Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	1J81.R0
True Name	Bursal Disease-Infectious Laryngotracheitis-Marek's Disease Vaccine, Serotype 3, Live Marek's Disease Vector
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	
Date of Compilation Summary	September 21, 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	Infectious Bursal Disease Virus (IBD), standard
Study Purpose	Demonstrate efficacy against standard bursal disease
Product Administration	One dose administered *in ovo* at 18-19 days of embryonation
Study Animals	SPF eggs divided into 2 groups Group 1 vaccinated with product and challenged Group 4 sham vaccinated and challenged (control)
Challenge Description	IBDV standard challenge administered at 31 days post vaccination
Interval observed after challenge	Observed daily for 4 days and then examined for gross bursal lesions.
Results	Vaccinates and controls were evaluated in terms of Bursal Disease grossly observable lesions per the criteria in 9 CFR 113.331(c). Birds with gross observable lesions: Group 1: 1/30 Group 4: 28/30 Requirements of 9 CFR 113.331(c) were met Raw data on attached page
USDA Approval Date	November 14, 2018

Raw data shown below for birds classified as positive. All other birds normal.

Group/Bird	Peri-Bursal Edema	Edema	Macroscopic Hemorrhage	Other Gross Lesions	COMMENTS
1/1	X			X	Atrophy
4/1		X		X	Necrosis
4/2		X		X	Necrosis
4/3	X				
4/4	X				
4/5	X				
4/6		X			
4/7	X			X	Necrosis
4/8	X		X	X	Necrosis
4/9	X			X	Necrosis
4/10	X	X			
4/11	X				
4/12	X				
4/13	X				
4/14	X				
4/15	X				
4/16			X	X	Necrosis
4/17	X	X			
4/18	X				
4/19			X	X	Necrosis
4/20		X			
4/21		X			
4/22		X		X	Necrosis
4/23	X				
4/24	X				
4/25	X			X	Atrophy
4/26			X	X	Necrosis
4/27	X				
4/28		X			

Study Type	Efficacy
Pertaining to	Infectious Bursal Disease Virus (IBD), standard
Study Purpose	Demonstrate efficacy against standard bursal disease
Product Administration	One dose administered subcutaneous route in day-old chicks
Study Animals	SPF day-old chicks divided into 2 groups Group 1 vaccinated with product and challenged Group 4 sham vaccinated and challenged (control)
Challenge Description	IBDV standard challenge administered at 28 days post vaccination
Interval observed after challenge	Observed daily for 4 days and then examined for gross bursal lesions.
Results	Vaccinates and controls were evaluated in terms of Bursal Disease grossly observable lesions per the criteria in 9 CFR 113.331(c). Birds with gross observable lesions: Group 1: 1/30 Group 4: 30/30 Requirements of 9 CFR 113.331(c) were met Raw data on attached page
USDA Approval Date	January 29, 2019

Raw data shown below for birds classified as positive. All other birds normal.

Group/Bird	Peri-Bursal Edema	Edema	Macroscopic Hemorrhage	Other Gross Lesions	COMMENTS
1/1		X			
4/1	X				
4/2	X				
4/3	X				
4/4	X				
4/5		X			Dead
4/6		X			
4/7	X				
4/8		X			Dead
4/9	X				
4/10		X			Dead
4/11	X				
4/12		X			
4/13	X				
4/14	X				
4/15		X		X	Depressed, Atrophy
4/16	X			X	Necrosis
4/17	X				
4/18	X				
4/19		X			
4/20		X			Depressed
4/21		X			Dead
4/22	X				
4/23	X				
4/24		X			
4/25	X				
4/26	X				
4/27	X				Depressed
4/28	X				
4/29		X	X		Dead
4/30		X			Dead

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Infectious Bursal Disease Virus (IBD), Variant E</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against IBD, Variant E</td></tr>
<tr><td>Product Administration</td><td>One dose administered in ovo at 18-19 days of embryonation</td></tr>
<tr><td>Study Animals</td><td>SPF day-old chicks divided into 3 groups, with 30 chicks per group

Group 1 vaccinated, challenged
Group 2 placebo-vaccinated, challenged (positive control)
Group 3 placebo-vaccinated, not challenged (negative control)</td></tr>
<tr><td>Challenge Description</td><td>IBDV Variant E challenge administered at 31 days post vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for 11 days and then euthanized. Body weight and bursal weight were recorded. Sex of birds was recorded.</td></tr>
<tr><td>Results</td><td>The body weight and bursal weight were collected and B/B weight ratio (bursa weight/body weight ratio) was calculated for each bird.

