Summary of Studies Supporting USDA Product Licensure

Establishment Name	Ceva Animal Health, LLC
USDA Vet Biologics Establishment Number	368
Product Code	1A91.R2
True Name	Bursal Disease-Marek's Disease-Newcastle Disease Vaccine, Serotypes 2 & 3, Live Virus, Live Marek's Disease Vector
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Ultifend IBD ND + SB1 - Biomune Company
Date of Compilation Summary	June 07, 2021

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 (IBDV) USDA Standard
Study Purpose	To demonstrate effectiveness against IBDV USDA Standard strain
Product Administration	One dose administered by the in ovo route
Study Animals	30 SPF chicken embryos per treatment group vaccinated at 18 days of incubation
Challenge Description	IBDV USDA Standard strain at five weeks of age
Interval observed after challenge	Daily observation for 4 days post challenge; necropsy at 4 days post challenge
Results	A chicken was considered affected by the challenge (positive) if grossly observable lesions caused by the IBDV USDA Standard challenge were present. 3/30 vaccinates, 30/30 positive controls and 0/30 negative controls were affected by the challenge, i.e 90% of vaccinates were protected against IBDV USDA Standard. Raw data are shown on the attached page.
USDA Approval Date	March 9, 2016

Vaccinate ID	Infectious Bursal Disease Lesions[1]	Positive Control ID	Infectious Bursal Disease Lesions	Negative Control ID	Infectious Bursal Disease Lesions
1	NA	31	P,A,Y	61	NA
2	NA	32	P,Y	62	NA
3	NA	33	E	63	NA
4	NA	34	P,A,Y	64	NA
5	NA	35	P,A,Y	65	NA
6	NA	36	A,E	66	NA
7	NA	37	P,E	67	NA
8	NA	38	P,A,Y	68	NA
9	NA	39	Y	69	NA
10	NA	40	Y	70	NA
11	NA	41	A,Y,E	71	NA
12	NA	42	P,A	72	NA
13	NA	43	P,A	73	NA
14	NA	44	P,Y	74	NA
15	NA	45	A,Y,E	75	NA
16	NA	46	A,E	76	NA
17	NA	47	A,Y,E	77	NA
18	NA	48	A,Y,E	78	NA
19	NA	49	E	79	NA
20	NA	50	P,A,Y	80	NA
21	A	51	A,Y,E	81	NA
22	NA	52	Y,E	82	NA
23	NA	53	Y	83	NA
24	A,M	54	A,E	84	NA
25	NA	55	P,A,Y	85	NA
26	NA	56	A,Y,E	86	NA
27	NA	57	P,A	87	NA
28	A	58	A	88	NA
29	NA	59	A,E	89	NA
30	NA	60	A,Y,E	90	NA

[1] Gross lesion: A=atrophy, Y=yellowish color, E=edema, P=peribursal edema, M=macroscopic hemorrhage, NA=not applicable (no lesions)

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Infectious Bursal Disease Virus Delaware Variant E Strain (IBDV-Var. E)</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness against IBDV-Var. E</td></tr>
<tr><td>Product Administration</td><td>One dose administered subcutaneously at day of age</td></tr>
<tr><td>Study Animals</td><td>1. Vaccinates: 30 SPF chickens at day of age were vaccinated with the test vaccine.
2. Controls: 30 SPF chickens were placebo-vaccinated (positive control group)</td></tr>
<tr><td>Challenge Description</td><td>Infectious Bursal Disease Virus Delaware Variant E challenge strain at 5 weeks of age for both the vaccinate and control groups (35 days post-vaccination).</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for eight days post-challenge and were observed for any adverse vaccine reaction. Tissues were examined at eight days post challenge for IBDV lesions.</td></tr>
<tr><td>Results</td><td>Vaccinates and Controls were evaluated in terms of 9 CFR 113.331 (Bursal Disease Vaccine) efficacy, except for the challenge time observed, the necropsy was done at 8 days post-challenge, and atrophy of the bursa was included as a gross lesion.

A chicken was considered negative if IBD-related gross lesions were not observed at the time of necropsy and was considered positive if any IBD-related gross lesions were observed. The IBD lesions included: peri-bursal edema, edema, macroscopic hemorrhage, discoloration, and atrophy of the bursa.

