Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	1281.R3
True Name	Bursal Disease-Marek's Disease Vaccine, Serotypes 1 & 3, Live Marek's Disease Vector, Live Herpesvirus Chimera
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	
Date of Compilation Summary	May 17, 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.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bursal disease virus 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 in ovo</td></tr>
<tr><td>Study Animals</td><td>3 groups of 20 SPF eggs each

Group 2 vaccinated and challenged
Group 4 sham vaccinated and challenged (challenge control/placebo)
Group 5 sham vaccinated and sham challenged (negative control)</td></tr>
<tr><td>Challenge Description</td><td>IBDV variant E challenge administered at 28 days of age (Study Day 31)</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for 11 post-challenge and target tissues examined for gross bursal lesions</td></tr>
<tr><td>Results</td><td>The body weight and bursal weight were collected and B/B wt. ratio (bursa weight/body weight ratio) was calculated for each bird and compared between vaccinates and challenge controls/placebos.

<table>
<tr><th>Gender</th><th>Group</th><th>Min</th><th>Q1</th><th>Med</th><th>Q3</th><th>Max</th></tr>
<tr><td>Female</td><td>Vaccinate</td><td>0.16</td><td>0.33</td><td>0.48</td><td>0.64</td><td>0.79</td></tr>
<tr><td></td><td>Placebo</td><td>0.05</td><td>0.10</td><td>0.11</td><td>0.13</td><td>0.16</td></tr>
<tr><td>Male</td><td>Vaccinate</td><td>0.06</td><td>0.35</td><td>0.44</td><td>0.45</td><td>0.54</td></tr>
<tr><td></td><td>Placebo</td><td>0.07</td><td>0.10</td><td>0.12</td><td>0.13</td><td>0.20</td></tr>
</table>

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

Raw data attached.</td></tr>
<tr><td>USDA Approval Date</td><td>November 14, 2017</td></tr>
</table>

				Bursa Weight (g)	Body Weight (g)	B/BW Ratio
Group	Vaccine	Challenge	ID			
2	Test vaccine	IBDV VAR-E (Day 31)	260	0.68	416.00	0.16
			273	2.25	509.00	0.44
			276	2.34	488.00	0.48
			279	1.03	458.00	0.22
			285	3.13	497.00	0.63
			287	2.30	527.00	0.44
			296	1.79	518.00	0.35
			303	2.58	531.00	0.49
			309	2.50	386.00	0.65
			319	2.34	537.00	0.44
			320	2.00	468.00	0.43
			325	4.06	516.00	0.79
			326	0.30	531.00	0.06
			334	2.34	529.00	0.44
			335	2.96	460.00	0.64
			336	1.53	459.00	0.33
			342	3.22	596.00	0.54
			343	2.81	564.00	0.50
			348	2.46	551.00	0.45
			355	0.71	542.00	0.13
4	Sham-vaccinated / IBDV VAR-E Challenge Controls	IBDV VAR-E (Day 31)	266	0.38	398.00	0.10
			272	0.51	423.00	0.12
			274	0.56	362.00	0.15
			275	1.04	520.00	0.20
			280	0.36	517.00	0.07
			292	0.52	428.00	0.12
			293	0.48	428.00	0.11
			294	0.87	623.00	0.14
			298	0.58	474.00	0.12
			304	0.58	426.00	0.14
			305	0.29	430.00	0.07
			311	0.45	405.00	0.11
			315	0.70	530.00	0.13
			316	0.75	458.00	0.16
			331	0.47	476.00	0.10
			344	0.54	454.00	0.12
			347	0.40	543.00	0.07
			349	0.42	394.00	0.11
			352	0.22	415.00	0.05
			354	0.48	421.00	0.11

