

Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	49K5.R1
True Name	Porcine Circovirus Vaccine, Type 2, Killed Baculovirus Vector, Mycoplasma Hyopneumoniae Bacterin
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	FLEXcombo - Boehringer Ingelheim Vetmedica GmbH FLEXcombo - No distributor specified
Date of Compilation Summary	December 02, 2020

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	Porcine Circovirus Vaccine, Type 2	2, Killed Baculoviru	s Vector								
Study Purpose	Demonstration of efficacy										
Product Administration	Single intramuscular administration	of vaccine. ORF2	gene of strain PCV2	a.							
Study Animals	Caesarian-derived, colostrum deprivided into 24 vaccinates and 24 c	ved pigs vaccinated	at 23-25 days of age	e and randomly							
Challenge	All pigs were challenged 14 days fo	ollowing vaccination	n with Porcine Circo	ovirus, Type 2a							
Description	challenge virus.										
Interval observed after challenge	Lymphoid tissues were examined 2	Lymphoid tissues were examined 25 days after challenge.									
Results	Summary of Lymphoid Tissue Efficacy Results										
	Group & Treatment	Lymphoid Depletion +/total (%)	Lymphoid Inflammation +/total (%)	Lymphoid IHC +/total (%)							
	PCV2 Vaccine	3/24 (12.5%)	3/24 (12.5%)	3/24 (12.5%)							
	Control Article	19/24 (79.2%)									
	Raw Data Tables of Positive Lym IHC = Immunohistochemistry MLN = Mesenteric Lymph Node ILN = Iliac Lymph Node TBLN = Tracheobronchial Lymph T Lymphoid Depletion Criteria: Negative (-) = No lymphoid depletin Positive (+) = Lymphoid depletion Lymphoid Inflammation Criteria Negative (-) = No lymphoid inflam Positive (+) = Lymphoid inflam Positive (+) = Lymphoid inflam Positive (+) = PCV2 antigen detector Raw data is presented on the follow	Node Node on present to some degree pres mation present tion to some degree with PCV2 antigen ed in lymphoid cells ving pages.	arameter and Tissu sent present	IE							

USDA Approval Date	June 28, 2007

Vaccinated pigs:

Pig	Lyı	nphoid	Depletic	on	Lym	phoid Iı	nflamma	ation		Lympho	id IHC	
ID	Tonsil	MLN	ILN	TBLN	Tonsil	MLN	ILN	TBLN	Tonsil	MLN	ILN	TBLN
5	-	-	-	-	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-	-	-	-	-	-
23	-	-	-	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	-	-	-	-	-
36	-	-	-	-	-	-	-	-	-	-	-	-
37	-	-	-	+	-	-	+	+	-	-	-	+
38	-	-	-	-	-	-	-	-	-	-	-	-
42	-	-	-	-	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-	-	-	-	-
46	-	-	-	-	-	-	-	-	-	-	-	-
47	-	-	-	-	-	-	-	-	-	-	-	-
50	-	-	+	-	+	+	+	+	+	-	+	-
85	-	-	-	-	-	-	-	-	-	-	-	-
87	-	-	-	-	-	-	-	-	-	-	-	-
88	-	-	-	-	-	-	-	-	-	-	-	-
89	-	-	-	-	-	-	-	-	-	-	-	-
90	-	-	-	-	-	-	-	-	-	-	-	-
91	-	-	-	-	-	-	-	-	-	-	-	-
92	-	+	+	+	+	+	+	+	+	-	-	+
94	-	-	-	-	-	-	-	-	-	-	-	-

Pig	Lym	phoid I	Deplet	ion	Lym	phoid Inf	lammat	ion	Lymphoid IHC			
ID	Tonsil	MLN	ILN	TBLN	Tonsil	MLN	ILN	TBLN	Tonsil	MLN	ILN	TBLN
1	-	-	-	-	-	-	-	-	+	-	-	-
2	-	-	+	-	-	+	+	+	-	+	+	+
4	+	+	+	+	+	+	+	+	+	+	+	+
7	-	-	-	-	-	-	-	-	-	-	-	-
10	-	-	+	-	-	-	+	+	-	-	+	-
11	-	-	-	-	-	-	-	-	-	-	-	-
13	+	+	+	+	+	+	+	+	+	+	+	+
15	-	-	1	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-	-	-	-
19	-	+	+	+	+	+	+	+	-	+	+	+
22	-	-	1	-	-	-	-	-	-	-	-	-
25	-	+	+	+	+	+	+	+	+	+	+	+
26	-	-	-	+	+	-	+	+	-	-	-	+
28	-	-	+	+	-	+	+	+	-	+	+	+
32	+	+	+	+	+	+	+	+	+	+	+	+
33	+	+	+	+	+	+	+	+	-	+	+	+
34	+	+	+	+	+	+	+	+	+	+	+	+
35	-	-	+	+	+	-	+	+	-	-	-	+
39	-	+	+	+	+	+	+	+	+	+	+	+
41	+	+	+	+	+	+	+	+	+	+	+	+
44	-	-	+	+	+	+	+	+	+	-	+	+
45	+	+	+	+	+	+	+	+	+	+	+	+
48	-	-	+	-	-	-	+	+	-	-	+	-
86	-	-	-	-	-	+	-	-	-	-	+	-