<table>
<tr><td>Group</td><td># birds</td><td>Min</td><td>Q1</td><td>Med</td><td>Q3</td><td>Max</td></tr>
<tr><td>1</td><td>30</td><td>0.09</td><td>0.36</td><td>0.58</td><td>0.69</td><td>0.93</td></tr>
<tr><td>2</td><td>30</td><td>0.09</td><td>0.11</td><td>0.14</td><td>0.16</td><td>0.20</td></tr>
<tr><td>3</td><td>30</td><td>0.25</td><td>0.53</td><td>0.65</td><td>0.76</td><td>0.94</td></tr>
</table>

Min is minimum
Q is quartile
Med is median
Max is maximum

Raw data on attached page</td></tr>
<tr><td>USDA Approval Date</td><td>January 28, 2020</td></tr>
</table>

Group	ID	Sex (M=male, F=female)	Body weight (g)	Bursal Weight (g)
1	706	M	542	3.36
1	709	M	555	3.51
1	710	F	462	1.23
1	719	M	615	3.64
1	724	M	505	3.09
1	725	F	438	1.93
1	726	M	467	3.19
1	727	M	561	2.70
1	729	F	477	0.93
1	737	F	441	3.17
1	739	M	571	2.78
1	742	M	572	0.49
1	745	F	465	1.65
1	748	F	479	3.97
1	756	F	424	0.47
1	758	F	419	1.44
1	759	F	445	2.78
1	762	M	532	1.32
1	763	M	557	3.21
1	764	M	563	4.40
1	765	M	519	3.76
1	766	F	496	2.51
1	771	M	607	4.19
1	776	F	480	1.49
1	778	F	466	3.03
1	780	F	428	2.15
1	786	F	451	1.71
1	788	M	593	4.15
1	793	M	457	3.61
1	795	M	569	5.28
2	712	F	397	0.41
2	713	F	460	0.79
2	715	M	521	0.85
2	717	F	431	0.45
2	718	M	537	0.76
2	720	M	415	0.60
2	721	F	394	0.60
2	723	F	376	0.57
2	731	M	561	0.51

2	734	M	491	0.75
2	735	F	398	0.62
2	736	F	368	0.56
2	746	F	399	0.50
2	750	M	517	0.72
2	751	F	493	0.48
2	753	M	546	0.77
2	754	F	431	0.46
2	755	F	451	0.45
2	760	M	544	0.80
2	767	M	529	0.91
2	769	M	587	1.17
2	774	M	466	0.61
2	777	M	478	0.97
2	779	F	437	0.76
2	783	F	427	0.48
2	784	F	393	0.38
2	789	F	373	0.43
2	790	F	385	0.49
2	792	M	486	0.89
2	794	F	371	0.37
3	707	F	380	2.08
3	708	M	527	3.10
3	711	M	526	2.98
3	714	F	453	2.26
3	716	F	414	2.76
3	722	F	465	4.39
3	728	F	463	3.39
3	730	M	612	1.79
3	732	M	530	4.37
3	733	F	493	3.36
3	738	F	474	3.81
3	740	M	465	3.32
3	741	M	527	3.14
3	743	F	481	3.79
3	744	F	451	2.90
3	747	F	475	2.21
3	749	M	604	2.09
3	752	F	461	4.12
3	757	M	484	3.25
3	761	F	428	2.58

