Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	4855.25
True Name	Encephalomyelitis-Rhinopneumonitis-Influenza-West Nile Virus Vaccine, Eastern & Western, Killed Virus, Tetanus Toxoid
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Vetera Goldxp - Boehringer Ingelheim (Canada) Ltd. Vetera Goldxp - No distributor specified
Date of Compilation Summary	February 06, 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.

Study Type	Efficacy
Pertaining to	Clostridium tetanus
Study Purpose	Demonstration of efficacy against Clostridium tetanus
Product Administration	One dose, administered intramuscularly
Study Animals	10 guinea pigs (10 vaccinates)
Challenge Description	Not applicable
Interval observed after challenge	Not applicable
Results	6 weeks after the injection, vaccinate serum samples were collected and pooled, then tested for antitoxin content by indirect Enzyme-Linked Immunosorbent Assay. A satisfactory value which met the requirements per 9 CFR 113.114(c) was achieved.
USDA Approval Date	February 15, 2011

Study Type	Efficacy
Pertaining to	Eastern equine encephalomyelitis
Study Purpose	Demonstration of efficacy against Eastern equine encephalomyelitis
Product Administration	Two doses, administered intramuscularly, 14 to 21 days apart
Study Animals	12 guinea pigs (10 vaccinates, 2 controls)
Challenge Description	Not applicable
Interval observed after challenge	Not applicable
Results	Serum samples were tested by a plaque reduction, serum neutralization test, 14 to 21 days after the second injection. Vaccinates and controls were evaluated in terms of Eastern equine encephalomyelitis per the criteria in 9 CFR 113.207(b) and the requirements were met.
USDA Approval Date	February 15, 2011

Study Type	Efficacy
Pertaining to	Western equine encephalomyelitis
Study Purpose	Demonstration of efficacy against Western equine encephalomyelitis
Product Administration	Two doses, administered intramuscularly, 14-21 days apart
Study Animals	12 guinea pigs (10 vaccinates, 2 controls)
Challenge Description	Not applicable
Interval observed after challenge	Not applicable
Results	Serum samples were tested by a plaque reduction, serum neutralization test, 14 days after the second injection. Vaccinates and controls were evaluated in terms of Western equine encephalomyelitis per the criteria in 9 CFR 113.207(b) and the requirements were met.
USDA Approval Date	February 15, 2011

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Equine herpesvirus type 1 (EHV-1)</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of efficacy against respiratory disease caused by EHV-1</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered intramuscularly, 21 days apart</td></tr>
<tr><td>Study Animals</td><td>40 horses (20 vaccinates, 20 controls), 4-5 months of age</td></tr>
<tr><td>Challenge Description</td><td>Equine herpesvirus type 1 administered 15 days post-final vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Horses were observed daily for 14 days post-challenge</td></tr>
<tr><td>Results</td><td>See raw data on following pages.

The horses were assessed for the presence of nasal discharge as signs of respiratory disease. The severity of nasal discharge was classified as “normal”, “mild”, or “moderate” according to the following classification of the nasal scores.

<table>
<tr><th>Disease status</th><th>MaximumNasal Score</th></tr>
<tr><td>Normal</td><td>0 or 1</td></tr>
<tr><td>Mild</td><td>1.5 or 2</td></tr>
<tr><td>Moderate</td><td>4 or 6</td></tr>
</table>

The number of horses in each category were:

<table>
<tr><th></th><th>Normal</th><th>Mild</th><th>Moderate</th></tr>
<tr><td>Control</td><td>0</td><td>10</td><td>10</td></tr>
<tr><td>Vaccine</td><td>6</td><td>11</td><td>3</td></tr>
</table>
</td></tr>
<tr><td>USDA Approval Date</td><td>January 28, 2009</td></tr>
</table>

Nasal Discharge:

Day Postchallenge

Treatment	ID	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Controls (20 horses)	1					1.5			1.5	1.5	1	1.5				
	2						1.5		1.5	1.5	1	1.5	1.5	1		
	3						1.5			1.5	2			1.5		
	4			1		2	1.5		1.5	1.5	1.5	1.5				1.5
	5				2	2	2	1	4	2	2	1.5	1.5		1.5	
	6			1		4	6	4	4	4	4	2	2	2		
	7					1.5	1.5	1.5	1.5	1.5	2	4	1		1	1
	8								1.5	2	2	4	1.5	4	2	1.5
	9				1	1.5	1.5	1.5	1.5	1.5	2	1.5				
	10			1			1		1.5	1.5	2	4	4		1.5	1.5
	11						1.5	1.5	1.5		2		1.5	1.5	1.5	
	12						1.5	1.5		2						1.5
	13						2	1.5	1.5	2	2	2	1.5	1.5	1.5	4
	14				1.5	2		1.5		1.5	1.5	1.5			2	2
	15				1	2	1.5	1	1.5		4		1		4	1.5
	16					1.5	1.5	2	2	2	2	1.5	1	1	4	2
	17					1.5		1			1.5	2		1.5	1.5	
	18						1	1.5	1.5	4	4	2	1.5	4	1.5	2
	19				1	2	1.5		1.5	2	4	1	1.5		1	
	20						1.5	1.5	2	1.5	2				1.5	
Vaccinates (20 horses)	1					1		1				1.5				
	2				1											
	3						1	1.5	4		1.5	1.5			1	
	4				1						2	1				
	5				1				1	1						
	6				1	1.5						1.5	2	2	2	1.5
	7							2					1.5			
	8															
	9					2	1.5	2	2	6	2	1.5		1.5	4	2
	10								1				1	1.5		
	11				1		1.5		2	2	1	1.5				
	12				1		1.5	2	1.5	2	2	2		2	2	1.5
	13				1.5						1.5	1.5			1.5	1.5
	14							1	1			1			1.5	
	15				1											
	16				1		1.5	1.5	1			1.5				
	17															
	18						1			1.5		1.5				
	19														6	2
	20															

