

Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	1501.20
True Name	Equine Influenza Vaccine, Modified Live Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Flu Avert I.N Merck Animal Health Flu Avert I.N No distributor specified
Date of Compilation Summary	February 08, 2018

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	Equine Influe	nza Virus (E	IV)									
Study Purpose	To demonstrat	te efficacy a	gainst EIV									
Product Administration	One dose adm	inistered int	ranasally (IN).									
Study Animals	13 vaccinates	and 9 control	ols horses were used	at 8.5 months of								
	age.											
Challenge Description	All horses we	re challenged	d with EIV strain A/e	equine/Kentucky/99								
	36 days post v	vaccination.										
Interval observed after	Horses were o	bserved dail	y for 14 days post-cl	hallenge for clinical								
challenge	signs. Nasal s	swabs were c	collected daily for vir	rus isolation.								
Results	A horse was c	onsidered af	fected if virus isolati	ion was detected at								
	any occasion	postchalleng	e.									
	# of											
	Group	Animals	Virus Isolation									
	Vaccinates	13	8 (61%)									
	Controls	9	9 (100%)									
	Derry data alter											
	Kaw data show	wn on attach	ed pages.									
USDA Approval Date	September 7, 2	2005										

	Control	Control	Control	Control	Control	Centrol	Control	Control	Control	Vaccinate	Group													
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Virus isolation from nasal swabs collected from horses on days post-challenge with virulent EIV

1501.20

Study Type	Efficacy
Pertaining to	Equine Influenza Virus (EIV)
Study Purpose	To demonstrate efficacy against EIV six months after vaccination
Product Administration	One dose administered intranasally (IN).
Study Animals	19 vaccinates and 10 controls horses were used at 11-12 months of
	age.
Challenge Description	All horses were challenged with EIV strain A/equine/Kentucky/91
	six months post vaccination.
Interval observed after	Horses were observed daily for 10 days post-challenge for clinical
challenge	signs. Nasal swabs were collected daily for virus isolation.
Results	
	Raw data shown on attached pages.
USDA Approval Date	May 20, 1999

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Dav n	ost-challence	4	-2	4 19	0	1	2	3	4	5	6	7	8	9
Group	Halter No.		Pre-cha	allenge						Post-ch	allenge			
Vaccinates	31	100.9*	100.5	101.1	100.4	100.4	104.7	102.5	100.2	102.6	100.0	100.0	100.2	100
(Group C)	32	100.5	100.4	100.2	101.0	101.5	104.1	103.6	104.1	104.1	103.0	100.2	99.8	99.
	33	100.4	100.5	101.2	101.4	100.2	104.1	104.0	102.7	101.2	100.9	100.2	101.2	100
	35	99.6	100.5	100.6	100.1	101.4	103.2	99.9	99.8	101.1	102.5	100.0	99.8	99.
	37	101.2	100.2	101.0	101.2	100.9	103.6	100.3	100.4	100.7	100.2	100.6	100.3	100
	39	100.5	100.3	100.1	100.8	100.3	103.0	100.7	100.3	100.9	100.6	101.2	100.4	10
	41	100.5	100.2	100.3	101.1	101.1	103.9	100.3	100.1	100.3	100.3	100.1	100.4	100
	42	100.4	100.6	100.4	100.2	100.5	101.7	100.2	100.5	101.2	101.2	102.5	100.9	100.
	45	100.1	100.9	100.2	100.3	100.4	104.3	104.8	106.2	105.7	103.4	100.5	100.5	100
	46	100.7	101.3	100.5	99.6	100.7	102.7	102.3	102.3	100.4	102.9	101.7	101.8	100.0
	47	100.6	101.1	101.4	101.6	101.3	105.4	105.3	102.6	104.9	103.3	102.3	100.9	100.9
	48	100.6	100.8	100.2	100.8	100.2	101.8	100.1	100.1	100.5	100.1	100.5	99.6	99.7
	50	100.6	101.2	100.3	100.4	100.3	104.2	101.2	100.8	100.1	100.2	101.0	100.2	100.4
	52	100.1	100.5	100.9	100.6	99.6	102.0	100.9	100.2	99.5	99.7	99.8	100.2	100.2
	53	101.1	100.2	100.8	100.5	100.5	104.0	100.2	99.9	101.4	101.0	101.0	101.0	100.5
	54	100.3	100.7	101.2	100.0	100.5	102.8	103.5	102.2	101.5	103.4	100.7	100.9	100.0
	57	100.6	101.4	100.5	100.7	100.2	104.3	100.1	101.0	100.4	101.2	99.9	100.2	99.9
	58	100.3	100.9	101.8	101.0	99.9	100.2	100.4	100.2	100.7	100.0	100.0	100.2	100.2
	59	99.9	100.4	100.6	100.8	100.4	105.0	104.6	104.0	104.7	101.5	101.3	100.4	99.6
Controls	34	101.0	100.7	100.9	101.2	100.5	103.4	101.2	101.3	104.7	105.1	100.5	101.4	100.2
(Group D)	36	100.4	100.7	100.8	101.0	100.2	105.6	103.2	100.1	100.8	100.2	100.5	100.8	100.2
	38	100.7	100.9	100.1	100.7	100.3	105.3	104.1	104.1	101.8	102.1	101.1	101.7	103.1
	40	100.7	100.7	100.6	100.9	100.2	104.2	104.5	105.5	105.6	104.6	104.6	101.2	100.1
	43	100.3	100.2	100.5	100.5	100.5	104.6	104.7	104.8	103.9	104.2	100.2	100.0	100.2
	44	100.5	101.2	100.4	101.0	100.2	104.8	103.6	101.5	102.5	102.9	101.9	104.0	99.1
	49	100.9	100.9	101.6	101.1	100.7	106.0	105.8	105.1	104.5	105.3	102.0	100.0	99.6
	51	101.1	100.5	100.7	100.3	100.6	105.5	104.8	101.6	104.6	102.2	103.1	100.2	100.2
	55	100.9	100.4	100.5	100.2	100.6	105.0	104.5	105.0	104.7	103.7	104.4	103.2	99.8
				100 0	100 8	100 4	104 1	102.3	102.9	105.0	105.2	104.8	101.9	100.3

