



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	4835.46
True Name	Encephalomyelitis-Influenza Vaccine, Eastern & Western, Killed Virus, Tetanus Toxoid
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Prestige 4 - Merck Animal Health
Date of Compilation Summary	April 12, 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	<i>Clostridium tetani</i>		
Study Purpose	Demonstrate efficacy against <i>C. tetani</i>		
Product Administration	One dose administered subcutaneously.		
Study Animals	Ten guinea pigs (5 females and 5 males, 450-550g)		
Challenge Description	Not applicable		
Interval observed after challenge	Six weeks after vaccination, guinea pigs were bled for serological testing.		
Results	<p>Efficacy of <i>C. tetani</i> was demonstrated in laboratory animals according to 9CFR 113.114(c).</p> <p>Satisfactory result is an antitoxin titer of at least 2.0 A.U. per mL for the serum pool.</p> <table border="1" data-bbox="579 920 989 1037"> <tr> <td>Pooled Guinea Pig Antitoxin titer (A.U./mL)</td> </tr> <tr> <td>2.082</td> </tr> </table>	Pooled Guinea Pig Antitoxin titer (A.U./mL)	2.082
Pooled Guinea Pig Antitoxin titer (A.U./mL)			
2.082			
USDA Approval Date	June 15, 2010		

Study Type	Efficacy								
Pertaining to	Eastern Equine Encephalomyelitis (EEE)								
Study Purpose	Demonstrate efficacy against EEE								
Product Administration	Two doses administered intramuscularly 3 weeks apart.								
Study Animals	Twelve guinea pigs, 10 vaccinates and 2 controls, each 300-500g								
Challenge Description	Not applicable								
Interval observed after challenge	14 days post 2nd vaccination, guinea pigs were bled for serological testing.								
Results	<p>Efficacy of EEE was demonstrated in laboratory animals according to 9CFR 113.207(b).</p> <p>Satisfactory test result is a Virus Neutralization Titer of $\geq 1:40$ in at least 9 out of 10 vaccinates (2nd stage - at least 17 out of 20 vaccinates).</p> <table border="1" data-bbox="579 920 1254 1072"> <thead> <tr> <th>Treatment group</th> <th>Results</th> <th>Test Disposition</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>17/20 $\geq 1:40$</td> <td rowspan="2">Satisfactory</td> </tr> <tr> <td>Controls</td> <td>2/2 $<1:4$</td> </tr> </tbody> </table>	Treatment group	Results	Test Disposition	Vaccinates	17/20 $\geq 1:40$	Satisfactory	Controls	2/2 $<1:4$
Treatment group	Results	Test Disposition							
Vaccinates	17/20 $\geq 1:40$	Satisfactory							
Controls	2/2 $<1:4$								
USDA Approval Date	June 15, 2010								

Study Type	Efficacy								
Pertaining to	Western Equine Encephalomyelitis (WEE)								
Study Purpose	Demonstrate efficacy against WEE								
Product Administration	Two doses administered intramuscularly 3 weeks apart.								
Study Animals	Twelve guinea pigs, 10 vaccinates and 2 controls, each 300-500g								
Challenge Description	Not applicable								
Interval observed after challenge	14 days post 2nd vaccination, guinea pigs were bled for serological testing.								
Results	<p>Efficacy of WEE was demonstrated in laboratory animals according to 9CFR 113.207(b).</p> <p>Satisfactory test result is a Virus Neutralization Titer of $\geq 1:40$ in at least 9 of the vaccinates.</p> <table border="1" data-bbox="587 884 1259 1037"> <thead> <tr> <th>Treatment group</th> <th>Results</th> <th>Test Disposition</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>9/10 $\geq 1:40$</td> <td rowspan="2">Satisfactory</td> </tr> <tr> <td>Controls</td> <td>2/2 $<1:4$</td> </tr> </tbody> </table>	Treatment group	Results	Test Disposition	Vaccinates	9/10 $\geq 1:40$	Satisfactory	Controls	2/2 $<1:4$
Treatment group	Results	Test Disposition							
Vaccinates	9/10 $\geq 1:40$	Satisfactory							
Controls	2/2 $<1:4$								
USDA Approval Date	June 15, 2010								

Study Type	Efficacy
Pertaining to	Equine Influenza Virus (EIV)
Study Purpose	To demonstrate efficacy of updated EIV strains FL/13 and RI/07
Product Administration	
Study Animals	
Challenge Description	
Interval observed after challenge	
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	March 8, 2016