3	768	M	553	4.33
3	770	M	506	2.77
3	772	M	536	2.58
3	773	M	571	3.80
3	775	M	437	2.31
3	781	M	580	2.98
3	782	F	412	2.88
3	785	F	453	1.15
3	787	F	484	4.15
3	791	M	597	4.63

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Infectious Bursal Disease Virus (IBD), Variant E</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against variant bursal disease</td></tr>
<tr><td>Product Administration</td><td>One dose administered subcutaneous route in day-old chicks</td></tr>
<tr><td>Study Animals</td><td>SPF day-old chicks divided into 3 groups

Group 1 vaccinated and challenged
Group 4 placebo-vaccinated and challenged (positive control)
Group 5 placebo-vaccinated and placebo-challenged (negative control)</td></tr>
<tr><td>Challenge Description</td><td>IBDV Variant E challenge administered at 28 days post vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for 11 days and then euthanized. Body weight and bursal weight were recorded. Sex of birds was recorded.</td></tr>
<tr><td>Results</td><td>The body weight and bursal weight were collected and B/B weight ratio (bursa weigh/body weight ratio) was calculated for each bird and compared between the challenged groups: vaccinates (Group 1) and placebo controls (Group 4).

Five Number Summary of Bursal Weight/Body Weight Ratios
<table>
<tr><td>Group</td><td># birds</td><td>Min</td><td>Q1</td><td>Med</td><td>Q3</td><td>Max</td></tr>
<tr><td>1</td><td>30</td><td>0.13</td><td>0.22</td><td>0.39</td><td>0.64</td><td>0.93</td></tr>
<tr><td>4</td><td>30</td><td>0.07</td><td>0.13</td><td>0.15</td><td>0.17</td><td>0.23</td></tr>
<tr><td>5</td><td>29</td><td>0.32</td><td>0.47</td><td>0.62</td><td>0.66</td><td>0.87</td></tr>
</table>
Min is minimum
Q is quartile
Med is median
Max is maximum

Raw data on attached page</td></tr>
<tr><td>USDA Approval Date</td><td>July 18, 2019</td></tr>
</table>

Raw data shown below.

Group	ID	Sex (M=male, F=female)	Body weight (g)	Bursal Weight (g)	B/BW Ratio
1	13	M	469	1.99	0.42
1	21	F	446	1.38	0.31
1	32	F	424	1.22	0.29
1	33	M	564	0.75	0.13
1	46	M	534	4.38	0.82
1	47	M	516	3.77	0.73
1	52	M	483	1.42	0.29
1	60	F	372	1.34	0.36
1	61	M	429	0.94	0.22
1	65	F	424	0.59	0.14
1	78	F	455	1	0.22
1	83	F	432	2.12	0.49
1	93	M	452	1.5	0.33
1	94	F	393	2.6	0.66
1	104	M	507	2.6	0.51
1	109	F	497	2.3	0.46
1	115	M	526	3.34	0.63
1	116	F	415	0.85	0.20
1	117	M	482	0.79	0.16
1	118	F	436	3.08	0.71
1	120	F	460	2.93	0.64
1	128	M	508	2.5	0.49
1	131	F	392	0.74	0.19
1	134	F	413	3.86	0.93
1	136	F	390	0.7	0.18
1	141	M	545	3.01	0.55
1	144	M	456	2.94	0.64
1	145	F	477	1.1	0.23
1	147	M	542	1.11	0.20
1	149	M	410	3.15	0.77
4	4	M	451	0.79	0.18
4	8	F	398	0.42	0.11
4	19	F	380	0.56	0.15
4	20	F	421	0.49	0.12
4	22	F	417	0.59	0.14
4	23	M	459	0.65	0.14
4	30	F	367	0.39	0.11
4	31	F	446	0.55	0.12