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Table A. Rectal temperature observations post-challenge.

*All temperatures in degrees Fahrenheit.

1	Study day		17	8	-		17	9			18	0			18	1			18	2			18	3			18	4	
Day post-	-chalienge		~	3			-2	2			-	1			C)			1				2	2			3	5	
Group	Halter No.	ç	N	R	D	С	N	R	D	С	N	R	D	С	N	R	D	С	Ν	R	D	c	N	R	D	С	N	R	D
Vaccinates	31	0"	0	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0	1	0	0
(Group C)	32	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	2	2	0	0
	33	0	0	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0	2	0	0	0	2	0	0
	35	0	2	0	0	0	2	0	0	0	1	0	0	0	2	0	0	2	3	0	0	0	3	0	0	0	3	0	0
	37	0	0	0	0	0.	2	0	0	0	2	0	0	0	2	0	0	0	0	0	0	2	3	0	0	0	3	0	0
	39	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0	0	2	3	0	0
	41	0	1	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0	2	0	0	1	2	0	1	0	3	0	0
	42	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0	2	0	0	1	3	0	0	0	2	0	0
	45	0	0	0	0	0	2	0	0	0	2	0	0	0	2	0	0.	0	2	0	0	0	2	0	0	2	2	0	0
	46	0	2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2	2	0	0
	47	0	2	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	1	0	0	2	2	0	0
	48	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0
	50	Ō	1	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0	0	0	0	1	1	0	0	1	3	0	0
	52	0	0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	1	2	0	0	0	3	0	0
	53	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0.	0	0	1	0	0	1	2	0	0	0	3	0	0
	54	0	2	0	0	0	·2	0	0	0	2	0	0	0	2	0	0	0	2	0	0	2	2	0	0	2	3	0	0
1	57	0	2	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0	3	0	0	2	2	0	0
	58	1	2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	1	2	0	1	0	2	0	0
	59	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	2	2	0	1
Controls	34	0	0	0	0	0	2	0	0	0	2	0	0	0	.2	0	0	0	1	0	0	0	3	0	0	2	3	0	0
(Group D)	36	0	0	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	3	0	0	0	3	0	0
	38	0	2	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0	2	0	0	2	3	0	0
	40	0	0	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	2	0	0	2	1	0	0
	43	0	0	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	0	0	0	2	2	0	0	0	3	0	0
1	44	0	1	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	11	0	0	0	1	0	0
	49	0	2	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0	2	0	0	1	3	0	0	2	3	0	11
	51	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0	2	0	0	2	13	1	-
	55	0	2	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0	1	0	1	2	3	0	0
	56	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0	2	0	0	2	2	0	0