Study Type	Efficacy	Efficacy										
Pertaining to	Porcine Circovirus	Vaccine, Type 2	2, Killed Baculov	virus Vector								
Study Purpose	Demonstration of 4	months duratio	n of immunity									
Product Administratio n	Single intramuscula	r administration	n of vaccine. ORI	F2 gene of stra	in PCV2a.							
Study Animals	Caesarian-derived c randomly divided in	Caesarian-derived colostrum deprived pigs vaccinated at 19 – 23 days of age and randomly divided into 24 vaccinates and 24 controls										
Challenge Description	All pigs were challenged 122 days (4months) following vaccination with Porcine Circovirus, Type 2a challenge virus.											
Interval observed after challenge	Lymphoid tissues were examined 25 days after challenge.											
	Summary of Efficacy Results											
	Group & Treatment	Lymphoid Depletion +/total (%)	Lymphoid Inflammation +/total (%)	Lymphoid IHC +/total (%)								
	Group # 1 – PCV2 Vaccine	0/24 (0%)	0/24 (0%)	0/24 (0%)								
	Group # 2 - Control Group	13/24 (54.2%)	20/24 (83.3%)	20/24 (83.3%)								
Results	Group $\# 2 -$ Control Group $13/24$ (54.2%) $20/24$ (83.3%) $20/24$ (83.3%) Observations of Lymphoid Tissue by Parameter and Tissue:IHC = Immunohistochemistry MLN = Mesenteric Lymph NodeILN = Iliac Lymph NodeLymphoid Depletion Criteria:Negative (-) = Normal, no lymphoid depletion present Positive (+) = Mild, moderate or severe depletionLymphoid Inflammation Criteria:Negative (-) = Normal, no lymphoid inflammation Positive (+) = Mild, moderate or severe histiocytic to granulomatous inflammationLymphoid IHC Criteria:Negative (-) = Zero lymphoid cells observed with PCV2 antigen staining Positive (+) = Lymphoid follicles have cells with PCV2 antigen staining Raw data is presented on the following pages.											

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	Lym	phoid I	Deplet	ion	Lymp	hoid In	flamm	ation	Lymphoid IHC			
Pig ID	Tonsil	MLN	ILN	TBLN	Tonsil	MLN	ILM	TBLN	Tonsil	MLN	ILN	TBLN
	Group	1: PCV2	Vacci	ne								
5	-	-	-	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-	-	-	-
15	-	-	-	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-	-	-	-	-
38	-	-	-	-	-	-	-	-	-	-	-	-
39	-	-	-	-	-	-	-	-	-	-	-	-
44	-	-	-	-	-	-	-	-	-	-	-	-
49	-	-	-	-	-	-	-	-	-	-	-	-
56	-	-	-	-	-	-	-	-	-	-	-	-
57	-	-	-	-	-	-	-	-	-	-	-	-
59	-	-	-	-	-	-	-	-	-	-	-	-
66	-	-	-	-	-	-	-	-	-	-	-	-
68	-	-	-	-	-	-	-	-	-	-	-	-
71	-	-	-	-	-	-	-	-	-	-	-	-
80	-	-	-	-	-	-	-	-	-	-	-	-
83	-	-	-	-	-	-	-	-	-	-	-	-
89	-	-	-	-	-	-	-	-	-	-	-	-
99	-	-	-	-	-	-	-	-	-	-	-	-
109	-	-	-	-	-	-	-	-	-	-	-	-
113	-	-	-	-	-	-	-	-	-	-	-	-
114	-	-	-	-	-	-	-	-	-	-	-	-
119	-	-	-	-	-	-	-	-	-	-	-	-

	Lymphoid Depletion				Lymphoid Inflammation				Lymphoid IHC			
Pig ID	Tonsil	MLN	ILN	TBLN	Tonsil	MLN	ILN	TBLN	Tonsil	MLN	ILN	TBLN
	Group 2: Control Group											
1	+	-	+	+	+	+	+	+	+	+	+	+
7	+	-	+	+	+	+	+	+	+	+	+	+
9	-	-	+	-	+	+	+	-	+	-	+	-
13	-	-	-	-	+	-	+	-	-	-	+	-
28	-	-	-	+	+	-	+	+	-	-	-	+
29	-	-	-	-	+	-	-	-	+	-	-	-

31	-	+	+	+	+	+	+	+	+	+	+	+
35	+	+	-	+	+	+	+	+	+	+	+	+
40	+	-	+	+	+	+	+	+	+	+	+	+
41	-	-	-	-	+	+	+	+	+	-	+	+
46	-	-	-	-	-	-	-	-	-	-	-	-
51	+	-	-	-	+	+	-	+	+	+	+	+
60	-	-	+	-	+	+	+	-	+	+	+	-
69	-	-	+	-	+	+	+	-	+	+	+	-
74	-	-	-	+	+	+	-	+	+	-	-	+
75	-	-	-	•	-	-	-	-	-	-	-	-
92	+	-	-	-	+	-	+	+	+	-	-	+
93	-	-	-	-	+	-	-	+	+	-	-	-
98	-	-	-	-	-	-	-	-	-	-	-	-
100	-	-	-	-	+	-	-	-	+	-	-	-
104	-	+	-	-	+	+	+	-	+	+	+	-
110	-	-	-	-	+	-	-	-	+	-	-	-
116	-	-	-	-	+	-	-	-	+	-	-	-
117	-	-	-	-	-	-	-	-	-	-	-	-