4	35	M	430	0.6	0.14
4	39	M	459	0.64	0.14
4	43	F	386	0.48	0.12
4	48	F	430	0.46	0.11
4	50	F	433	0.89	0.21
4	57	M	496	0.86	0.17
4	64	M	438	0.56	0.13
4	66	F	355	0.52	0.15
4	67	F	342	0.58	0.17
4	76	F	423	0.59	0.14
4	86	M	480	0.76	0.16
4	89	F	411	0.68	0.17
4	97	F	452	0.75	0.17
4	99	F	437	0.66	0.15
4	101	M	930	0.69	0.07
4	108	F	408	0.36	0.09
4	125	F	392	0.72	0.18
4	132	F	384	0.64	0.17
4	137	M	402	0.68	0.17
4	138	F	348	0.8	0.23
4	139	M	440	0.72	0.16
4	143	M	464	0.75	0.16
5	1	M	460	1.79	0.39
5	3	F	342	2.11	0.62
5	5	M	527	2.3	0.44
5	6	M	514	2.49	0.48
5	17	M	478	2.75	0.58
5	27	F	480	1.55	0.32
5	37	F	450	2.07	0.46
5	40	M	575	4.44	0.77
5	44	M	542	2.48	0.46
5	45	F	369	2.36	0.64
5	49	F	400	1.88	0.47
5	53	F	392	2.04	0.52
5	56	M	500	3.08	0.62
5	59	M	480	3.25	0.68
5	70	F	436	2.44	0.56
5	74	M	537	3.87	0.72
5	77	F	398	2.06	0.52
5	92	M	547	3.84	0.70
5	98	F	503	2.11	0.42

5	100	M	507	3.25	0.64
5	107	F	391	2.77	0.71
5	114	M	493	3.11	0.63
5	119	F	438	2.9	0.66
5	124	F	521	3.52	0.68
5	127	F	434	2.8	0.65
5	129	M	442	1.53	0.35
5	135	M	481	2.98	0.62
5	142	M	445	2.87	0.64
5	146	F	397	3.44	0.87

Study Type	Efficacy
Pertaining to	Infectious Laryngotracheitis Virus (ILT)
Study Purpose	Demonstrate efficacy against ILT
Product Administration	One dose administered *in ovo* at 18-19 days of embryonation
Study Animals	SPF eggs divided into 2 groups Group 2 vaccinated with product and challenged Group 4 sham vaccinated and challenged (control)
Challenge Description	ILT challenge administered at 28 days post vaccination
Interval observed after challenge	Observed daily for 10 days for mortality and individually observed for ILT clinical signs.
Results	Vaccinates and controls were evaluated in terms of fowl laryngotracheitis per the criteria in 9 CFR 113.328(c). Birds with ILT clinical signs: Group 2: 1/30 Group 4: 26/30 Requirements of 9 CFR 113.328(c) were met Raw data on attached page
USDA Approval Date	November 7, 2018

Raw data shown below for birds classified as positive. All other birds normal.

Group/Bird	Depression/Breathing	Infraorbital Sinus/Conjunctiva
2/1		X
4/1		X
4/2		X
4/3		X
4/4		X
4/5		X
4/6		X
4/7	X	X
4/8		X
4/9		X
4/10		X
4/11		X
4/12		X
4/13		X
4/14		X
4/15		X
4/16		X
4/17		X
4/18	X	X
4/19	X	X
4/20		X
4/21		X
4/22		X
4/23	X	X
4/24	X	X
4/25		X
4/26	X	

Study Type	Efficacy
Pertaining to	Infectious Laryngotracheitis Virus (ILT)
Study Purpose	Demonstrate efficacy against ILT
Product Administration	One dose administered subcutaneous route to day-old chicks
Study Animals	SPF day-old chicks divided into 2 groups Group 3 vaccinated with product and challenged Group 4 sham vaccinated and challenged (control)
Challenge Description	ILT challenge administered at 28 days post vaccination
Interval observed after challenge	Observed daily for 10 days for mortality and individually observed for ILT clinical signs.
Results	Vaccinates and controls were evaluated in terms of fowl laryngotracheitis per the criteria in 9 CFR 113.328(c). Birds with ILT clinical signs: Group 3: 2/30 Group 4: 30/30 Requirements of 9 CFR 113.328(c) were met Raw data on attached page
USDA Approval Date	January 25, 2019

Raw data shown below for birds classified as positive. All other birds normal.