Table B. Clinical observations by clinical sign post-challenge.

* C, coughing

N, nasal discharge

R, respiration

D, depression

Table 2. Clinical signs and scoring index.

Clinical Sign	Description	Score
Coughing	normal during observation period of 15 min	0
	coughing once during observation	1
	coughing twice or more during observation	2
Nasal discharge	normal	0
	abnormal, serous	1
	abnormal, mucopurulent	2
	abnormal, profuse	3
Respiration	normal	0
	abnormal (dyspnea, tachypnea)	1
Depression	normal	0
-	depression present	1

[†]Depression was assessed by subjective evaluation of individual animal behavior that included the following: failure to approach food rapidly, general lethargy, inappetence, and anorexia.

:	Study day		18	5			18	6			18	7			18	8			18	9			15	90			19	1	
Day post-	challenge		4	ł			5				6	1	1		7		-		8)			Ş	9			1	0	
Group	Halter No.	ċ	N	R	D	С	N	R	D	С	N	R	D	С	N	R	D	С	N	R	D	C	N	R	D	С	N	R	D
Vaccinates	31	0"	3	0	0	1	1	0	0	1	0	0	0	1	2	0	0	0	1	0	0	1	0	0	0	0	1	0	0
(Group C)	32	2	3	0	0	2	2	0	0	0	3	1	0	0	2	0	0	0	2	0	0	0	2	0	0	0	1	0	0
	33	1	3	0	0	0	3	0	0	2	3	0	0	0	3	0	0	0	3	0	0	2	3	0	0	0	2	0	0.
	35	1	3	0	0	1	3	0	0	1	3	0	0	0	3	0	0	2	3	0	0	0_	3	0	0	0	3	0	0
	37	0	3	0	0	0	2	0	0	1	2	0	0	0	2	0	0	0	2	0	0	0	3	0	0	0	2	0	0
	39	1	3	0	0	0	.3	0	0	0	3	0	0	1	3	0	0	2	3	0	0	0	3	0	0	0	3	0	0
	41	0	3	0	0	0	2	0	0	0	2	0	0	0	3	0	0	0	3	0	0	1	2	0	0	0	2	0	0
1	42	0	2	0	0	1	3	0	0	2	3	0	0	1	3	0	0	2	3	0	0	0	3	0	0	0	3	0	0
	45	2	2	1	0	2	3	1	0	0	3	1	0	0	3	0	0.	1	3	1	0	0	3	0	0	0	2	0	0
	46	0	3	0	0	1	3	0	0	2	3	0	0	2	3	0	0	2	3	0	0	2	3	0	0	2	3	0	0
	47	0	3	0	0	2	2	1	0	2	3	1	0	2	3	0	0	0	3	0	0	2	3	0	0	2	3	0	0
	48	1	2	0	0	1	2	0	0	0	0	0	0	0	2	0	0	0	2	0	0	1	2	0	0	0	0	0	0
	50	0	3	0	0	0	3	0	0	0	3	0	0	0	3	0	0	0	2	0	0	0	3	0	0	0	3	0	0
	52	0	3	0	0	0	0	0	0	0	3	0	0	0	3	0	0	0	2	0	0	1	3	0	0	0	2	0	0
	53	0	0	0	0	0	0	0	0	0	2	0	0	0	3	0.	0	1	3	0	0	0	3	0	0	0	3	0	0
	54	2	3	0	0	2	.3	0	0	2	3	0	0	1	3	0	0	1	3	0	0	0	3	0	0	0	3	0	0
1	57	1	2	0	0	0	2	0	0	0	2	0	0	0	3	0	0	0	3	0	0	1	3	0	0	0	3	0	0
1	58	0	2	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0	0	D	0
	59	2	3	1	1	2	3	1	1	2	2	1	1	2	3	0	0	2	3	0	0	0	3	0	0	0	3	0	0
Controls	34	1	3	0	0	0	3	0	0	1	3	0	0	2	3	0	0	2	3	0	0	1	3	0	0	1.1	3	0	0
(Group D)	36	2	3	0	0	2	3	0	0	2	3	0	0	2	3	0	0	2	3	0	0	0	3	0	0	0	3	0	0
	38	2	3	0	0	2	3	0	0	0	3	0	0	0	3	0	0	0	3	0	0	2	3	0	0	1	3	0	0
	40	0	3	0	0	0	3	0	0	2	2	0	0	0	3	1	1	2	3	0	0	0	3	0	0	0	3	0	0
	43	2	3	1	1	2	3	0	0	1	3	1	1	1	3	1	1	0	3	0	0	0	3	0	0	11	3	0	0
	44	2	3	0	0	0	3	1	0	1	3	0	0	2	3	0	0	2	3	0	0	1	3	10	10	11	3	0	0
	49	2	3	0	1	2	3	0	1	1	3	0	1	0	3	0	0	1	3	0	0	1	3	0	0	10	3	0	0
	51	0	3	0	0	1	3	0	0	1	3	0	0	0	3	0	0	0	3	0	0	0	3	10	10	10	3	10	0
1	55	0	2	0	0	2	3	1	1	2	3	1	1	0	3	Ľ	11	2	3	+	0	1	3	ᆤ	0	10	13	10	0
	56	1	2	0	0	2	3	0	0	2	3	0	1	2	3	1	1	2	3	1	0	2	13	10	0	10	3	10	U