Day 31 denotes day of study and day of challenge

				Bursa Weight (g)	Body Weight (g)	B/BW Ratio
5	Sham-vaccinated, sham-challenged (Negative Controls)	Sham Challenge (Day 31)	259	1.09	493.00	0.22
			262	4.31	622.00	0.69
			264	2.41	569.00	0.42
			267	3.73	444.00	0.84
			269	3.74	444.00	0.84
			270	2.41	548.00	0.44
			271	2.42	519.00	0.47
			282	2.97	560.00	0.53
			283	2.69	492.00	0.55
			295	1.78	475.00	0.37
			308	2.22	670.00	0.33
			312	2.36	470.00	0.50
			322	2.63	594.00	0.44
			324	2.04	514.00	0.40
			328	2.65	520.00	0.51
			332	1.93	445.00	0.43
			339	3.56	568.00	0.63
			345	2.00	503.00	0.40
			350	2.81	471.00	0.60
			356	3.56	479.00	0.74

Day 31 denotes day of study and day of challenge

Study Type	Efficacy
Pertaining to	Bursal disease virus standard
Study Purpose	Demonstrate efficacy against bursal disease standard strain
Product Administration	One dose administered in ovo route
Study Animals	SPF eggs divided into 2 groups Group 1 vaccinated and challenged Group 2 sham vaccinated and challenged (positive control)
Challenge Description	IBDV standard challenge administered at 28 days of age
Interval observed after challenge	Observed daily for 4 days and necropsied to examine 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: 2/40 Group 2: 38/40 Requirements of 9 CFR 113.331(c) were met. Raw data on attached page
USDA Approval Date	October 19, 2017

Group/Bird	Peri-Bursal Edema	Edema	Macroscopic Hemorrhage	Bursal Disease Score	Comments
1/1		X		Positive	
1/2		X		Positive	
2/1		X		Positive	
2/2		X		Positive	
2/3		X		Positive	
2/4		X		Positive	
2/5		X		Positive	
2/6	X			Positive	
2/7		X		Positive	
2/8		X		Positive	
2/9		X		Positive	
2/10		X		Positive	
2/11	X		X	Positive	Found Dead
2/12		X		Positive	
2/13		X		Positive	
2/14		X		Positive	
2/15		X		Positive	
2/16		X		Positive	
2/17		X		Positive	
2/18		X		Positive	
2/19		X		Positive	
2/20		X		Positive	
2/21		X		Positive	
2/22		X		Positive	
2/23		X		Positive	
2/24		X		Positive	
2/25		X		Positive	
2/26		X		Positive	
2/27		X		Positive	
2/28		X		Positive	
2/29		X		Positive	
2/30		X		Positive	
2/31		X		Positive	
2/32		X		Positive	
2/33		X		Positive	
2/34		X		Positive	
2/35		X		Positive	Found Dead
2/36		X		Positive	
2/37		X		Positive	
2/38		X		Positive	

Study Type	Efficacy
Pertaining to	Infectious bursal disease virus, standard
Study Purpose	Demonstrate efficacy against infectious bursal disease, standard
Product Administration	One dose subcutaneously (SQ) at day of age
Study Animals	One-day-old SPF chicks, 20 per group Group 1: Vaccinated, challenged Group 7: Placebo vaccinated, challenged (Control)
Challenge Description	IBDV Classical STC challenge, 28 days after vaccination
Interval observed after challenge	Observed for 4 days post-challenge then examined for gross bursal lesions at necropsy
Results	Animals were evaluated for signs of gross bursal lesions per the criteria in 9 CFR 113.331(b)(2)(i). Birds with observable lesions: Group 1: 0/20 Group 7: 20/20 Requirements of 9 CFR 113.331(c)(3)(ii) were met. Raw data of affected chickens on attached page
USDA Approval Date	January 28, 2014

Group	Bird ID	Bursal Disease Score
7	257	Positive
7	258	Positive
7	262	Positive
7	256	Positive
7	255	Positive
7	261	Positive
7	251	Positive
7	259	Positive
7	254	Positive
7	260	Positive
7	263	Positive
7	264	Positive
7	265	Positive
7	266	Positive
7	268	Positive
7	270	Positive
7	271	Positive
7	272	Positive
7	273	Positive
7	275	Positive

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Infectious bursal disease virus, variant E</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against variant infectious bursal disease variant E</td></tr>
<tr><td>Product Administration</td><td>One dose subcutaneously (SQ) at day of age</td></tr>
<tr><td>Study Animals</td><td>One-day-old SPF chicks, 20 per group

Group 2: Vaccinated, challenged
Group 3: Vaccinated, sham challenged
Group 8: Placebo vaccinated, challenged
Group 9: Placebo vaccinated, sham challenged</td></tr>
<tr><td>Challenge Description</td><td>IBDV Variant (VAR-E) challenge, 28 days after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Body and bursal weights collected 11 days post-challenge. Sex of birds was recorded.</td></tr>
<tr><td>Results</td><td>Bursal ratios (bursa weight/body weight ratio X 100) were calculated for each animal

5-number summary for the bursal to body weight ratio per treatment group.