Study Type	Efficacy																		
Pertaining to	Equine Influenza Virus (EIV)																		
Study Purpose	To demonstrate efficacy against EIV six months after vaccination.																		
Product Administration	Two doses administered intramuscularly (IM) three weeks apart.																		
Study Animals	18 vaccinate and 7 control horses were used at 6 months of age.																		
Challenge Description	All horses were challenged with EIV strain A/equine/Kentucky/99 six months post second vaccination.																		
Interval observed after challenge	Horses were observed daily for 14 days post-challenge for clinical signs. Nasal swabs were collected daily for virus isolation.																		
Results	<p>Disease Prevalence – presence/absence of any clinical sign at any occasion during the observation period (nasal discharge, coughing, respiration, temperature >102.5°F).</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th>Presence of clinical signs</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>18</td> <td>14</td> </tr> <tr> <td>Controls</td> <td>7</td> <td>7</td> </tr> </tbody> </table> <p>Virus shedding prevalence – a horse was considered negative for shedding if all 14 daily post-challenge swabs were virus negative, otherwise it was positive.</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th>Virus Isolation</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>18</td> <td>12</td> </tr> <tr> <td>Controls</td> <td>7</td> <td>7</td> </tr> </tbody> </table> <p>Raw data shown on attached pages.</p>	Group	# of Animals	Presence of clinical signs	Vaccinates	18	14	Controls	7	7	Group	# of Animals	Virus Isolation	Vaccinates	18	12	Controls	7	7
Group	# of Animals	Presence of clinical signs																	
Vaccinates	18	14																	
Controls	7	7																	
Group	# of Animals	Virus Isolation																	
Vaccinates	18	12																	
Controls	7	7																	
USDA Approval Date	August 8, 2005																		

Table 1. Rectal body temperatures of horses vaccinated with vaccine 111103 on days post-challenge with virulent EIV KY99.

Horse No.	Group	Body temperatures (°F) on days post challenge with EIV KY99:															
		-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	Vaccinates	100.3	100.0	99.6	99.9	101.5	101.1	100.0	99.8	100.2	99.1	100.2	98.1	100.7	99.9	100.1	100.6
2		99.2	100.0	99.7	99.0	99.5	99.8	98.9	99.3	100.0	99.1	99.8	99.2	100.8	99.6	100.3	100.1
4		98.8	99.1	99.9	100.1	98.6	99.8	98.9	99.3	98.9	97.8	99.2	99.2	100.5	99.9	101.7	100.0
14		99.8	100.9	100.6	101.9	99.8	99.8	99.9	100.0	99.2	99.1	100.3	99.2	100.8	99.9	100.2	99.7
16		99.1	100.1	99.3	102.8	100.5	101.5	100.1	98.9	98.8	98.5	98.3	98.8	100.1	99.4	100.0	100.6
19		99.7	100.6	99.9	100.0	99.6	100.2	99.4	100.0	99.7	99.5	100.0	98.6	100.0	100.6	100.9	100.2
29		100.3	100.5	99.6	99.7	99.7	100.0	99.3	99.2	99.2	100.5	99.8	100.0	100.5	100.9	100.2	100.3
30		101.2	100.1	100.5	105.4	102.6	104.4	102.1	100.9	99.6	100.4	101.5	100.7	102.4	101.3	102.1	101.4
32		98.8	100.8	100.0	100.4	99.3	100.5	99.6	99.7	99.7	98.3	99.6	100.0	101.2	100.0	100.4	102.7
33		99.2	100.0	99.4	104.6	100.0	100.0	98.7	100.0	100.8	98.6	99.0	99.3	100.6	99.6	100.9	100.6
34		99.8	100.2	99.7	103.6	100.0	101.3	102.1	102.7	102.1	101.5	102.9	102.0	100.4	100.1	99.8	99.4
35		99.2	99.7	99.1	99.5	99.5	100.6	100.4	99.7	98.8	98.5	100.1	100.1	101.6	100.2	100.3	100.5
36		99.7	99.6	99.8	100.5	100.0	100.5	99.6	99.4	100.4	98.6	99.2	99.0	100.6	100.7	99.9	100.4
39		99.7	100.4	100.0	100.5	100.3	100.5	98.8	100.0	99.4	98.7	100.8	99.6	100.5	100.1	100.9	100.0
40		99.4	100.4	99.9	102.2	99.9	101.6	100.1	100.1	99.1	99.1	99.7	99.5	100.3	99.2	99.9	100.4
41		99.2	100.0	99.4	102.6	99.7	99.7	99.4	99.6	99.7	99.3	99.6	98.8	100.2	99.0	100.1	100.2
43	99.7	100.4	99.8	99.4	99.8	100.1	98.6	99.8	98.7	99.0	99.4	99.6	99.6	99.9	99.6	99.9	
47	100.2	100.2	100.1	101.6	99.2	100.1	99.9	100.5	99.6	99.3	98.8	99.5	99.3	99.7	99.5	100.6	
3	Controls	99.5	100.2	99.6	104.5	103.1	103.8	103.7	103.6	102.6	102.4	104.7	102.7	102.4	101.8	102.0	100.9
8		99.0	99.9	98.8	101.9	100.8	103.0	99.1	100.7	100.2	98.9	99.9	99.3	100.4	100.1	100.3	99.6
11		100.4	100.5	100.1	101.9	99.9	99.8	100.9	100.1	99.2	100.6	101.3	99.2	101.0	99.9	100.6	100.3
13		99.5	99.7	100.3	103.6	102.4	102.8	99.5	99.3	100.4	99.5	99.2	98.8	101.0	100.1	100.7	99.8
25		100.1	100.6	99.5	104.7	103.6	102.2	103.1	104.2	103.2	102.3	105.4	99.5	99.8	99.8	99.7	100.1
38		99.2	100.0	99.0	104.7	103.7	104.0	104.6	104.7	103.0	103.6	103.3	101.6	101.2	99.5	99.2	99.5
44		99.1	99.9	99.8	103.2	102.6	104.4	97.2	99.8	100.4	104.6	103.8	102.6	102.9	100.6	100.0	99.4