<table>
<tr><th rowspan="2">Group</th><th rowspan="2">Treatment</th><th rowspan="2">Vaccine Route</th><th colspan="2">IBDV-Var. E Challenge</th></tr>
<tr><th>No. Protected/ Total No.</th><th>% Protected</th></tr>
<tr><td>Vaccinates</td><td>rHVT/ND/IBD & SB-1</td><td>SQ</td><td>27/30</td><td>90%</td></tr>
<tr><td>Positive controls</td><td>Placebo-vaccinated</td><td>SQ</td><td>2/30</td><td>7%</td></tr>
</table>
3/30 vaccinates and 28/30 Positive Controls were affected by the challenge, IBDV-Var. E.

Raw data are shown on the attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>November 25, 2020</td></tr>
</table>

Vaccinate ID	IBD Lesions	Bursal Lesion	Control ID	IBD Lesions	Bursal Lesion
141	Neg[1]	NA[2]	146	Pos[1]	Atrophy
142	Pos[3]	Atrophy	147	Pos	Atrophy
143	Neg	NA	148	Pos	Atrophy
144	Neg	NA	150	Pos	Atrophy
145	Neg	NA	151	Neg[2]	NA[3]
149	Pos	Atrophy	152	Pos	Atrophy
156	Neg	NA	153	Pos	Atrophy
160	Neg	NA	154	Pos	Atrophy
163	Neg	NA	155	Pos	Atrophy
165	Neg	NA	157	Pos	Atrophy
166	Neg	NA	158	Pos	Atrophy
167	Neg	NA	159	Pos	Atrophy
169	Neg	NA	164	Pos	Atrophy
171	Neg	NA	172	Pos	Atrophy
174	Neg	NA	173	Pos	Atrophy
175	Neg	NA	176	Pos	Atrophy
179	Pos	Atrophy	178	Pos	Atrophy
181	Neg	NA	182	Neg	NA
184	Neg	NA	183	Pos	Atrophy
185	Neg	NA	186	Pos	Atrophy
187	Neg	NA	191	Pos	Atrophy
188	Neg	NA	194	Pos	Atrophy
190	Neg	NA	195	Pos	Atrophy
193	Neg	NA	196	Pos	Atrophy
197	Neg	NA	198	Pos	Atrophy
200	Neg	NA	199	Pos	Atrophy
201	Neg	NA	202	Pos	Atrophy
203	Neg	NA	208	Pos	Atrophy
204	Neg	NA	209	Pos	Atrophy
207	Neg	NA	210	Pos	Atrophy

[1] Neg = negative for gross lesions of IBD
[2] NA = not applicable
[3] Pos = positive for gross lesions of IBD

Study Type	Efficacy
Pertaining to	Newcastle Disease Virus (NDV) Texas GB strain and Infectious Bursal Disease Virus (IBDV) USDA Standard strain
Study Purpose	To demonstrate effectiveness against NDV Texas GB and IBDV USDA Standard infections
Product Administration	One dose administered by the subcutaneous route
Study Animals	30 SPF chickens per treatment group vaccinated at day of age
Challenge Description	For one vaccinate group and one control group: NDV Texas GB at four weeks of age; for a second vaccinate group and a second control group: IBDV USDA Standard at five weeks of age
Interval observed after challenge	For NDV Texas GB challenged chickens: daily observation for 14 days post challenge; for IBDV USDA Standard: daily observation for four days post challenge and necropsy at four days post challenge
Results	For NDV Texas GB challenged chickens, a chicken was considered affected by the challenge (positive) if clinical signs of Newcastle Disease were present. 0/30 vaccinates, 30/30 positive controls and 0/32 negative controls were affected by the challenge, i.e 100% of vaccinates were protected against NDV Texas GB. For IBDV USDA Standard challenged chickens, a chicken was considered affected by the challenge (positive) if gross lesions of Infectious Bursal Disease were present. 1/30 vaccinates, 29/30 positive controls and 0/20 negative controls were affected by the challenge, i.e. 97% of vaccinates were protected against IBDV USDA Standard. Raw data are shown on the attached pages.
USDA Approval Date	January 28, 2016