Study Type	Efficacy							
Pertaining to	Porcine Circovirus Vaccine, T	ype 2, Killed	l Baculoviru	is Vector				
Study Purpose	Efficacy of Porcine Circovirus	s Vaccine, Ty	/pe 2					
Product Administration	Administration of one dose int	tramuscularly	. Product te	ested				
	contained ORF2 gene of strair	n PCV2a.						
Study Animals	3 week old caesarian derived.	colostrum de	prived pigs.	divided				
	into 24 vaccinates and 24 cont	trols	1 10					
Challenge Description	Challenged with Porcine Circo	ovirus Type 2	2a at 31 days	s after				
F	vaccination							
Interval observed after	Pigs were observed daily for 2	25 days. At 2	5 davs. tissu	es were				
challenge	assessed for lymphoid depletion	on. lymphoid	and lung					
ge	inflammation and immunohist	ochemistry (IHC)					
Results	Summary of Results:)					
	Tissues were assessed for lym	nhoid denleti	ion lympho	id and				
	lung inflammation and immu	nohistochemi	istry (IHC) f	for both				
	lymphoid and lung tissue			or com				
	Tymphote and rang ussue.							
	An animal was considered nos	sitive for lym	nhoid denle	tion				
	lymphoid inflammation or lymphoid	nnhoid IHC	if depletion	tion,				
	inflammation or PCV2 antique	n respective	ly were pre	cont in				
	tongil tiggue magentaria lump	h nodo (MIN	D tiggue ilia	sont m				
	rodo (II N) tiggue or trachach	n node (MLN	"haid (TDI					
	node (ILN) ussue, of tracheob	ronemai tym		iv) tissue.				
	An animal was considered nos	vitivo for lun	inflommati	ion if				
	All allinar was considered pos		t and Lyna l					
	nicroscopic lung inflammatio	n was presen	t and Lung	INC				
	positive if FC v2 antigen was		ing cens.					
	Tissues	Vaccinates	Controls					
	Lymphoid depletion (LyD)	0/24	20/24					
	Lymphoid inflammation (LyI)	1/24	21/24					
	Lung Inflammation	3/24	18/24					
	Lymphoid IHC	2/24	22/24					
	Lung IHC	0/24	14/24					
	Any pig: (LyD or Lyl)	2/24	22/24					
		£. 1 (
	See tables on the following pa	ges for data.						
USDA Approval Date	June 5, 2008							