Table 2. Coughing observations of horses vaccinated with vaccinated 111103 on days post-challenge with virulent EIV KY99.

Horse No	Group	Coughing observations on days post-challenge with EIV KY99:															
		-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1		N	N	N	N	C	C	C,C	C	C	N	N	N	N	N	N	N
2		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
4		N	N	N	N	N	N	N	N	N	N	N	N	C	N	N	N
14		N	N	N	N	N	N	C	N	N	C	C	C	N	N	N	N
16		N	N	N	C,C	C	C,C	C,C	C,C	N	C,C	C,C	N	N	N	N	N
19		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
29		N	N	N	N	N	N	N	N	C	N	N	N	N	N	N	N
30		N	N	N	C,C	C	C,C	C,C	C,C	N	C,C	N	N	N	N	N	N
32		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
33	Vaccinates	N	N	N	C,C	C	C	N	N	N	C,C	C	N	N	N	N	N
34		N	N	N	N	N	N	C,C	C,C	C,C	C,C	C	N	N	N	N	N
35		N	N	N	N	N	N	N	N	N	N	C	N	N	N	N	N
36		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
39		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
40		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
41		N	N	N	N	N	N	N	C	N	N	N	C	N	N	N	N
43		N	N	N	N	N	N	N	N	N	C	C,C	N	N	N	N	N
47		N	N	N	N	N	N	N	N	N	N	C	N	N	N	N	N
3		N	N	N	C,C	C,C	C,C	C,C	C	C	C,C	C,C	N	N	N	N	N
8		N	N	N	C,C	C	C,C	C,C	C,C	C,C	C,C	C,C	N	N	N	N	N
11		N	N	N	N	N	N	N	C	C	C,C	C	N	N	N	N	N
13		N	N	N	C	C,C	C,C	C,C	C,C	C,C	C,C	C	N	N	N	N	N
25		N	N	N	N	C,C	C	C,C	C,C	N	N	C,C	N	N	N	N	N
38		N	N	N	C,C	C,C	C,C	C,C	C,C	C,C	C,C	C,C	N	N	N	N	N
44		N	N	N	C,C	C	C	C,C	N	N	C	N	C,C	N	N	N	N

N=no coughing, C=coughing 1 time during the observation period, C,C=coughing 2 or more times during the observation period

Table 3. Nasal discharge observations of horses vaccinated with vaccine 111103 on days post-challenge with virulent EIV KY99.

Horse No.	Group	Nasal discharge observations on days post-challenge with EIV KY99:															
		-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1		N	N	N	N	N	N	CM	N	N	N	N	N	N	N	N	N
2		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
4		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
14		N	N	N	N	N	N	N	N	N	N	SM	CM	SM	N	N	N
16		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
19		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
29		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
30		N	N	N	N	N	N	SM	SM	SM	N	N	N	N	N	SM	N
32		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
33		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
34		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
35		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
36		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
39		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
40		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
41		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
43		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
47		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
3		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
8		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
11		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
13		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
25		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
38		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
44		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N=normal (score of 0), S=copious serous discharge (score of 1), SM=slight mucopurulent discharge (score of 2), CM=copious mucopurulent discharge (score of 4)

Table 4. Abnormal respiration and depression observations of horses vaccinated with vaccine 111103 on days post-challenge with virulent EIV KY99.