<table>
<tr><th>Group</th><th>Min.</th><th>Q1</th><th>Median</th><th>Q3</th><th>Max.</th></tr>
<tr><td>2</td><td>0.31</td><td>0.44</td><td>0.49</td><td>0.53</td><td>0.84</td></tr>
<tr><td>3</td><td>0.31</td><td>0.44</td><td>0.49</td><td>0.57</td><td>0.69</td></tr>
<tr><td>8</td><td>0.08</td><td>0.10</td><td>0.12</td><td>0.13</td><td>0.16</td></tr>
<tr><td>9</td><td>0.33</td><td>0.46</td><td>0.49</td><td>0.56</td><td>0.87</td></tr>
</table>
Min. is minimum
Q is quartile
Max. is maximum

Raw data on attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>January 28, 2014</td></tr>
</table>

Raw data shown below

Group	ID No.	Sex (M=male, F=female)	Body weight (g)	Bursa weight (g)
2	235	M	469	2.26
2	236	M	416	2.34
2	232	F	385	1.7
2	234	F	356	1.82
2	233	F	502	4.21
2	229	F	468	2.46
2	230	M	480	2.53
2	237	M	461	1.44
2	228	F	462	2.07
2	226	M	436	2.2
2	240	M	555	3.09
2	247	F	514	2.33
2	244	F	463	1.87
2	243	F	449	2.2
2	238	F	451	1.78
2	249	F	441	2.68
2	250	M	526	2.54
2	248	M	497	1.78
2	246	M	471	2.4
2	241	M	407	1.84
3	162	M	523	3.6
3	157	M	576	2.67
3	158	F	420	1.94
3	152	M	483	2.84
3	153	M	487	2.64
3	151	M	496	2.88
3	154	F	377	1.17
3	155	F	425	1.32
3	161	F	393	1.85
3	156	M	483	2.35
3	169	M	477	2.46
3	164	F	381	2.15
3	175	F	419	2.23
3	167	F	393	2.34
3	170	M	472	2.85
3	163	F	461	1.94
3	172	M	505	2.15
3	174	M	557	2.62
3	165	F	427	2.07

3	173	M	511	1.76
8	307	M	470	0.59
8	303	M	614	0.87
8	310	F	445	0.54
8	306	F	441	0.54
8	311	F	433	0.43
8	305	F	473	0.41
8	308	F	386	0.63
8	302	M	472	0.61
8	304	F	410	0.55
8	301	M	508	0.67
8	322	M	505	0.62
8	323	M	546	0.65
8	317	F	443	0.68
8	316	M	528	0.63
8	319	M	500	0.72
8	314	F	479	0.47
8	320	F	482	0.44
8	313	F	468	0.39
8	315	F	476	0.37
8	321	F	438	0.47
9	206	M	570	2.77
9	204	M	435	2.14
9	201	M	550	2.52
9	207	F	497	2.53
9	209	M	498	2.27
9	211	M	515	3.07
9	208	F	512	3.5
9	212	F	429	3.75
9	203	M	522	2.96
9	202	F	458	1.52
9	215	F	503	3.13
9	221	M	535	2.72
9	220	M	504	2.41
9	219	M	491	2.02
9	222	M	525	2.89
9	225	F	410	2.05
9	216	F	409	1.87
9	223	M	521	2.56
9	217	F	433	1.76
9	224	F	444	2.24