Individual Lymphoid Depletion

ID - - - 22 - - - - 23 - - - - 26 - - - - 29 - - - - 31 - - - - 32 - - - - 34 - - - - 39 - - - - 43 - - - - 44 - - - - 45 - - - - 45 - - - - 45 - - - - 45 - - - - 53 - - - - 60 - - - - 72 - - - -	Group	Animal	Tonsil	MLN	ILN	TBLN
22 - - - - 23 - - - - 26 - - - - 29 - - - - 31 - - - - 34 - - - - 39 - - - - 43 - - - - 43 - - - - 44 - - - - - 45 - - - - - 47 - - - - - 51 - - - - - 52 - - - - - 72 - - - - - 74 - - - - - 74 - -	- · · r	ID				
Vaccinates		22	-	-	-	-
26 - - - 29 - - - 31 - - - 32 - - - 34 - - - 39 - - - 43 - - - 44 - - - 45 - - - 45 - - - 45 - - - 45 - - - 45 - - - 45 - - - 45 - - - 45 - - - 51 - - - 57 - - - 62 - - - 74 - - - 74 - - - 88 - - - 95 - - -		23	-	-	-	-
Vaccinates (24) 29 $ 31$ $ 34$ $ 39$ $ 43$ $ 43$ $ 43$ $ 44$ $ 45$ $ 47$ $ 51$ $ 57$ $ 62$ $ 74$ $ 74$ $ 87$ $ 88$ $ 88$ $ 88$ $ 40$ $ 41$ $+$ $ 41$ $+$ $ 41$ $+$ $ 41$ $+$ $ 55$ $+$ $+$ $+$ 66 $ 58$ $ 58$ $ 64$ $ +$ $+$ 75 $+$ $+$ $+$ 75 $+$ $+$ $+$ 77 $+$ $+$ $+$ 77 $+$ $+$ $+$ 77 $ 77$ $ -$ <		26	-	-	-	-
31 - - - 32 - - - 34 - - - 39 - - - 43 - - - 43 - - - 44 - - - 45 - - - 45 - - - 45 - - - 45 - - - 45 - - - 45 - - - 51 - - - 53 - - - 67 - - - 67 - - - 74 - - - 74 - - - 74 - - - 74 - - - 74 <td></td> <td>29</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td>		29	-	-	-	-
32 - - - 34 - - - 39 - - - 43 - - - 44 - - - 44 - - - 45 - - - 45 - - - 47 - - - 45 - - - 47 - - - 51 - - - 57 - - - 62 - - - 67 - - - 72 - - - 74 - - - 82 - - - 84 + + + 95 - - - 95 - - - 10 + + + 38 - - -		31	-	-	-	-
34 - - - 39 - - - 43 - - - 44 - - - 45 - - - 47 - - - 47 - - - 47 - - - 51 - - - 53 - - - 62 - - - 67 - - - 69 - - - 74 - - - 74 - - - 74 - - - 74 - - - 74 - - - 74 - - - 74 - - - 95 - - - 95 - - - 95 - - -		32	-	-	-	-
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Vaccinates (24) 43 $ 44$ $ 45$ $ 47$ $ 51$ $ 53$ $ 57$ $ 62$ $ 67$ $ 69$ $ 72$ $ 74$ $ 82$ $ 74$ $ 88$ $ 88$ $ 95$ $ 88$ $ 74$ $ 88$ $ 74$ $ 88$ $ 74$ $ 88$ $ 88$ $ 88$ $ 95$ $ 40$ $ 40$ $ 58$ $ 64$ $ +$ 77 $+$ $+$ 77 $+$ $+$ 78 $+$ $+$ 79 $+$ $+$ 79 $+$ $+$ 79 $+$ $+$ 77 $+$ $+$ <t< td=""><td></td><td>39</td><td>-</td><td>-</td><td>-</td><td>-</td></t<>		39	-	-	-	-
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Vaccinates (24) 45 $ 51$ $ 53$ $ 57$ $ 62$ $ 67$ $ 69$ $ 72$ $ 74$ $ 87$ $ 87$ $ 88$ $ 87$ $ 88$ $ 88$ $ 88$ $ 88$ $ 88$ $ 95$ $ 28$ $+$ $+$ 44 $ 40$ $ 40$ $ 41$ $+$ $ 42$ $ +$ 44 $ 41$ $+$ $ 41$ $+$ $ 55$ $+$ $+$ 66 $ 57$ $+$ $+$ 77 $+$ $+$ 77 $+$ $+$ 78 $+$ $+$ 77 $+$ $+$ 78 $+$ $+$ 79 $+$ $+$ 79 $+$ $+$ 80 $+$ $+$ 79 $+$ $+$ 79 $+$ $+$ 79 $+$ $+$ 79 $-$		44	-	-	-	-
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Controls (24) $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Vaccinates	47	-	-	-	-
53 - - - - 57 - - - - 62 - - - - 67 - - - - 69 - - - - 72 - - - - 74 - - - - 74 - - - - 74 - - - - 74 - - - - 87 - - - - 87 - - - - 87 - - - - 88 - - - - 95 - - - - 30 + + + + 36 * + + + 40 - - - - 55 + + + +	(24)	51	-	-	-	-
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$Controls (24) \begin{array}{c cccccccccccccccccccccccccccccccc$		82	-	-	-	-
88 - - - - 95 - - - - 28 + + + + 30 + + + + 36 * + + + 36 * + + + 36 * + + + 38 - - - - 40 - - - - 41 + - - - 42 - + + + 42 - + + + 44 - - - - 44 - - - - - 55 + + + + + 56 - + - - - 61 - + + + +		87	-	-	-	-
95 $ 28$ $+$ $+$ $+$ $+$ 30 $+$ $+$ $+$ $+$ 36 $*$ $+$ $+$ $+$ 36 $*$ $+$ $+$ $+$ 36 $*$ $+$ $+$ $+$ 38 $ 40$ $ 41$ $+$ $ 41$ $+$ $ 41$ $+$ $ 41$ $+$ $ 42$ $ +$ $+$ $+$ 46 $ 58$ $ 61$ $ +$ $+$ $+$ 71 $-$		88	-	-	-	-
Controls (24) 28 ++++ 30 ++++ 36 *+++ 36 *+++ 38 40 41 ++ 42 -+++ 46 55 ++++ 56 -+ 58 58 60 + 64 -+++ 71 + 75 ++++ 77 ++++ 78 ++++ 79 ++++ 80 ++++ 81 ++++ 86 94		95	-	-	-	-
30 + + + + + 36 * + + + + 38 - - - - 40 - - - - 41 + - - + 41 + - - + 41 + - - + 42 - + + + 46 - - - - 55 + + + + 56 - + - - 58 - - - - 58 - - - - 58 - - - - 61 - + + + 64 - + + + 75 + + + + 78 + + + + 79 + +		28	+	+	+	+
36 * + + + + 38 - - - - 40 - - - - 41 + - - + 42 - + + + 42 - + + + 46 - - - - 55 + + + + 56 - + + + 56 - + - - 58 - - - - 58 - - - - 58 - - - - 60 - - - + 61 - + + + 71 - - - + 75 + + + + 79 + + + + 79 + + +		30	+	+	+	+
38 - - - - 40 - - - - 41 + - - + 42 - + + + 46 - - - - 55 + + + + 46 - - - - 55 + + + + 56 - + + - 58 - - - - 58 - - - - 58 - - - - 58 - - - - 60 - - - - 64 - + + + 71 - - - + 75 + + + + 77 + + + + 79 + + + +		36	*	+	+	+
40 - - - - 41 + - - + 42 - + + + 46 - - - - 55 + + + + 56 - + + + 56 - + - - 58 - - - - 58 - - - - 58 - - - - 60 - - - - 64 - + + + 71 - - - + 75 + + + + 75 + + + + 78 + + + + 79 + + + + 80 + + + + 86 - - - + 94 -		38	-	-	-	-
41++ 42 -+++ 46 55 ++++ 56 -+ 58 58 60 61 -++ 64 -++ 71 75 +++ 77 +++ 78 +++ 79 +++ 80 +++ 81 +++ 86 94		40	-	-	-	-
42 - + + + 46 - - - - 55 + + + + 56 - + - - 58 - - - - 60 - - - + 61 - + + + 64 - + + + 65 + + + + 71 - - - + 75 + + + + 77 + + + + 78 + + + + 79 + + + + 80 + + + + 81 + + + + 94 - - - +		41	+	-	-	+
46 - - - - 55 + + + + + 56 - + - - - 58 - - - - - 58 - - - - - 60 - - - + + 61 - + + + + 64 - + + + + 65 + + + + + 71 - - - + + 75 + + + + + 78 + + + + + 79 + + + + + 80 + + + + + 86 - - - + + 94 - - - + +		42	-	+	+	+
55 + + + + + 56 - + - - 58 - - - - 60 - - - + 61 - + - - 64 - + + + 65 + + + + 71 - - - + 75 + + + + 77 + + + + 78 + + + + 79 + + + + 80 + + + + 81 + + + + 86 - - - + 94 - - - +		46	-	-	-	-
56 $ +$ $ 58$ $ 60$ $ +$ 61 $ +$ $ 64$ $ +$ $+$ $+$ 65 $+$ $+$ $+$ $+$ 71 $ +$ 75 $+$ $+$ $+$ 77 $+$ $+$ $+$ 78 $+$ $+$ $+$ 79 $+$ $+$ $+$ 80 $+$ $+$ $+$ 81 $+$ $+$ $+$ 86 $ +$ 94 $ +$		55	+	+	+	+
Solution Solutity is a solity is a solity is a solution Solution		56	-	+	-	-
Controls (24) 60 $ +$ $+$ $ 61$ $ +$ $+$ $ 64$ $ +$ $+$ $+$ $+$ 65 $+$ $+$ $+$ $+$ 71 $ +$ 75 $+$ $+$ $+$ $+$ 75 $+$ $+$ $+$ $+$ 77 $+$ $+$ $+$ $+$ 78 $+$ $+$ $+$ $+$ 78 $+$ $+$ $+$ $+$ 79 $+$ $+$ $+$ $+$ 80 $+$ $+$ $+$ $+$ 81 $+$ $+$ $+$ $+$ 86 $ +$ 94 $ +$		58	-	-	-	-
$(24) \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Controls	60	-	-	-	+
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	(24)	61	-	+	-	-
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$		64	-	+	+	+
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$		65	+	+	+	+
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$		71	_	-	-	+
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		75	+	+	+	+
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		77	+	+	+	+
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$		78	+	+	+	+
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		79	+	+	+	+
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		80	+	+	+	+
		81	+	+	+	+
94 +		86	_	-	-	+
		94	-	-	-	+