Scoring:

Blank is 0 = none;
1 = slight serous, as may be observed in both normal and diseased horses;
1.5 = very slight mucopurulent discharge;
2 = moderate clear serous discharge, or slight mucopurulent discharge;
3 = abundant serous discharge;
4 = moderate mucopurulent discharge;
6 = heavy mucopurulent discharge

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Equine herpesvirus type 4 (EHV-4)</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of efficacy against respiratory disease caused by EHV-4</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered intramuscularly, 21 days apart</td></tr>
<tr><td>Study Animals</td><td>40 horses (20 vaccinates, 20 controls), 4 months of age</td></tr>
<tr><td>Challenge Description</td><td>Equine herpresvirus type 4 administered 14 days post-final vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Horses were observed daily for 14 days post-challenge</td></tr>
<tr><td>Results</td><td>See raw data on following pages.

The horses were assessed for the presence of nasal and ocular discharge as signs of respiratory disease. The severity of the combined findings (nasal and ocular discharge) were classified as “mild” or “moderate” according to the following classification:

<table>
<tr><th>Disease status</th><th>Nasal score</th><th>Ocular score</th></tr>
<tr><td>Normal = 0</td><td>0 or 1</td><td>0 or 1</td></tr>
<tr><td>Mild = 1</td><td>0 or 1</td><td>2</td></tr>
<tr><td>Mild = 1</td><td>1.5, 2, or 3</td><td>any</td></tr>
<tr><td>Moderate = 2</td><td>4 or 6</td><td>any</td></tr>
</table>

Moderate respiratory disease was observed in 8/20 placebo controls and 1/20 vaccinated horse, and mild disease was observed in 12/20 placebo controls and 17/20 vaccinated horses.

None of the placebo controls remained healthy following challenge, whereas 2 vaccinates showed no signs of respiratory disease.</td></tr>
<tr><td>USDA Approval Date</td><td>May 31, 2011</td></tr>
</table>

Ocular Discharge:

		Day Postchallenge														
Treatment	**Animal**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Controls	1								2		2	2	2		2	2
	2				2	2	2	2	2	2	2	2	2	2	2	
	3				2	2		2	2	2		2	2	2	2	2
	4				2	2	2	2	2		2	2	2		2	
	5					2					2			2	2	2
	6				2		2	2	2	2	2	2	2	2	2	
	7					2	2	2	2	2	2	2		2		2
	8				2		2	2		2						
	9				2	2	2	2	2	2	2	2	2	2	2	2
	10				2	2	2	2	2	2		2	2	2	2	
	11				2	2	2	2	2	2	2	2	2	2	2	2
	12												2		2	
	13															
	14				2	2	2	2	2		2	2	2	2		2
	15					2	2	2		2	2	2	2			
	16							2		2	2	2	2			
	17					2		2		2	2	2	2	2	2	2
	18				2	2	2	2	2	2	2	2	2	2		
	19				2	2	2	2			2				2	2
	20				2	2	2	2	2	2	2	2				
Vaccinates	1											2	2	2		
	2					2										
	3						2		2	2				2	2	2
	4				2			2			2					
	5								2							2
	6									2	2					
	7						2	2								
	8					2	2	2	2		2					
	9															2
	10							2					2		2	2
	11															
	12										2	2	2			2
	13					2	2		2					2	2	2
	14															
	15						2	2								
	16															
	17				2			2	2	2		2		2	2	2
	18									2		2		2	2	
	19															
	20															

Scoring:
Blank is 0=none
1=mild or moderate
2=severe

Nasal Discharge: Day Postchallenge

Day Postchallenge

Treatment	Animal		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Controls	1					1	1			1	2	3		3		3	
	2					2	3	3	2	2	3	3	2	4	3	3	2
	3					3	3		2	4			3	3	2	2	
	4						4	4	3	3	4	3	3			2	2
	5						2	3	3	3		3	2	2		2	3
	6							3		2	4	3	3	2	3	2	
	7					1	2	1	2	2	2	2	3	2		2	2
	8									2		2					
	9								2	2	3	2	2	2	3		
	10					3	4	3	3	3	2		2	2	2	2	2
	11																1
	12							3		2	2	2				3	3
	13						3	2	2	2	2	1	2	2			
	14					2	3	4	4	2	4	2	4	3	4	3	
	15					1		3	3	3	3		3	3			2
	16					3	3	3	4	2	4	4	3	4	2	2	2
	17						1		2	2	3	2		3	3		
	18					2		3	3	2	2	2	2	3	2	2	2
	19							1	4	2	3		3			2	3
	20					2			2	2		3		2	2	2	
Vaccinates	1									2					2	3	
	2																
	3										1	2				3	
	4					1											
	5									2				3			2
	6											3					
	7						1										
	8								2	3	1	3					
	9												1				2
	10											3		2			
	11									2							
	12									3	2	3	1	3			2
	13								1	3				2	2	2	
	14										2				2		
	15									2							
	16												1				
	17					2					3				3	2	
	18										4	2		2		2	
	19																
	20									2			3	3			