Horse No	Group	Observations on days post-challenge with EIV KY99:															
		-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
2		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
4		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
14		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
16		N	N	N	D	N	N	N	N	N	N	N	N	N	N	N	N
19		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
29		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
30		N	N	N	D	D, Ab	D	D, Ab	D, Ab	N	D, Ab	N	N	N	N	N	N
32		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
33	Vaccinates	N	N	N	Ab	N	N	N	N	N	N	N	N	N	N	N	N
34		N	N	N	N	N	N	N	D, Ab	D, Ab	N	N	D, Ab	Ab	N	N	N
35		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
36		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
39		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
40		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
41		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
43		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
47		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
3		N	N	N	N	N	D, Ab	D, Ab	D	D, Ab	D	D	D	D	D	D	D
8		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
11		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
13		N	N	N	N	D	N	N	N	N	N	N	N	N	N	N	N
25	Controls	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
38		N	N	N	N	N	D, Ab	D	D	N	N	N	D, Ab	D	D	D	D
44		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N=normal, Ab=abnormal respiration of >36 per minute, D=depression, lethargy or inappetence. Observations were scored as not observed (score of 0) and observed (score of 1)

Table 5. Virus isolation from nasal swabs from horses vaccinated with vaccine 111103 on days post-challenge with virulent EIV KY99.

Horse No	Group	Isolation of virus on days post-challenge with EIV KY99:															
		-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1		-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-
2		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
14		-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
16		-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
19		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
29		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30		-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
32		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
33	Vaccinates	-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
34		-	-	+	+	+	-	+	+	-	-	-	-	-	-	-	-
35		-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-
36		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
39		-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
40		-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-
41		-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-
43		-	-	-	+	+	-	+	-	-	-	-	-	-	-	-	-
47		-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
3		-	-	+	+	+	-	+	+	-	-	-	-	-	-	-	-
8		-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
11		-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
13		-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
25	Controls	-	-	+	+	+	-	+	+	-	-	-	-	-	-	-	-
38		-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-
44		-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-

(-) = no virus isolated from the nasal swab, (+) = virus recovered from the nasal swab

Study Type	Safety																					
Pertaining to	ALL																					
Study Purpose	To demonstrate safety under field conditions																					
Product Administration	298 horses received 2 doses intramuscularly 3 to 4 weeks apart for primary immunization. 254 horses received 1 dose intramuscularly.																					
Study Animals	552 horses of various ages, breeds and sex in 5 different states. 177 horses were 4-months of age or younger at the time of the initial vaccination.																					
Challenge Description	Not applicable																					
Interval observed after challenge	Horses were observed immediately following vaccination and then daily for 3 days post-vaccination																					
Results	<p>Doses are reported due to difference in vaccination schedule.</p> <table border="1"> <thead> <tr> <th>Score</th> <th># of Cases</th> <th>% of Total</th> </tr> </thead> <tbody> <tr> <td>0</td> <td>820</td> <td>96.47</td> </tr> <tr> <td>1</td> <td>25</td> <td>2.94</td> </tr> <tr> <td>2</td> <td>3</td> <td>0.35</td> </tr> <tr> <td>3</td> <td>2</td> <td>0.24</td> </tr> <tr> <td>4</td> <td>0</td> <td>0</td> </tr> <tr> <td>5</td> <td>0</td> <td>0</td> </tr> </tbody> </table> <p>Total # of Doses administered = 850</p> <p>Score Overview: 0 – No reaction 1 – Localized swelling at or near the injection site, which is not visible; detectable only by palpation. Not clinically significant. 2 – Localized visible swelling at or near the injection site. Not painful. 3 – Localized visible swelling at or near the injection site. Raised, circumscribed and painful. 4 – Visible diffused swelling involving a substantial area around the injection site. Very painful and hot. Horse is stiff and/or reluctant to move. 5 – Generalized or systemic reaction, including anaphylaxis or elevated temperature.</p>	Score	# of Cases	% of Total	0	820	96.47	1	25	2.94	2	3	0.35	3	2	0.24	4	0	0	5	0	0
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