p>	<b>Clinical Observation</b>	<b>MO Site N=499</b>	<b>NC Site N=250</b>	<b>IA Site N=248</b>	<b>None*</b>	<b>470</b>	<b>42</b>	<b>229</b>	Depression	0	174	0	Loss of condition	5	82	5	Conjunctivitis	0	47	0	Panting	0	46	0	Lameness	1	22	2	Laceration/trauma	0	21	0	Ataxia	1	15	0	Anorexia	0	15	0	Mortality	15	14	6	Unthrifty	0	9	0	Aggression	0	6	0	Decreased appetite	0	6	0	Reddening of the skin	0	6	0	Dehydrated	0	5	0	Sneezing	0	4	0	Localized swelling (not at the injection site)	0	3	0	Hernia	0	2	0	Ocular discharge	0	2	0	Bursitis	0	2	0	Abnormal breathing	1	1	11	Cough	0	1	1	Nasal discharge	0	1	0	Diarrhea	23	0	0
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