Scoring:

Blank is 0 = none

1 = slight clear serous, as may be observed in both normal and diseased horses;

1.5 = very slight mucopurulent discharge, one or both nostrils;

2 = moderate clear serous discharge, easily seen in one or both nostrils;

3 = abundant clear serous discharge typically seen only in diseased horses;

4 = moderately mucopurulent, in large quantities in both nostrils;

5 = heavy mucopurulent discharge in large amounts in both nostrils

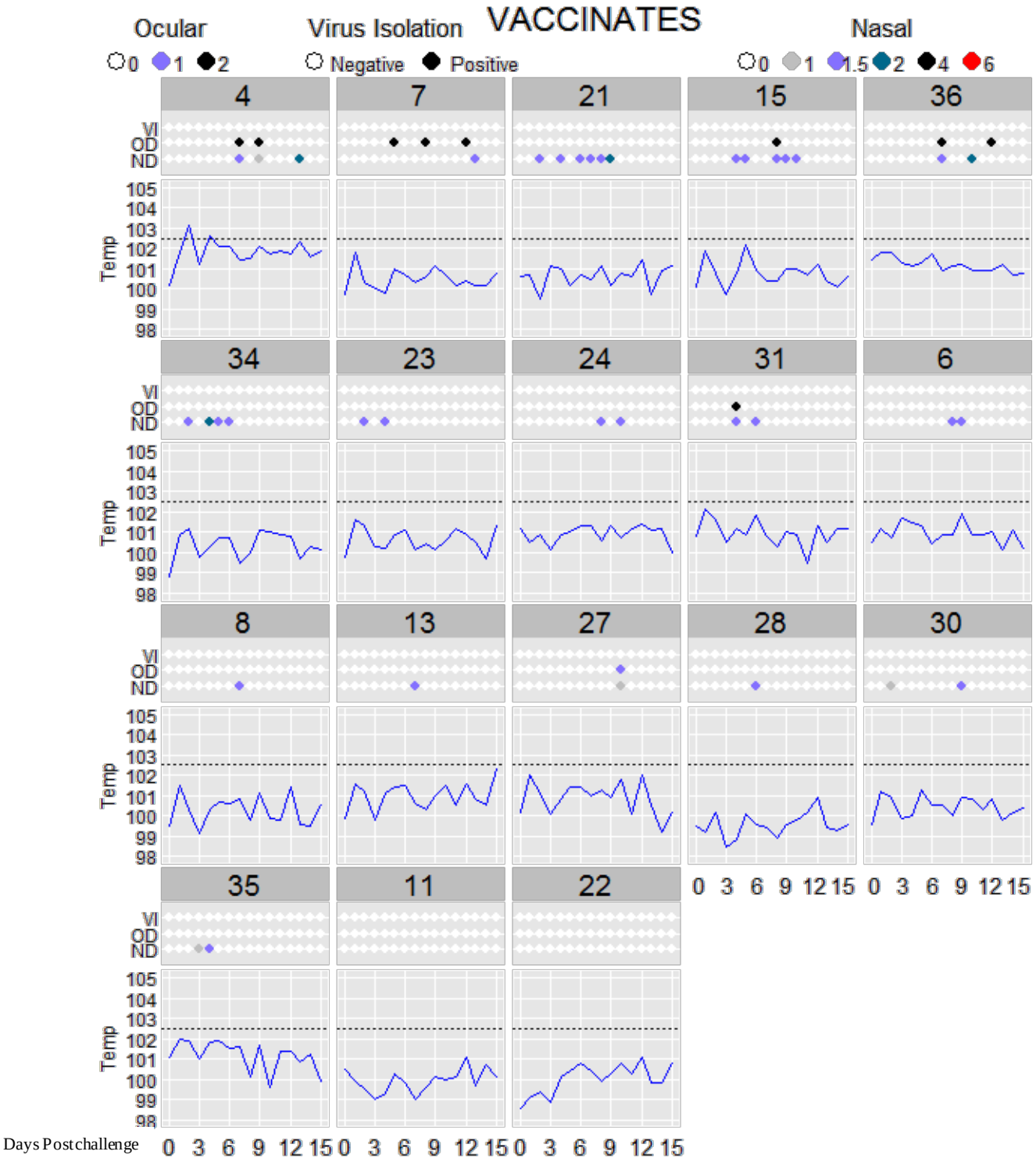
Study Type	Efficacy
Pertaining to	Equine influenza virus
Study Purpose	Demonstration of 6-month duration of immunity against respiratory disease caused by equine influenza
Product Administration	Two doses, administered intramuscularly, 21 days apart. Vaccinates received test product, and controls received adjuvanted diluent.
Study Animals	30 horses (20 vaccinates, 10 controls), 5-6 months of age
Challenge Description	Influenza A/eq/Ohio/2003 administered 184 days post-final vaccination
Interval observed after challenge	Horses were observed daily for 10 days post-challenge
Results	**See tables at the end of document for data.** **Clinical Signs:** An animal was considered positive (affected by challenge) if the animal exhibited: • Fever (temperature >102.5ºF), OR • Nasal discharge (moderate serous discharge or mucopurulent discharge), OR • Ocular discharge A total of 9/10 (90%) controls were positive as compared to only 9/20 (45%) vaccinates. There were no adverse reactions to vaccine administration at any timepoint.
USDA Approval Date	September 7, 2010