Group/Bird	Depression/Breathing	Infraorbital Sinus/Conjunctiva
3/1		X
3/2		X
4/1		X
4/2		X
4/3		X
4/4		X
4/5		X
4/6		X
4/7		X
4/8		X
4/9		X
4/10		X
4/11		X
4/12		X
4/13		X
4/14	X	X
4/15		X
4/16		X
4/17		X
4/18		X
4/19		X
4/20		X
4/21		X
4/22		X
4/23		X
4/24		X
4/25		X
4/26		X
4/27		X
4/28		X
4/29		X
4/30		X

Study Type	Efficacy
Pertaining to	Marek's Disease Virus (MDV)
Study Purpose	Demonstrate efficacy against Marek's disease
Product Administration	One dose administered *in ovo* at 18-19 days of embryonation
Study Animals	SPF eggs divided into 3 groups Group 1 vaccinated with product and challenged Group 2 sham vaccinated and challenged (positive control) Group 3 sham vaccinated and sham challenged (negative control)
Challenge Description	Serotype-1 GA 22 strain administered at 7 days post vaccination
Interval observed after challenge	Observed daily for clinical signs for 7 weeks and then examined for gross lesions.
Results	Vaccinates and controls were evaluated in terms of Marek's disease grossly observable lesions per the criteria in 9 CFR 113.330(c). Birds with gross observable lesions: Group 1: 4/34 Group 2: 27/32 Group 3: 0/33 Requirements of 9 CFR 113.330(c) were met Raw data on attached page
USDA Approval Date	November 5, 2018

Raw data shown below for birds classified as positive. All other birds normal.

Group/Bird	PARALYSIS	LOCOMOTIVE SIGNS	EMACIATION	DEPRESSION	LIVER	SPLEEN	HEART	MUSCLE	GONADS	KIDNEYS	Other Gross Lesions	Comments
1/1						X		X	X	X		
1/2						X				X		
1/3		X		X					X	X		
1/4	X					X			X		X	Gross Lesion on skin
2/1				X		X				X		
2/2				X	X	X		X				
2/3				X	X	X						
2/4				X		X						
2/5			X		X	X				X	X	Gross Lesion on skin
2/6						X				X		
2/7				X		X						
2/8				X	X	X				X	X	Gross Lesion on skin
2/9				X	X	X						
2/10			X			X			X	X		
2/11			X	X	X	X				X	X	Gross Lesion on skin
2/12			X	X	X	X						
2/13				X		X				X	X	Gross Lesion on skin
2/14					X	X				X	X	Gross Lesion on skin
2/15			X		X	X				X	X	Gross Lesion on skin
2/16						X				X		
2/17			X	X	X	X					X	Gross Lesion on skin
2/18										X		
2/19		X		X						X		
2/20				X		X						
2/21		X	X	X	X	X				X		
2/22			X		X				X	X		
2/23				X	X	X				X		
2/24				X	X	X	X					
2/25				X	X	X	X					
2/26		X		X		X						
2/27			X	X	X	X	X			X		

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Marek’s Disease Virus (MDV)</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against MDV</td></tr>
<tr><td>Product Administration</td><td>One dose administered subcutaneous route to day-old chicks</td></tr>
<tr><td>Study Animals</td><td>SPF day-old chicks divided into 3 groups with 35 chicks per group

Group 1 vaccinated, challenged
Group 2 placebo-vaccinated, challenged (positive control)
Group 3 placebo-vaccinated, not challenged (negative control)</td></tr>
<tr><td>Challenge Description</td><td>Serotype-1 GA 22 strain given subcutaneously at 4 days post vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for clinical signs for 7 weeks and then examined for gross lesions.</td></tr>
<tr><td>Results</td><td>Vaccinates and controls were evaluated in terms of Marek’s disease grossly observable lesions per the criteria in 9 CFR 113.330(c).

