Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	4845.20
True Name	Encephalomyelitis-Rhinopneumonitis-Influenza Vaccine, Eastern & Western, Killed Virus, Tetanus Toxoid
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Equi-Jec 5 - 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	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	May 1, 2008

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	May 1, 2008

Study Type	Efficacy
Pertaining to	Western equine encephalomyelitis
Study Purpose	Demonstration of efficacy against Western 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 Western equine encephalomyelitis per the criteria in 9 CFR 113.207(b) and the requirements were met.
USDA Approval Date	May 1, 2008

<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 (EHV) type 1</td></tr>
<tr><td>Study Purpose</td><td>Demonstration of efficacy against 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>37 horses (24 vaccinates, 13 controls), 4 to 5 months of age</td></tr>
<tr><td>Challenge Description</td><td>Equine herpesvirus type 4 was administered 15 days following second vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Horses were observed daily for 14 days following challenge</td></tr>
<tr><td>Results</td><td>The horses were assessed for the presence of nasal and ocular discharge as signs of respiratory disease. The severity of the nasal and ocular discharge resulted in the classification of the observed clinical signs as “mild” or “moderate” according to the following table:
<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 rowspan="2">Mild = 1</td><td>0 or 1</td><td>2</td></tr>
<tr><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>
Respiratory disease was observed as follows:
<table>
<tr><th></th><th>Controls</th><th>Vaccinates</th></tr>
<tr><td>Normal</td><td>0 out of 13</td><td>9 out of 24</td></tr>
<tr><td>Mild</td><td>12 out of 13</td><td>14 out of 24</td></tr>
<tr><td>Moderate</td><td>1 out of 13</td><td>1 out of 24</td></tr>
</table>
See raw data on the following pages.</td></tr>
<tr><td>USDA Approval Date</td><td>September 17, 2009</td></tr>
</table>

Ocular Discharge:

Treatment	Horse ID	Days Post-challenge														
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Controls (13 horses)	8300															
	8861								1		1	2	1	1	1	1
	0327										1	1				1
	1029								1	1	1		1		1	1
	2603											1				
	8822															
	5542												1	1	1	2
	3280				1				1				1	1	1	1
	5597														1	2
	9331								2	2	2	2	1		2	1
	9339											1	1			1
	5103															
	6528															
Vaccinates (24 horses)	1278							1					1		1	
	1602							1	1	1	1	1	1	2		
	8026															
	3857									1	1	1				1
	5560															
	5636															
	0261											1	1			
	0285						1	1								1
	6051															
	6311							1			1					
	1310															
	5381															
	8023												1			
	8881				1	1		1					1			
	0019											1				
	1381															
	2333															1
	3086															
	3347															
	5379												1			
	7297															
	7580							1					1			
	7806							1	1							
	8004															

Scoring:

No entry indicates 0 = horse is normal

1 = normal

2 = mild

Nasal Discharge:

Treatment	Horse #	Days Post-challenge														
		0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Controls (13 horses)	**8300**							1.5	1.5	1.5	1.5			1.5		
	8861							1.5	1	1			1.5			1.5
	0327							1	1		1.5	1.5		2		1
	1029				1.5						1.5			1.5	1.5	
	2603				1.5			1.5			1.5					
	8822					2	1.5	1.5		2						
	5542								1.5	1.5	2	1.5	1		1.5	2
	3280					1		2								
	5597					1.5		1	1.5	2	1.5		1		1.5	1.5
	9331						1.5	1.5	1.5	4	1.5	1			1.5	1.5
	9339							1.5	1.5	1.5	1.5	1.5	2	1		
	5103					1	1.5	2	1.5	2	1.5	2				
	6528							1.5	1.5			1.5		1		
Vaccinates (24 horses)	**1278**					1.5		1								
	1602							1.5	1.5	2	2	2	2	4		
	8026					2	1.5	1				2	1.5	2		
	3857									1.5	1.5					
	5560															1.5
	5636									1.5						
	0261										1.5					
	0285										1.5					
	6051				1.5					1						1.5
	6311							1.5			2					
	1310															
	5381															
	8023															
	8881				1.5	1.5					1.5		1.5			
	0019															
	1381							1.5			1.5					
	2333															
	3086															
	3347				1.5											
	5379														2	
	7297															
	7580					1										1.5
	7806															
	8004										1					

Scoring:

No entry is 0 = horse is normal

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 or slightly mucopurulent discharge, in one or both nostrils;

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

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

6 = heavy mucopurulent discharge in large amounts filling 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
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

Study Type	Efficacy
Pertaining to	Equine influenza
Study Purpose	Demonstration of efficacy against respiratory disease caused by equine influenza A2 strain New Market 2/93
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	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

<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</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered intramuscularly approximately 3 – 4 weeks apart</td></tr>
<tr><td>Study Animals</td><td>880 horses, including 218 foals 3 months of age and 52 foals 5 months of age</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>Not applicable</td></tr>
<tr><td>Results</td><td>Horses were observed at least daily following each vaccination, until resolution of any observed reactions.