(+) = positive (-) = negative (*)=missing tissue

mar i auar By mphora innannauon

Group	Animal ID	Tonsil	MLN	ILN	TBLN
	22	-	-	-	-
	23	-	-	-	-
	26	-	-	-	-
	29	-	-	-	-
	31	-	-	-	-
	32	-	-	-	-
	34	-	-	-	-
	39	-	-	-	-
	43	-	-	-	-
	44	-	-	-	-
	45	-	-	-	-
Vaccinates	47	-	-	-	-
(24)	51	-	-	-	+
	53	-	-	-	-
	57	-	-	-	-
	62	-	-	-	-
	67	-	-	-	-
	69	-	-	-	-
	72	-	-	-	-
	74	-	-	-	-
	82	-	-	-	-
	87	-	-	-	-
	88	-	-	-	-
	95	-	-	-	-
	28	+	+	+	+
	30	+	+	+	+
	36	*	+	+	+
	38	-	-	-	-
	40	-	-	-	-
	41	+	+	+	+
	42	+	+	+	+
	46	+	-	+	-
	55	+	+	+	+
	56	+	+	+	+
	58	-	-	-	-
Controls	60	-	-	+	+
(24)	61	+	+	+	-
	64	+	+	+	+
	65	+	+	+	+
	71	+	_	+	+
	75	+	+	+	+
	77	+	+	+	+
	78	+	+	+	+
	79	+	+	+	+
	80	+	+	+	+
	81	+	+	+	+
	86	+	_	+	+
	94	+	-	+	+