<table>
<tr><th>Treatment</th><th>Number positive for Marek’s Disease</th><th>Number negative for Marek’s Disease</th></tr>
<tr><td>Vaccinates</td><td>3/35 (8.6%)</td><td>32/35 (91.4%)</td></tr>
<tr><td>Positive controls</td><td>31/35 (88.6%)</td><td>4/35 (11.4%)</td></tr>
<tr><td>Negative controls</td><td>0/35 (0.0%)</td><td>35/35 (100%)</td></tr>
</table>

Requirements of 9 CFR 113.330(c) were met

Raw data on attached page</td></tr>
<tr><td>USDA Approval Date</td><td>July 2, 2019</td></tr>
</table>

Raw data shown below for birds classified as positive. All other birds normal.

Group/Bird	Clinical Signs				Gross Lesions at Necropsy								Lesions Consistent with Mareks	Comments
	Paralysis	Locomotive Signs	Emaciation	Depression	Liver	Spleen	Heart	Nerve Enlargement	Muscle	Gonads	Kidneys	Other Gross Lesions		
1/1						X	X			X	X		X	
1/2													X	TOO DECOMPOSED TO NECROPSY
1/3											X		X	
2/1				X	X	X					X		X	
2/2						X							X	
2/3	X				X	X					X		X	
2/4		X		X		X	X				X		X	
2/5	X	X	X	X	X	X	X						X	
2/6		X		X		X					X		X	
2/7						X							X	
2/8				X	X	X					X		X	
2/9				X		X				X	X		X	
2/10				X		X					X		X	
2/11	X					X							X	
2/12				X	X	X			X				X	
2/13				X		X	X				X		X	
2/14				X	X	X				X	X	X	X	SKIN
2/15						X							X	
2/16		X		X	X	X				X	X		X	
2/17		X	X	X	X	X			X		X		X	
2/18						X							X	
2/19					X	X	X						X	
2/20						X							X	
2/21				X	X	X				X	X		X	
2/22					X	X				X	X		X	
2/23				X	X	X			X				X	
2/24				X		X							X	
2/25				X	X	X					X		X	
2/26				X	X	X	X						X	
2/27		X		X		X							X	
2/28	X	X		X		X							X	
2/29	X			X		X					X		X	
2/30			X	X	X	X					X		X	
2/31					X	X			X	X	X		X	

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>ALL</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate safety of product under typical use conditions</td></tr>
<tr><td>Product Administration</td><td>1 dose by either the in ovo or subcutaneous route</td></tr>
<tr><td>Study Animals</td><td>Commercial chicken eggs at 18 to 19 days of embryonation or chickens at one day of age. At each of the three sites, one group received the test vaccine and one group received vaccinations according to site standard practices.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>No challenge. Animals were observed daily for mortality for 21 days. Hatchability for in ovo vaccinated groups was recorded.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><th>Location</th><th>Treatment</th><th>Total Placed</th><th>% Mortality</th><th>% Hatchability</th></tr>
<tr><td>1</td><td>Subcutaneous</td><td>22,900</td><td>1.4</td><td>N/A</td></tr>
<tr><td>1</td><td>Subcutaneous Control</td><td>22,900</td><td>2.8</td><td>N/A</td></tr>
<tr><td>2</td><td>In ovo</td><td>26,900</td><td>1.5</td><td>86.5</td></tr>
<tr><td>2</td><td>In ovo Control</td><td>26,800</td><td>1.8</td><td>86.2</td></tr>
<tr><td>3</td><td>In ovo</td><td>26,527</td><td>2.3</td><td>96.4</td></tr>
<tr><td>3</td><td>In ovo Control</td><td>-*</td><td>2.3</td><td>88.4*</td></tr>
</table>
N/A = not applicable
* Based on all the eggs vaccinated that day

No adverse reactions attributable to the vaccine were recorded.
</td></tr>
<tr><td>USDA Approval Date</td><td>September 2, 2020</td></tr>
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