Treatment	Clinical Sign	Days Post-challenge										
		0	1	2	3	4	5	6	7	8	9	10
Controls												
1	Fever											
	Nasal discharge						+	+	+	+		
	Ocular discharge						+			+		+
2	Fever											
	Nasal discharge			+			+		+	+	+	
	Ocular discharge						+	+			+	+
3	Fever											
	Nasal discharge							+		+		
	Ocular discharge			+			+			+		+
4	Fever											
	Nasal discharge											
	Ocular discharge						+	+	+			+
5	Fever											
	Nasal discharge					+	+	+	+	+	+	
	Ocular discharge											
6	Fever											
	Nasal discharge					+			+		+	+
	Ocular discharge											+
7	Fever											
	Nasal discharge			+			+		+			+
	Ocular discharge			+				+				
8	Fever								+			
	Nasal discharge						+	+	+			+
	Ocular discharge			+	+		+	+				+
9	Fever											
	Nasal discharge											
	Ocular discharge											
10	Fever											
	Nasal discharge						+	+	+	+	+	
	Ocular discharge					+	+		+	+	+	

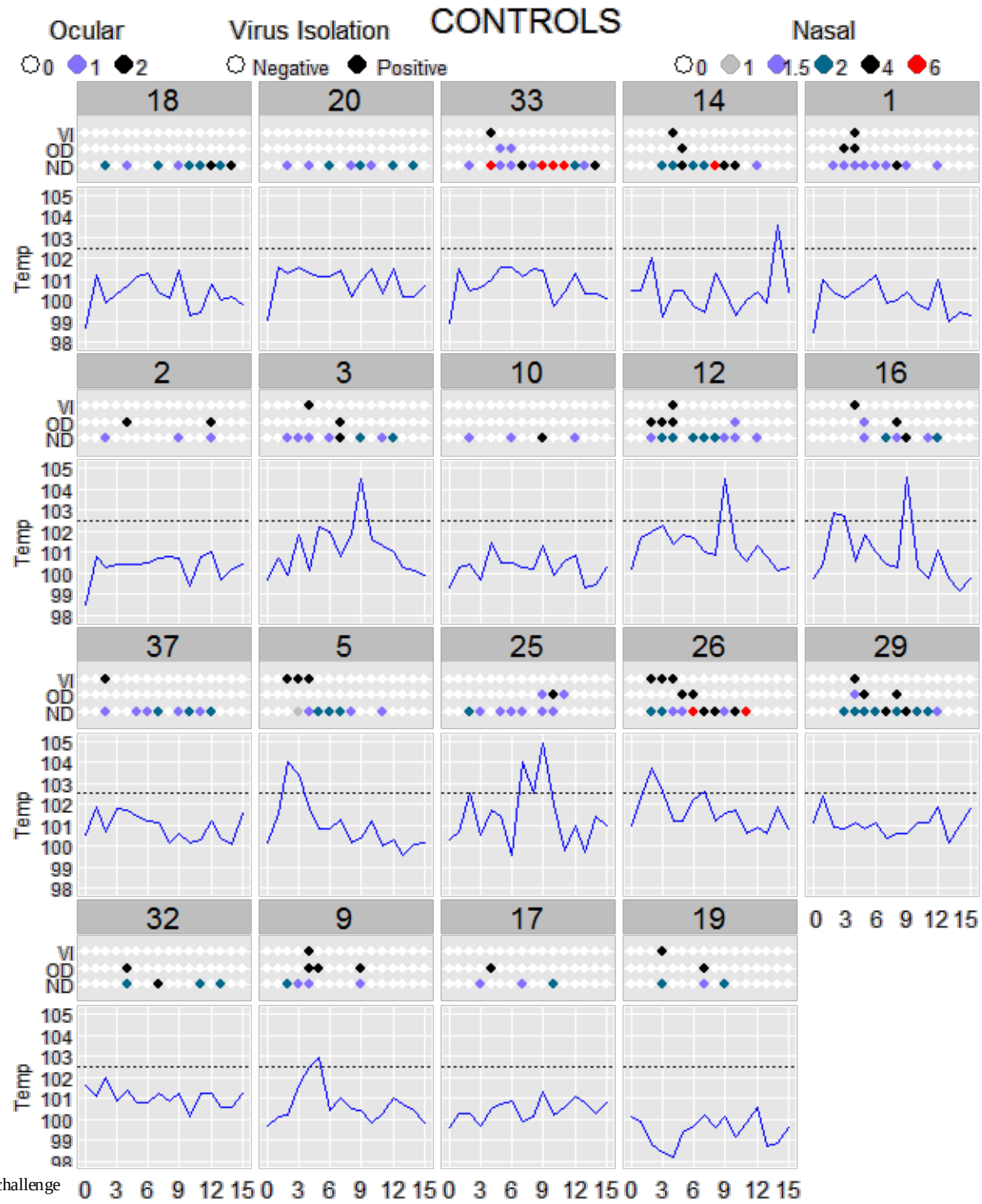
Treatment	Clinical Sign	Days Post-challenge										
		0	1	2	3	4	5	6	7	8	9	10
Vaccinates												
1	Fever											
	Nasal discharge											
	Ocular discharge											
2	Fever											
	Nasal discharge											
	Ocular discharge											
3	Fever											
	Nasal discharge											
	Ocular discharge						+			+	+	
4	Fever											
	Nasal discharge								+			
	Ocular discharge											
5	Fever											
	Nasal discharge											
	Ocular discharge											
6	Fever											
	Nasal discharge											
	Ocular discharge											
7	Fever											
	Nasal discharge											
	Ocular discharge											
8	Fever											
	Nasal discharge											
	Ocular discharge											
9	Fever											
	Nasal discharge											
	Ocular discharge											
10	Fever						+					
	Nasal discharge							+	+			
	Ocular discharge									+		+
11	Fever											
	Nasal discharge						+			+	+	+
	Ocular discharge											
12	Fever											
	Nasal discharge									+		
	Ocular discharge											