(+) = positive

(-) = negative

(*)=missing tissue

Individual Lymphoid IHC Results

Group	Animal	Tonsil	MLN	ILN	TBLN
-	ID				
	22	-	-	-	-
	23	-	-	-	-
	26	-	-	-	-
	29	-	-	-	-
	31	-	-	-	-
	32	-	-	-	-
	34	-	-	-	-
	39	+	+	-	-
	43	-	-	-	-
	44	-	-	-	-
	45	-	-	-	-
Vaccinates	47	-	-	-	-
(24)	51	-	-	-	+
	53	-	-	-	-
	57	-	-	-	-
	62	-	-	-	-
	67	-	-	-	-
	69	-	-	-	-
	72	-	-	-	-
	74	-	-	-	-
	82	-	-	-	-
	87	-	-	-	-
	88	-	-	-	-
	95	-	-	-	-
	28	+	+	+	+
	30	+	+	+	+
	36	*	+	+	+
	38	-	-	-	-
	40	-	+	-	-
	41	+	+	+	+
	42	+	+	+	+
	46	+	-	+	-
	55	+	+	+	+
	56	+	+	+	-
	58	-	-	-	-
Controls	60	-	-	-	+
(24)	61	+	+	+	-
	64	+	+	+	+
	65	+	+	+	+
	71	+	-	+	+
	75	+	+	+	+
	77	+	+	+	+
	78	+	+	+	+
	79	+	+	+	+
	80	+	+	+	+
	81	+	+	+	+
	86	+	-	+	+
	94	+	-	+	+

(+) = positive (-) = negative (*)=missing tissue

Group	Animal ID	Lung Inflammation Result
	22	-
	23	-
	26	_
	29	_
	31	-
	32	_
	34	-
	39	+
	43	-
	44	_
	45	_
Vaccinates	47	_
(24)	51	+
()	53	+
	57	-
	62	-
	67	_
	69	_
	72	_
	74	_
	82	_
	87	_
	88	_
	95	_
	28	+
	30	+
	36	+
	38	_
	40	_
	41	+
	42	+
	46	
	55	+
	56	+
	58	-
Controls	60	+
(24)	61	-
(2.)	64	+
	65	+
	71	+
	75	+
	77	+
	78	+
	70	+
	80	+
	<u> </u>	+
	01	1
	86	

Individual Lung Inflammation Results

(+) = positive (-) = negative

Individual Lung IHC Results

Group	Animal	Lung IHC Result
Group	ID	Lung me Kesuk
	22	
	22	-
	25	-
	20	-
	29	-
	31	-
	32	-
	34	-
	39	-
	43	-
	44	-
	45	-
Vaccinates	47	-
(24)	51	-
	53	_
	57	_
	62	-
	67	-
	69	
	72	_
	74	
	82	
	87	-
	0/	-
	88	-
	95	-
	28	+
	30	+
	36	+
	38	-
	40	-
	41	+
	42	+
	46	+
	55	+
	56	-
	58	_
Controls	60	+
(24)	61	-
()	64	-
	65	+
	71	-
	75	+
	77	+
	70	Г
	/ 0	+
	/9	+
	80	-
	81	+
	86	-
1	94	-

(+) = positive (-) = negative

Study Type	Efficacy	Efficacy						
Pertaining to	Mycoplasma	Нуропеи	moniae					
Study Purpose	Efficacy of N	Efficacy of Mycoplasma Hyopneumoniae Bacterin						
Product Administration	Administratio	Administration of one dose intramuscularly						
Study Animals	Pigs 3 weeks	Pigs 3 weeks of age, divided into 19 vaccinates and 20 controls						
Challenge Description	Challenged w vaccination	Challenged with <i>Mycoplasma hyopneumoniae</i> 33 days post vaccination						
Interval observed after	Pigs were observed for 28 days. Lungs were examined for lung							
chanenge	post challenge.							
Results	Summary of Results: Lung lesions were evaluated visually and by palpation for each pig to determine the percent pathology for each lung lobe. The following is a summary of statistics for Total Lung Lesion scores (%) results:							
	Treatment	Min	Q1	Median	Q3	Max		
	Vaccinates	0	0	2	6	16		
	Controls 0 7 12 17 50							
USDA Annroval Data	See tables on the following pages for data.							

Individual Lung Lesion Second	cores in Vaccinates (19):
Pig ID	Total Lung Score*
516	0.00
517	0.10
522	0.40
529	0.20
535	1.40
538	5.50
547	0.00
551	2.70
555	14.25
571	4.60
712	9.95
714	1.10
716	0.20
717	1.50
719	8.50
735	16.00
736	6.05
864	0.20
866	1.50

Individual Lung Lesion Sco	ores in Controls (20):
Pig ID	Total Lung Score*
519	8.00
525	4.95
526	11.95
534	0.00
540	17.00
546	2.00
549	50.25
554	20.00
556	9.25
562	25.50
563	12.45
576	10.50
709	6.25
711	13.20
715	17.25
724	5.00
723	29.50
732	NA**
734	17.50
876	10.50