Table B (continued). Clinical observations by clinical sign post-challenge.

* C, coughing

N, nasal discharge

R, respiration

D, depression

Table 2. Clinical signs and scoring index.

Clinical Sign	Description	Score
Coughing	normal during observation period of 15 min	0
	coughing once during observation	1
	coughing twice or more during observation	2
Nasal discharge	normal	0
	abnormal, serous	1
	abnormal, mucopurulent	2
	abnormal, profuse	3
Respiration	normal	0
	abnormal (dyspnea, tachypnea)	1
Depression	normal	0
-	depression present [†]	1

[†]Depression was assessed by subjective evaluation of individual animal behavior that included the following: failure to approach food rapidly, general lethargy, inappetence, and anorexia.

St	udy day	179	182	183	184	185	186	187	188	189	
Days post-cl	allenge	-1	1	2	3	4	5	6	7	8	
Group	Halter No.				Dete	ction of v	irus*				No. days positive per horse
Vaccinates	31	neg**	1.0E+02	1.0E+02	neg	1.8E+02	neg	neg	neg	neg	3
	32	neg	neg	5.6E+02	1.8E+02	3.9E+03	1.8E+02	neg	neg	neg	4
	33	neg	2.5E+05	3.2E+05	3.9E+04	2.3E+03	neg	neg	5.6E+02	neg	5
	35	neg	1.0E+05	2.5E+04	1.8E+03	1.0E+05	neg	neg	neg	neg	4
	37	neg	1.8E+02	3.2E+04	3.9E+02	3.2E+03	neg	neg	neg	neg	4
	39	neg	1.0E+03	3.2E+05	2.9E+03	3.2E+04	3.2E+03	neg	neg	neg	5
	41	neg	5.6E+02	3.2E+04	5.6E+03	1.8E+03	neg	neg	neg	neg	4
	42	neg	4.0E+03	4.4E+04	neg	2.5E+04	neg	neg	neg	neg	3
	45	neg	neg	3.2E+04	6.3E+03	3.2E+03	1.0E+04	1.0E+03	neg	neg	5
	46	neg	neg	1.0E+05	3.2E+05	1.8E+05	4.0E+02	neg	neg	neg	4
	47	neg	3.2E+03	3.2E+05	2.5E+03	2.5E+05	5.0E+02	neg	neg	neg	5
	48	neg	neg	3.2E+03	2.0E+03	1.0E+04	neg	neg	neg	neg	3
	50	neg	3.2E+03	3.9E+04	6.3E+03	5.0E+03	5.6E+03	neg	neg	neg	5
	52	neg	neg	1.0E+05	1.0E+02	3.2E+03	2.5E+02	neg	neg	neg	4
	53	neg	neg	5.6E+04	1.0E+04	3.2E+03	neg	neg	neg	neg	3
	54	neg	5.0E+03	4.0E+04	3.9E+03	5.6E+04	7.4E+03	2.5E+02	neg	neg	6
	57	neg	neg	1.8E+04	2.0E+02	1.0E+03	neg	neg	neg	neg	3
	58	neg	2.5E+02	1.8E+02	neg	3.2E+02	neg	neg	neg	neg	3
	59	neg	2.5E+02	2.5E+05	3.9E+03	3.2E+03	3.2E+02	neg	neg	neg	5
No. horses per da	positive y (of 19)	0	12	19	16	19	9	2	1	0	
Controls	34	neg	3.2E+05	3.2E+05	5.6E+03	3.2E+05	5.6E+03	5.6E+03	ncg	neg	6
	36	neg	5.6E+03	1.8E+05	1.4E+02	3.9E+04	3.2E+03	neg	neg	neg	5