Study Type	Efficacy
Pertaining to	Marek's Disease Virus, serotype 1
Study Purpose	Demonstrate efficacy against very virulent Marek's disease
Product Administration	One dose administered *in ovo*
Study Animals	SPF eggs divided into 4 groups Group 1 vaccinated with test product and challenged Group 2 sham vaccinated and challenged (control) Group 3 sham vaccinated and not challenged (control) Group 4 vaccinated with a serotype 3 Marek's vaccine and challenged (control)
Challenge Description	Serotype-1 (SR-1) RB1B strain administered at 5 days of age
Interval observed after challenge	Observed daily for 50 days and then evaluated for internal lesions
Results	Vaccinates and controls were evaluated in terms of Marek's disease clinical signs and/or grossly observable lesions per the criteria in 9 CFR 113.330(c)(4) & (5). Birds with clinical signs and/or observable lesions: Group 1: 6/33 Group 2: 35/35 Group 3: 0/35 Group 4: 11/35 Requirements of 9 CFR 113.330(c)(4) & (5) were met. Raw data on attached page
USDA Approval Date	November 30, 2016

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

Group/Bird	Paralysis	Locomotive_Signs	Emaciation	Depression	Other Clinical Signs	Liver	Spleen	Heart	Muscle	Gonads	Kidneys	Other Gross Lesions	Comments
1/1						X	X				X		
1/2				X						X	X		
1/3						X	X			X	X		
1/4						X	X			X	X		
1/5							X			X	X		
1/6				X			X				X		
2/1				X			X				X		
2/2		X				X					X		
2/3		X		X							X		
2/4		X		X			X				X		
2/5				X							X		
2/6				X			X						
2/7				X			X			X	X		
2/8				X		X					X		
2/9				X		X		X			X		
2/10				X			X						
2/11				X			X				X		
2/12				X			X				X		
2/13				X			X				X		
2/14				X			X			X			
2/15				X							X		
2/16				X			X			X	X		
2/17				X									
2/18				X			X			X	X		
2/19				X			X			X	X		
2/20				X		X	X						
2/21				X			X						

Group/Bird	Paralysis	Locomotive_Signs	Emaciation	Depression	Other Clinical Signs	Liver	Spleen	Heart	Muscle	Gonads	Kidneys	Other Gross Lesions	Comments
2/22				X			X				X		
2/23		X		X									
2/24				X							X		
2/25				X			X						
2/26				X			X				X		
2/27				X			X		X	X			
2/28		X		X		X	X						
2/29				X		X	X				X		
2/30				X			X				X		
2/31				X			X				X		
2/32				X			X						
2/33				X		X	X				X		
2/34				X			X						
2/35		X		X			X			X			
4/1										X	X		
4/2		X		X						X			
4/3						X	X			X	X		
4/4		X		X						X	X		
4/5		X		X						X	X		
4/6										X			
4/7											X		
4/8											X		
4/9			X							X	X		
4/10						X	X				X		
4/11		X							X	X	X		

Study Type	Efficacy
Pertaining to	Marek's disease virus, serotype 1
Study Purpose	Demonstrate efficacy against very virulent Marek's disease virus (vvMDV)
Product Administration	One dose subcutaneously (SQ)
Study Animals	One-day-old SPF chicks, 34-35 per group Group 1: Vaccinated, challenged Group 5: Placebo vaccinated, challenged (challenge control) Group 6: Placebo vaccinated, placebo challenged (nonchallenge control) Group 7: Vaccinated with serotype 3 Marek's vaccine and challenged (challenge severity group)
Challenge Description	Marek's virus (SR-1) RB1B strain at 4 days post vaccination
Interval observed after challenge	Observed daily until necropsied at 45 days post-challenge (49 days post-hatch) to examine for gross lesions associated with Marek's disease
Results	Vaccinates and controls were evaluated in terms of Marek's disease clinical signs and/or grossly observable lesions per the criteria in 9 CFR 113.330(c)(4) & (5). Birds with clinical signs and/or observable lesions: Group 1: 2/35 Group 5: 33/34 Group 6: 0/35 Group 7: 10/35 Requirements of 9 CFR 113.330(c)(4) & (5) were met. Raw data on attached page.
USDA Approval Date	July 16, 2013