***Total Lung Score** = Sum of scores for all lung lobes **Animal died on Study day 33. No necropsy was performed.

Study Type	Efficacy								
Pertaining to	Mycoplasma	Нуропеито	niae						
Study Purpose	To demonstra	ate efficacy of	of the Mycop	olasma Hy	poneumonic	ie			
	component o	component of the combination package product							
Product	Administratio	on of one do	se intramusc	cularly					
Administration									
Study Animals	40 pigs, 24-2	40 pigs, 24-25 days old divided into 20 vaccinates and 20 controls							
Challenge	Challenged w	with virulent	Mycoplasma	а Нуропеі	umoniae 35 o	days after			
Description	vaccination								
Interval observed	Pigs were observed for 28 days after challenge, and then tissues were								
after challenge	examined for lung lesions								
Results	Summary of	Results:							
	Lungs were e	examined an	d scored for	percent lu	ng patholog	у.			
		•				·			
	Group	Minimum	25 th	Median	75 th	Maximum			
			percentile		percentile				
	Vaccinates	<1	1	4	11	35			
	Controls	<1	7	15	20	30			
	See tables on	the following	ng pages for	data.					
USDA Approval	August 10, 20	006							
Date									

10#	R.	R.	R.	L.	L.	L.	Intermedicto	Total
ID#	Apical	Cardiac	Diaphragmatic	Apical	Cardiac	Diaphragmatic	Intermediate	Total
184	0.0	0.2	0.0	0.0	0.2	0.0	0.0	0.4
187	0.0	0.5	0.25	0.0	1.0	0.25	0.1	2.1
188	0.0	1.0	0.25	0.0	2.0	0.0	0.0	3.25
189	0.0	5.0	0.25	0.0	2.0	0.5	0.5	8.25
193	4.0	7.0	2.5	4.0	7.0	1.25	9.0	34.75
194	0.0	0.1	0.25	0.0	0.2	0.25	0.0	0.8
195	0.5	2.0	1.25	0.1	4.0	0.0	5.0	12.85
200	0.1	0.2	0.0	0.0	0.1	0.0	0.0	0.4
201	1.0	3.0	0.5	0.0	3.0	0.5	8.0	16.0
202	0.5	3.0	0.0	0.0	2.0	0.0	0.0	5.5
217	0.5	3.0	0.5	0.0	3.0	0.0	3.0	10.0
218								
219	0.0	3.0	1.25	0.0	2.0	0.5	0.2	6.95
220	0.0	3.0	1.25	0.0	2.0	0.5	0.2	14.95
222	0.2	2.0	0.25	0.0	1.0	0.25	0.5	4.2
223	0.1	0.5	0.0	0.0	0.0	0.0	1.0	1.6
224	0.1	0.2	0.5	0.1	1.0	0.25	1.0	3.15
226	0.0	0.2	0.0	0.0	1.0	0.0	0.0	1.2
227	0.5	5.0	0.0	1.0	7.0	0.0	0.0	13.5
228	0.0	0.2	0.0	0.0	1.0	0.0	0.0	1.2

Individual Pig Lung Lesion Scoes (%) in Vaccinates

. = no data

ID#	R.	R.	R.	L.	L.	L.	Intermediate	Total
ID#	Apical	Cardiac	Diaphragmatic	Apical	Cardiac	Diaphragmatic	Intermediate	Total
181	2.0	6.0	2.5	0.5	5.0	2.5	7.0	25.5
182	0.0	1.0	0.0	0.2	0.5	0.0	5.0	6.7
183	0.1	0.5	0.5	0.1	2.0	0.5	0.2	3.9
185	0.5	4.0	1.25	0.5	5.0	2.5	6.0	19.75
186	0.1	1.0	0.25	0.0	6.0	0.25	0.5	8.1
191	0.0	0.1	0.0	0.0	0.5	0.0	0.0	0.6
192	1.0	7.0	1.25	0.2	7.0	0.0	4.0	20.45
196								•
198	0.0	1.0	1.25	0.1	7.0	0.25	8.0	17.6
204	0.2	2.0	0.25	0.2	2.0	0.0	1.0	5.65
205	0.2	3.0	0.0	0.1	1.0	0.0	3.0	7.3
207	0.2	5.0	0.5	0.2	5.0	0.5	3.0	14.4
211	1.0	5.0	1.25	1.0	6.0	0.5	4.0	18.75
212	0.2	6.0	1.25	0.1	5.0	0.25	7.0	19.8
215	1.0	3.0	1.25	0.1	4.0	0.5	5.0	14.85
225	0.1	1.0	0.25	0.0	2.0	0.5	0.1	3.95
230	0.2	4.0	0.5	0.1	3.0	0.25	2.0	10.05
231	0.0	3.0	0.5	3.0	6.0	1.25	1.0	14.75
232	1.0	8.0	1.25	1.0	8.0	1.25	9.0	29.5
233	2.0	6.0	1.25	2.0	7.0	0.25	3.0	21.5