Treatment	Clinical Sign	Days Post-challenge										
		0	1	2	3	4	5	6	7	8	9	10
Vaccinates												
13	Fever											
	Nasal discharge					+						+
	Ocular discharge											
14	Fever											
	Nasal discharge											
	Ocular discharge											
15	Fever											
	Nasal discharge											
	Ocular discharge						+		+			
16	Fever											
	Nasal discharge							+				
	Ocular discharge											
17	Fever											
	Nasal discharge											
	Ocular discharge											
18	Fever											
	Nasal discharge											
	Ocular discharge											
19	Fever											
	Nasal discharge							+		+		
	Ocular discharge											
20	Fever											
	Nasal discharge											
	Ocular discharge											

Study Type	Efficacy
Pertaining to	Equine influenza virus
Study Purpose	Demonstration of efficacy against respiratory disease and shedding caused by equine influenza
Product Administration	Two doses, administered intramuscularly, 21 days apart.
Study Animals	37 horses (18 vaccinates, 19 controls), approximately 9-10 months of age
Challenge Description	Influenza A/eq/Ohio/2003 administered 3 weeks post-final vaccination
Interval observed after challenge	Horses were observed, and nasal swabs were collected, daily for 15 days post-challenge.
Results	**See tables at the end of document for data.** **Clinical Signs:** An animal was considered positive (affected by challenge) if the animal exhibited the following at any post-challenge observation point: • Fever (temperature $\geq$102.5°F), OR • Ocular discharge, OR • Nasal discharge (very slight mucopurulent discharge, or worse) **Duration** of disease was calculated from the date the animal was first observed to be positive to the date of last positive observation for that animal. Based on this calculation, the median duration of disease for the controls was determined to be 11 days as compared to 3 days for the vaccinates. **Nasal shedding** of influenza virus was evaluated through nasal swab virus isolation results. An animal was considered positive if virus was isolated from nasal swabs on one or more occasions following challenge. 0/18 vaccinates shed virus and 12/19 controls shed virus. There were no adverse reactions to vaccine administration at any timepoint.
USDA Approval Date	April 8, 2013



Ocular Discharge: 0=none; 1=mild to moderate; 2=severe
Nasal Discharge: 0=none; 1=slight clear serous, as may be observed in both normal and diseased horses; 1.5=very slight mucopurulent discharge, one or both nostrils; 2=moderate clear serous discharge, easily seen in one or both nostrils; 3=Abundant clear serous discharge typically seen only in diseased horses; 4=moderately mucopurulent, in large quantities in both nostrils; 5=heavy mucopurulent discharge in large amounts in both nostrils



Ocular Discharge: 0=none; 1=mild to moderate; 2=severe

Nasal Discharge: 0=none; 1=slight clear serous, as may be observed in both normal and diseased horses; 1.5=very slight mucopurulent discharge, one or both nostrils; 2=moderate clear serous discharge, easily seen in one or both nostrils; 3=Abundant clear serous discharge typically seen only in diseased horses; 4=moderately mucopurulent, in large quantities in both nostrils; 5=heavy mucopurulent discharge in large amounts in both nostrils

Study Type	Efficacy
Pertaining to	Equine influenza
Study Purpose	Demonstration of efficacy against respiratory disease caused by equine influenza A2 strain Richmond 07
Product Administration	Two doses, administered intramuscularly, 21 days apart
Study Animals	20 horses (20 vaccinates), 12 months of age
Challenge Description	Not applicable
Interval observed after challenge	Not applicable
Results	This product class allows the manufacturer to update micro-organisms in this vaccine under expedited procedures to respond to emerging needs. Abbreviated data to support influenza strain updates to the product composition were evaluated by USDA-APHIS and found to be acceptable based on regulations and policies at the time of approval. Full vaccination-challenge studies may not have been required for these updates.
USDA Approval Date	February 2, 2012