	38	neg	1.0E+05	5.6E+04	1.8E+05	1.0E+04	neg	NT	neg	neg	4
	40	neg	1.8E+02	3.2E+05	3.9E+04	2.5E+04	2.5E+03	neg	1.8E+02	neg	6
	43.	neg	4.0E+03	3.2E+04	3.9E+03	1.0E+04	1.8E+03	1.0E+03	neg	neg	6
	44	neg	neg	1.0E+05	3.2E+05	3.9E+03	NT	2.5E+03	neg	neg	4
	49	neg	1.0E+03	3.2E+05	2.5E+03	3.9E+03	3.2E+03	1.8E+02	neg	neg	6
	51	neg	2.0E+03	2.5E+05	2.3E+03	3.9E+03	5.6E+03	1.0E+03	neg	neg	6
	55	neg	1.8E+02	5.6E+04	2.5E+03	1.0E+04	1.4E+03	2.3E+02	2.5E+02	neg	7
	56	neg	3.2E+02	3.2E+05	3.9E+04	5.6E+03	2.5E+03	2.3E+02	neg	neg	5
No. horses per day (of	positive (10 or 9)	0	9	10	10	10	8	7	2	0	

Table C. Virus shedding post-challenge detected by cell culture.

*Values are in TCID₅₀ units per ml of sample (1.0E+02 corresponds to 1.0 x 10²). **Negative: less than 1.0E+01 (assay detection limit). *Not tested.

Study Type	Safety										
Pertaining to	ALL										
Study Purpose	To demonstrate safety under fiel	d condition	S								
Product Administration	One dose administered intranasa	lly. Four h	orses in Study 2 were								
	given a 2 nd dose intranasally 3 m	onths after	initial vaccination.								
Study Animals	Study 1: 435 horses from 6 state	s. 53 horse	s were 11 months of								
	age or younger at time of vaccin	ation. 11 pr	egnant mares were								
	enrolled. Study 2: 47 horses from	n 3 states. 4	6 horses were 6								
	months of age or younger at time	e of vaccina	ation.								
Challenge Description	Not applicable										
Interval observed after	Horses were observed immediate	ely followir	ng vaccination and								
challenge	then daily for 14 days post-vacci	ination.									
Results	Study 1:										
	Adverse Events	Number									
	Nasal Discharge22Ocular Discharge3Coughing2										
	Nasar Discharge22Ocular Discharge3Coughing2Uttiggeig2										
	Ocular Discharge3Coughing2Urticaria3										
	Coughing2Urticaria3Founder1										
	Coughing2Urticaria3Founder1										
	Swelling	1									
	Fever (>102.0°F)	1									
	Lethal white foal	1									
	Horses with no reaction	407									
	<u>Study 2:</u>	T									
	Adverse Events	Number									
	Nasal Discharge	2									
	Horses with no reaction	45									
USDA Approval Date	September 23, 1999										