Individual Pig Lung Lesion Scoes (%) in Controls

. = no data

Study Type	Efficacy				
Pertaining to	Mycoplasma Hyponeumoniae				
Study Purpose	Demonstration of a 26 week Duration of Immunity				
Product Administration	Administration of one dose intramuscularly				
Study Animals	Pigs approximately 3 weeks of age, divided into 20 vaccinates and 20 controls				
Challenge Description	Challenged with <i>Mycoplasma hyopneumoniae</i> 184 days post vaccination				
Interval observed after challenge	Pigs were observed for 33 days post-challenge for clinical signs of <i>Mycoplasma hyopneumoniae</i> infection and then tissues were examined for lung lesions consistent with <i>Mycoplasma</i> <i>hyopneumoniae</i> infection.				
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.				
USDA Approval Date	August 7, 2006				

Study Type	Safety							
Pertaining to	All fractions							
Study Purpose	To demonstrate safety of the product under field conditions							
Product Administration	Administration of one dose intramuscularly							
Study Animals	1349 nigs 18-25 days of age at three different geographical							
Study Annais	locations divided in	193 0 10 6'	1 age, 72 vac	cinates	and 67	$\frac{17}{2}$ contr	als	ui
	locations divided into 672 vaccinates and 677 controls							
Challenge Decemintion	Not Applicable							
Chanenge Description			£	1	1	<u> </u>		
Interval observed after	Animals were observed for at least 2 hours after vaccination and							
challenge	then daily for 14 days after vaccination							
Results	Results Summary:							
	No injection site reactions were observed.							
	The number of pigs by site with specific clinical observations							
	post-vaccination are presented in the following table:							
	Clinical ObservationSite 1Site 2Site 3					e 3		
			Vac.	Cont.	Vac.	Cont.	Vac.	Cont.
	Cough		1	1	0	0	0	0
	Gaunt	.1	4	1	0	0	2	0
	Lacking vigor / growt	rth	1	2	0	0	0	0
	Red anus Red aars		0	1	0	0	0	0
	Swollen joint/foot /le	eσ	0	1	2	0	2	2
	Inflamed umbilicus	5	3	0	0	0	0	0
	Greasy pig disease		0	0	0	0	8	14
	Pneumonia		0	0	0	0	3	0
	Scours		0	0	0	0	18	15
	Streptococcus infectio	on	0	0	0	0	1	0
	Lame		0	0	1	0	2	5
	Additional observations were affirmed by licensee to be due to							
	causes other than vaccination.							
	Vac. is vaccinate; Cont. is control.							
	I ne total number of animals exhibiting clinical signs for at least							
	one day at an three	sites	are as $1 \leq 1 $		vs:	Dama	n4	
		nnica resent	i signs t		al Absent	Cline	al Signe	
	Vaccinates 48	3	•	624	ADJUIT	7%	ai oigno	
	Controls 43	3		634	634 6%			
						1		
USDA Annroval Date	June 18, 2009							

Study Type	Safety						
Pertaining to	All						
Study Purpose	To demonstrate safety under field conditions						
Product Administration	Single intramuscular administration						
Study Animals	1355 pigs at 10 - 30 days of age, (≥200 pigs from each of three						
	different geographical locations were vaccinated, and a similar						
	number at each site were not vaccinated for comparison)						
Challenge Description	Not applicable						
Interval observed after	Pigs were observed immediately following vaccination and then						
challenge	for 14 days following vaccination. No challenge was conducted.						
Results	Observations of Vaccinated Pigs:						
	Clinical Observation ^a	MO Site N=244	NE Site N=229	IN Site N=207			
	None ^b	241	210	193			
	Poor Condition ^c	0	15	0			
	Dead ^d	3	2	3			
	Scours	0	1	10			
	Lame	0	1	0			
	Swollen Joint(s)	2	0	0			
	Cough	0	0	1			
	Skin Abnormalities ^e	0	1	1			
	 ^a Pigs may have exhibited more than one clinical observation. ^b For an observation of "None" a pig had to be without clinical observations for the entire 14 days of the study. ^c Observations of "Poor Condition" included: thin starve, small thin, small, gaunt, gaunt weak, and thin. ^d Observation of "Dead" included: Dead, Died, and Euthanized Observation of "Skin Abnormalities" included: scabbed knee and skin spots 						

	Observations of Control Pigs:					
	Clinical Observation ^a	MO Site N=241	NE Site N=228	IN Site N=206		
	None ^b	237	209	195		
	Poor Condition ^c	0	13	0		
	Dead ^d	4	2	1		
	Scours	0	0	9		
	Lame ^e	0	3	1		
	Swollen Joint(s)	2	0	0		
	Hernia ^f	0	2	0		
	 ^a Pigs may have exhibited more than one clinical observation. ^b For an observation of "None" a pig had to be without clinical observations for the entire 14 days of the study. ^c Observations of "Poor Condition" included: thin, gaunt, gaunt/weak, and gaunt-purple ears. ^d Observation of "Dead" included: dead, died, and euthanized. ^e Observation of "Lame" included: lame, sore right front foot, a shoulder ^f Observation of "Hernia" included: hernia and surgery. 					
USDA Approval Date	April 5, 2006					