Study Type	Efficacy
Pertaining to	Equine influenza
Study Purpose	Demonstration of efficacy against respiratory disease caused by equine influenza A2 strain Kentucky 95
Product Administration	Two doses, administered intramuscularly, 21 days apart
Study Animals	20 horses (20 vaccinates), 12 months of age
Challenge Description	Not applicable
Interval observed after challenge	Not applicable
Results	This product class allows the manufacturer to update micro-organisms in this vaccine under expedited procedures to respond to emerging needs. Abbreviated data to support influenza strain updates to the product composition were evaluated by USDA-APHIS and found to be acceptable based on regulations and policies at the time of approval. Full vaccination-challenge studies may not have been required for these updates.
USDA Approval Date	February 2, 2012

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>West Nile Virus (WNV)</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of twelve month duration of immunity against disease caused by WNV</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered intramuscularly, 25 days apart</td></tr>
<tr><td>Study Animals</td><td>30 horses (20 vaccinates, 10 placebo controls) 4-5 months of age</td></tr>
<tr><td>Challenge Description</td><td>West Nile Virus was administered at 380 days (10 vaccinated and 5 placebo control animals) or 408 days (10 vaccinated and 5 placebo control animals) post-final vaccination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Horses were observed twice daily for 14 days post-challenge and once daily for an additional 7 days post-challenge.</td></tr>
<tr><td>Results</td><td>An animal was considered affected by challenge if it developed neurological disease, as measured by mortality and microscopic evidence of virus-induced brain disease (histopathology).

Animals were also monitored for viremia (detection of WNV in the blood).

Results are summarized as follows:
<table>
<tr><th>Outcome</th><th>Controls</th><th>Vaccinates</th></tr>
<tr><td>Mortality</td><td>7/10 (70%)</td><td>1/20 (5%)</td></tr>
<tr><td>Viremia at least one day</td><td>10/10 (100%)</td><td>2/20 (10%)</td></tr>
</table>

See raw data on following pages.</td></tr>
<tr><td>USDA Approval Date</td><td>September 3, 2010</td></tr>
</table>

Treatment	#	Died or Euthanized due to disease severity	Severity Histopathological lesions	
			Medulla	Pons
Controls (10 horses)	**1**	Yes	3	3
	2	Yes	3	3
	3	Yes	3	3
	4	Yes	3	3
	5	Yes	3	3
	6	Yes	2	2
	7	Yes	1	1
	8	No	1	1
	9	No	1	1
	10	No	1	0.5
Vaccinates (20 horses)	**1**	Yes	3	3
	2	No	2	0.5
	3	No	1	1
	4	No	1	0.5
	5	No	1	0.5
	6	No	1	0.5
	7	No	0.5	0.5
	8	No	0.5	0.5
	9	No	0.5	0
	10	No	0	0.5
	11	No	0	0
	12	No	0	0
	13	No	0	0
	14	No	0	0
	15	No	0	0
	16	No	0	0
	17	No	0	0
	18	No	0	0
	19	No	0	0
	20	No	0	0

Scoring of histopathological lesions:	
0 =	No significant lesions.
0.5 =	Rare, small, multifocal glial nodules scattered throughout the parenchyma.
1 =	Mild, nonsuppurative encephalitis characterized by mild multifocal perivascular cuffs with lymphocytes and plasma cells and a rare neutrophil and scattered multifocal glial nodules composed of glial cells with a few mononuclear inflammatory cells. Occasionally within this grade, there may be minimval perivascular cuffing and more moderate scattered glial nodules.
2 =	Moderate nonsuppurative encephalitis characterized by moderate lymphoplasmacytic perivascular cuffs around many vessels and multifocal accumulations of glial nodules scattered throughout the parenchyma.
3 =	Severe nonsuppurative encephalitis characterized by severe and thick lymphoplasmacytic perivascular cuffing with multiple scattered glial nodules throughout the parenchyma.

Viremia: Days Post-challenge

Treatment	#	0	1		2		3		4		5		6		7	8	9	10	14	21
			AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM						
Controls (10 horses)	1				15	25	10				5								D	D
	2					30		5	20		5								D	D
	3				25	470	160	210	175	75	100							D	D	D
	4			5	20	205	175	90	75	50								D	D	D
	5			40	130	30	25	50	10									D	D	D
	6				165	110	65	55	10										D	D
	7			10	330	200	180	225	115	15									N	D
	8				50	90	35	105	20	10										
	9			5	30	95	25	135	240	40	20									
	10					80	70	40	10											
Vaccinates (20 horses)	1																		D	D
	2																			
	3																			
	4																			
	5																			
	6				95															
	7																			
	8				40															
	9																			
	10																			
	11																			
	12																			
	13																			
	14																			
	15																			
	16																			
	17																			
	18																			
	19																			
	20																			