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

Group/Unit/Bird	Positive for Marek's	Comments
1/91/1	Yes	Emaciated. NVL
1/91/11	Yes	
5/81/1	Yes	Emaciated. NVL
5/81/10	Yes	Emaciated. MD tumors in kidney.
5/81/2	Yes	NVL
5/81/3	Yes	Emaciated. Kidneys
5/81/4	Yes	NVL
5/81/5	Yes	Emaciated. MD tumors in heart, muscle breast & kidneys.
5/81/6	Yes	MD tumors in liver, kidneys & gonads.
5/81/7	Yes	Emaciated. MD tumors in kidney.
5/81/8	Yes	Bird was down sick. Terminated. Emaciated. NVL.
5/81/9	Yes	MD tumors in liver & spleen
5/89/10	Yes	MD tumors in kidneys.
5/89/11	Yes	Heart, kidneys, gonads, breast muscle
5/89/12	Yes	Kidneys
5/89/2	Yes	MD tumors in liver, kidneys, spleen
5/89/3	Yes	MD tumors in kidneys & gonad
5/89/4	Yes	NVL
5/89/5	Yes	Emaciated. NVL
5/89/6	Yes	Emaciated. MD tumors in liver, gonads, kidneys, spleen.
5/89/7	Yes	Emaciated. MD tumors in liver, heart, spleen, kidneys & gonads.
5/89/8	Yes	Emaciated. MD tumors in kidneys.
5/89/9	Yes	Bird was down sick. Terminated. MD tumors in heart & gonads.
5/90/1	Yes	MD tumors in gonads
5/90/10	Yes	Terminated. Emaciated. Down with extended leg. MD tumors kidneys & gonads.
5/90/11	Yes	Terminated. Emaciated. MD in heart, spleen & kidneys.
5/90/12	Yes	Liver, spleen
5/90/2	Yes	MD tumors in heart, liver, gonads, & kidneys
5/90/3	Yes	Emaciated. NVL.
5/90/4	Yes	Emaciated. MD kidneys & heart.
5/90/5	Yes	MD spleen
5/90/6	Yes	MD tumors in liver & kidneys
5/90/7	Yes	MD tumors in heart, kidneys & gonads

5/90/8	Yes	MD tumors in spleen
5/90/9	Yes	Emaciated. Tumors in kidneys & gonads.
7/37/1	Yes	Bird was down w/ NVL
7/37/2	Yes	Emaciated. MD tumors in kidneys & gonads.
7/37/8	Yes	Gonads
7/38/1	Yes	Bird was down. NVL.
7/38/2	Yes	NVL
7/39/1	Yes	MD tumor in gonads. Emaciated
7/39/12	Yes	
7/39/2	Yes	MD tumor in proventriculus
7/39/3	Yes	Bird down. MD tumors gonads & breast muscle.
7/39/4	Yes	Bird down. Tumors in kidneys & gonads.

NVL – No visible lesions
MD – Marek's disease

<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. Hatchability for in ovo vaccinated groups was recorded. Animals were observed daily for mortality for 21 days.</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>
<table>
<tr><th>Location</th><th>Treatment</th><th>Total Placed</th><th>21 Day Mortality</th><th>% Mortality</th><th>% Hatchability</th></tr>
<tr><td rowspan="2">1</td><td rowspan="2">In ovo</td><td>15,500</td><td>677</td><td>4.4</td><td rowspan="2">74.1</td></tr>
<tr><td>15,500</td><td>561</td><td>3.6</td></tr>
<tr><td>1</td><td>Control</td><td>27,200</td><td>367</td><td>1.3</td><td>86.5</td></tr>
<tr><td>2</td><td>In ovo</td><td>20,000</td><td>291</td><td>1.5</td><td>91.4</td></tr>
<tr><td>2</td><td>Control</td><td>20,000</td><td>277</td><td>1.4</td><td>91.8</td></tr>
<tr><td>3</td><td>SQ</td><td>22,543</td><td>351</td><td>1.6</td><td>N/A</td></tr>
<tr><td>3</td><td>Control</td><td>22,540</td><td>756</td><td>3.4</td><td>N/A</td></tr>
</table>
N/A = not applicable

No adverse reactions attributable to the vaccine were recorded.
</td></tr>
<tr><td>USDA Approval Date</td><td>July 2, 2018</td></tr>
</table>