There were no systemic reactions observed at any of the sites. Two foals and one horse died from causes affirmed by licensee not attributed to vaccination.

Adverse events were limited to transient, non-painful swellings at the injection site that resolved without treatment.

Local injection site reactions are summarized below across the four sites:
<table>
<tr><th rowspan="2">Site</th><th rowspan="2">Total Number Of Vaccinates</th><th rowspan="2">Number Of Vaccinates Administered 2 doses</th><th colspan="2">Vaccinates With Transient Injection Site Swelling</th><th colspan="2">Number Of Normal Vaccinates</th></tr>
<tr><td>After 1st dose</td><td>After 2nd dose</td><td>After 1st dose</td><td>After 2nd dose</td></tr>
<tr><td>North Dakota</td><td>378</td><td>378</td><td>4</td><td>0</td><td>374</td><td>378</td></tr>
<tr><td>California</td><td>43</td><td>43</td><td>4</td><td>3</td><td>39</td><td>40</td></tr>
<tr><td>Missouri</td><td>292</td><td>290</td><td>0</td><td>0</td><td>292</td><td>290</td></tr>
<tr><td>Texas</td><td>170</td><td>169</td><td>6</td><td>1</td><td>164</td><td>168</td></tr>
<tr><td>Total</td><td>883</td><td>880</td><td>14 (1.6%)</td><td>4 (0.5%)</td><td>869 (98.4%)</td><td>876 (99.5%)</td></tr>
</table>
Results from each site are summarized on the following pages.</td></tr>
</table>

North Dakota Site:

Summary	Number Of Vaccinates	Number Of Vaccinates Administered 2 doses	Vaccinates With Transient Injection Site Swelling		Number Of Normal Vaccinates	
Age			After 1st dose	After 2nd dose	After 1st dose	After 2nd dose
2-4 months	179	179	0	0	179	179
5-7 months	0	0	n/a	n/a	n/a	n/a
8-11 months	0	0	n/a	n/a	n/a	n/a
1-5 years*	121	121	2	0	119	121
6-15 years*	78	78	2	0	76	78
>16 years	0	0	n/a	n/a	n/a	n/a
Total	**378**	**378**	**4**	**0**	**374**	**378**

*Swellings were 3cm in size observed 1-3 days post vaccination that resolved within 3 days.

California Site:

Summary	Number Of Vaccinates	Number Of Vaccinates Administered 2 doses	Vaccinates With Transient Injection Site Swelling		Number Of Normal Vaccinates	
Age			After 1st dose	After 2nd dose	After 1st dose	After 2nd dose
2-4 months*	7	7	0	2	7	5
5-7 months**	1	1	1	0	0	1
8-11 months	0	0	n/a	n/a	n/a	n/a
1-5 years***	19	19	2	0	17	19
6-15 years****	15	15	1	1	14	14
>16 years	1	1	0	0	1	1
Total	**43**	**43**	**4**	**3**	**39**	**40**

*Swellings were 3cm in size observed within hours post vaccination that resolved within several hours.
**Swelling was 3cm in size observed immediately post vaccination that resolved within several hours.
***1 horse had a swelling 1cm in size observed immediately post vaccination that resolved within several hours. 1 horse had a swelling observed on day 1 that increased in size to 9cm on day 3 post vaccination and resolved by day 5.
****Same horse had a swelling after each vaccination that resolved within 3 weeks. Size after the first vaccination was 24cm. Size after the second vaccination was 10cm.

Missouri Site:

Summary	Number Of Vaccinates	Number Of Vaccinates Administered 2 doses	Vaccinates With Transient Injection Site Swelling		Number Of Normal Vaccinates	
Age			After 1st dose	After 2nd dose	After 1st dose	After 2nd dose
2-4 months	33	32	0	0	33	32
5-7 months	0	0	n/a	n/a	n/a	n/a
8-11 months	0	0	n/a	n/a	n/a	n/a
1-5 years	225	224	0	0	225	224
6-15 years	32	32	0	0	32	32
>16 years	2	2	0	0	2	2
Total	**292**	**290**	**0**	**0**	**292**	**290**

Texas Site:

Summary	Number Of Vaccinates	Number Of Vaccinates Administered 2 doses	Vaccinates With Transient Injection Site Swelling		Number Of Normal Vaccinates	
Age			After 1st dose	After 2nd dose	After 1st dose	After 2nd dose
2-4 months	0	0	n/a	n/a	n/a	n/a
5-7 months	52	51	1	1	51	50
8-11 months	0	0	n/a	n/a	n/a	n/a
1-5 years	114	114	5	0	109	114
6-15 years	0	0	n/a	n/a	n/a	n/a
>16 years	4	4	0	0	4	4
Total	**170**	**169**	**6***	**1****	**164**	**168**

*Swellings were <1.5cm were observed 4-7 days post vaccination and resolved within 6 days.
**Swelling was 5cm observed 1 day post vaccination that resolved within 2 days.

USDA Approval Date	November 1, 2010