Actual value in plaque-forming units per milliliter equivalents (PFUeq/mL) = Positive for virus isolation
Blank = Negative for virus isolation (<5 PFUeq/mL)
D = Dead
N = Not recorded; horse was circling with sporadic head / neck tremors.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>West Nile Virus (WNV)</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of seven month duration of immunity against WNV</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered intramuscularly 22 days apart</td></tr>
<tr><td>Study Animals</td><td>30 horses (20 vaccinates, 10 placebo controls) 4-5 months of age</td></tr>
<tr><td>Challenge Description</td><td>Challenged with West Nile Virus at 201 days (Group 1: 10 vaccinated and 5 placebo control animals) or 222 days (Group 2: 10 vaccinated and 5 placebo control animals) after the second vaccination.</td></tr>
<tr><td>Interval observed after challenge</td><td>Horses were bled on the day of challenge, twice daily for 6 days post-challenge, once daily for an additional 4 days post-challenge, and on day 14 post-challenge</td></tr>
<tr><td>Results</td><td>The primary outcome was viremia (detection of WNV in the blood). An animal was considered to be positive if virus was detected in the blood on one or more occasions post-challenge.

The number of animals positive for viremia at least once is summarized for as follows:
<table>
<tr><th>Challenge Group</th><th>Controls</th><th>Vaccinates</th></tr>
<tr><td>1</td><td>5/5 (100%)</td><td>1/10 (10%)</td></tr>
<tr><td>2</td><td>5/5 (100%)</td><td>3/10 (30%)</td></tr>
</table>

The outcome for viremia is as follows for the first group of horses challenged 201 days following the second vaccination:
<table>
<tr><th></th><th>Horse ID</th><th>Challenge Group 1</th></tr>
<tr><td rowspan="5">Controls (5 horses)</td><td>S16</td><td>Positive</td></tr>
<tr><td>S21</td><td>Positive</td></tr>
<tr><td>S23</td><td>Positive</td></tr>
<tr><td>S26</td><td>Positive</td></tr>
<tr><td>S30</td><td>Positive</td></tr>
<tr><td rowspan="10">Vaccinates (10 horses)</td><td>S17</td><td>Negative</td></tr>
<tr><td>S18</td><td>Negative</td></tr>
<tr><td>S19</td><td>Negative</td></tr>
<tr><td>S20</td><td>Negative</td></tr>
<tr><td>S22</td><td>Positive</td></tr>
<tr><td>S24</td><td>Negative</td></tr>
<tr><td>S25</td><td>Negative</td></tr>
<tr><td>S27</td><td>Negative</td></tr>
<tr><td>S28</td><td>Negative</td></tr>
<tr><td>S29</td><td>Negative</td></tr>
</table>
Positive = WNV detected in blood on one or more occasions post-challenge
Negative = WNV detected in blood on zero occasions post-challenge</td></tr>
</table>

The outcome for **viremia** is as follows for the second group of horses challenged 222 days following the second vaccination:

	Horse ID	Challenge Group 2
Controls (5 horses)	S32	Positive
	S36	Positive
	S39	Positive
	S40	Positive
	S43	Positive
Vaccinates (10 horses)	S31	Negative
	S33	Positive
	S34	Negative
	S35	Positive
	S37	Negative
	S38	Negative
	S41	Negative
	S42	Negative
	S44	Negative
	S45	Positive

Positive = WNV detected in blood on one or more occasions post-challenge
Negative = WNV detected in blood on zero occasions post-challenge

USDA Approval Date	November 2, 2009

<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 under field conditions at three different test sites</td></tr>
<tr><td>Product Administration</td><td>2 doses given intramuscularly 21 days apart</td></tr>
<tr><td>Study Animals</td><td>622 horses vaccinated with two doses including:
203-two to four month-old foals
19-five to seven month-old foals
400-1 year or older horses</td></tr>
<tr><td>Challenge Description</td><td>Not Applicable</td></tr>
<tr><td>Interval observed after vaccination</td><td>Horses were observed on Days 0, 1 and 3 following the first vaccination and on Days 1, 3 and 7 following the second vaccination for systemic and local injection site reactions.</td></tr>
<tr><td>Results</td><td>There were no systemic reactions observed at any of the three sites. Local injection site reactions are summarized below.

North Dakota Site:
<table>
<tr><th>Summary</th><th>Total Number</th><th>Number with 2 doses</th><th colspan="2">Transient Injection Site Swelling</th><th colspan="2">Number Normal</th></tr>
<tr><td>Age</td><td></td><td></td><td>1st dose</td><td>2nd dose</td><td>1st dose</td><td>2nd dose</td></tr>
<tr><td>2-4 mo</td><td>149</td><td>149</td><td>0</td><td>0</td><td>149</td><td>149</td></tr>
<tr><td>5-7 mo</td><td>0</td><td>0</td><td>n/a</td><td>n/a</td><td>n/a</td><td>n/a</td></tr>
<tr><td>8-11 mo</td><td>0</td><td>0</td><td>n/a</td><td>n/a</td><td>n/a</td><td>n/a</td></tr>
<tr><td>1 yr-5yr</td><td>23</td><td>23</td><td>0</td><td>0</td><td>23</td><td>23</td></tr>
<tr><td>6-15 yr</td><td>121</td><td>121</td><td>0</td><td>0</td><td>121</td><td>121</td></tr>
<tr><td>>16 yr</td><td>3</td><td>3</td><td>0</td><td>0</td><td>3</td><td>3</td></tr>
<tr><td>Total</td><td>296</td><td>296</td><td>0</td><td>0</td><td>296</td><td>296</td></tr>
</table>
California Site:
<table>
<tr><th>Summary</th><th>Total Number</th><th>Number with 2 doses</th><th colspan="2">Transient Injection Site Swelling</th><th colspan="2">Number Normal</th></tr>
<tr><td>Age</td><td></td><td></td><td>1st dose</td><td>2nd dose</td><td>1st dose</td><td>2nd dose</td></tr>
<tr><td>2-4 mo</td><td>0</td><td>0</td><td>n/a</td><td>n/a</td><td>n/a</td><td>n/a</td></tr>
<tr><td>5-7 mo</td><td>5</td><td>5</td><td>0</td><td>0</td><td>5</td><td>5</td></tr>
<tr><td>8-11 mo</td><td>0</td><td>0</td><td>n/a</td><td>n/a</td><td>n/a</td><td>n/a</td></tr>
<tr><td>1 yr-5yr</td><td>25</td><td>25</td><td>0</td><td>4</td><td>25</td><td>21</td></tr>
<tr><td>6-15 yr</td><td>15</td><td>15</td><td>0</td><td>3</td><td>15</td><td>12</td></tr>
<tr><td>>16 yr</td><td>6</td><td>6</td><td>0</td><td>1</td><td>6</td><td>5</td></tr>
<tr><td>Total</td><td>51</td><td>51</td><td>0</td><td>8*</td><td>51</td><td>43</td></tr>
</table>
*Postvaccination reactions were minimal. The reported reactions were mild, transient, non-painful injection swellings.</td></tr>
</table>

Missouri Site:

Summary	Total Number	Number with 2 doses	Transient Injection Site Swelling		Number Normal	
Age			1st dose	2nd dose	1st dose	2nd dose
2-4 mo	55	54	0	0	55	54
5-7 mo	15	14	0	0	15	14
8-11 mo	0	0	n/a	n/a	n/a	n/a
1 yr-5yr	134	132	0	0	134	132
6-15 yr	68	68	0	0	68	68
>16 yr	7	7	0	0	7	7
Total	**279**	**275**	**0**	**0**	**279**	**275**

Total Across Three Sites:

Site	Total Number	Number with 2 doses	Transient Injection Site Swelling		Number Normal	
			1st dose	2nd dose	1st dose	2nd dose
North Dakota	296	296	0	0	296	296
California	51	51	0	8*	51	43
Missouri	279	275	0	0	279	275
Total	**626**	**622**	**0**	**8***	**626**	**614**

*Postvaccination reactions were minimal and described as mild, transient, non-painful swellings after the second vaccination in eight (8) older, heavily vaccinated horses. There were no systemic reactions observed.

USDA Approval Date	February 14, 2012

Study Type	Safety
Pertaining to	All fractions
Study Purpose	To demonstrate safety in pregnant mares under field conditions at two different test sites
Product Administration	Two intramuscular doses, given 16-28 days apart. 54 pregnant mares were injected with placebo and 325 pregnant mares were vaccinated with test product.
Study Animals	Three hundred seventy-nine pregnant mares at two locations were included in the study. The mares were confirmed to be pregnant by serum hormonal evaluation on the day of the first vaccination.
Challenge Description	Not applicable
Interval observed after vaccination	1st and 2nd trimester: Mares observed immediately after vaccination and daily for overall health and for abortion. Resulting foals were observed daily for 7 days following birth. 3rd trimester: Mares observed immediately after vaccination and daily for overall health and for abortion. Resulting foals were observed daily for 30 days following birth.
Results	Results shown on next page

Results

Study 2013-PM-1009
North Dakota Site:

Group	Vaccinated	Confirmed Pregnant	Foals	Parturition Rate
1st trimester/ product	143	127	114	90%
1st trimester/ placebo	59	54	49	91%
2nd trimester/ product	6	6	6	100%
3rd trimester/ product	140	117	117	100%
Total – all animals	**348**	**304**	**286**	**94%**
Total – product only	**289**	**250**	**237**	**95%**
Total – placebo only	**59**	**54**	**49**	**91%**

Study 2013-PM-1009
Misssouri Site:

Group	Vaccinated	Confirmed Pregnant	Foals	Parturition Rate
2011 3rd trimester	5	5	5	100%
2012 1st trimester	1	1	1	100%
2012 2nd trimester	53	43	39	91%
2012 3rd trimester	26	26	25	96%
Total – product	**85**	**75**	**70**	**93%**

Study 2014-PM-1009
North Dakota Site:

Group	Vaccinated	Confirmed Pregnant	Foaled	Parturition Rate	Foals Survived to End of Observation Period
2nd trimester vaccinated	52	52	52	100%	51*
3rd trimester vaccinated	69	69	67**	97.1%	67

*Lost foal affirmed by study cooperator to be due to causes other than vaccination.
**One mare died due to causes other than vaccination, as affirmed by study cooperator.
All other foals were normal and healthy

USDA Approval Date	September 12, 2014