NDV Texas GB challenge

Vaccinate ID	Clincial Signs of Newcastle Disease	Positive Control ID	Clincial Signs of Newcastle Disease	Negative Control ID	Clincial Signs of Newcastle Disease
1	Neg	31	Pos	121	Neg
2	Neg	32	Pos	122	Neg
3	Neg	33	Pos	123	Neg
4	Neg	34	Pos	124	Neg
5	Neg	35	Pos	125	Neg
6	Neg	36	Pos	126	Neg
7	Neg	37	Pos	127	Neg
8	Neg	38	Pos	128	Neg
9	Neg	39	Pos	129	Neg
10	Neg	40	Pos	130	Neg
11	Neg	41	Pos	131	Neg
12	Neg	42	Pos	132	Neg
13	Neg	43	Pos	133	Neg
14	Neg	44	Pos	134	Neg
15	Neg	45	Pos	135	Neg
16	Neg	46	Pos	136	Neg
17	Neg	47	Pos	137	Neg
18	Neg	48	Pos	138	Neg
19	Neg	49	Pos	139	Neg
20	Neg	50	Pos	140	Neg
21	Neg	51	Pos	141	Neg
22	Neg	52	Pos	142	Neg
23	Neg	53	Pos	143	Neg
24	Neg	54	Pos	144	Neg
25	Neg	55	Pos	145	Neg
26	Neg	56	Pos	146	Neg
27	Neg	57	Pos	147	Neg
28	Neg	58	Pos	148	Neg
29	Neg	59	Pos	149	Neg
30	Neg	60	Pos	150	Neg
				151	Neg
				152	Neg

IBDV USDA Standard challenge

Vaccinate ID	Lesions of Infectious Bursal Disease	Positive Control ID	Lesions of Infectious Bursal Disease	Negative Control ID	Lesions of Infectious Bursal Disease
61	NA	91	A	121	NA
62	A	92	A,P	122	NA
63	NA	93	A,P	123	NA
64	NA	94	A,E	124	NA
65	NA	95	Y,P	125	NA
66	NA	96	A,E	126	NA
67	NA	97	Y,P,E	127	NA
68	NA	98	A	128	NA
69	NA	99	A,M	129	NA
70	NA	100	A	130	NA
71	NA	101	A	131	NA
72	NA	102	A	132	NA
73	NA	103	A,E	133	NA
74	NA	104	P,Y,E	134	NA
75	NA	105	A,E	135	NA
76	NA	106	A,P	136	NA
77	NA	107	A,P	137	NA
78	NA	108	A,M	138	NA
79	NA	109	A	139	NA
80	NA	110	A,P	140	NA
81	NA	111	A,M,E		
82	NA	112	P,Y		
83	NA	113	P,M,E		
84	NA	114	NA		
85	NA	115	A,E		
86	NA	116	A,M		
87	NA	117	E		
88	NA	118	E		
89	NA	119	A,M		
90	NA	120	A,M,E		

[1] Gross lesion: A=atrophy, Y=yellowish color, E=edema, P=peribursal edema, M=macroscopic hemorrhage, NA=not applicable (no lesions)

Study Type	Efficacy
Pertaining to	Marek's Disease Virus (MDV) RB1/B
Study Purpose	To demonstrate effectiveness against MDV RB1/B
Product Administration	1. One dose administered by the subcutaneous route 2. One dose administered by the in ovo route
Study Animals	1. 45 SPF chickens per treatment group vaccinated at day of age 2. 45 SPF chicken embryos per treatment group vaccinated at 18 days of incubation
Challenge Description	MDV RB1/B at five days of age
Interval observed after challenge	Daily observation for 44 days post challenge; necropsy at 44 days post challenge
Results	A chicken was considered affected by the challenge (positive) if grossly observable lesions caused by the MDV RB1/B challenge were present. In ovo vaccination: 5/45 vaccinates were affected by the challenge, i.e 89% of vaccinates were protected against MDV RB1/B. SQ vaccination: 7/45 vaccinates were affected by the challenge, i.e 84% of vaccinates were protected against MDV RB1/B. Controls: 10/43 HVT serotype 3 controls, 42/45 positive controls and 0/45 negative controls were affected by the challenge. Raw data are shown on the attached page.
USDA Approval Date	October 18, 2016

SQ Vaccinate ID	Marek's Lesions[1]	In ovo Vaccinate ID	Marek's Lesions	HVT Serotype 3 Control ID	Marek's Lesions	Positive Control ID	Marek's Lesions	Negative Control ID	Marek's Lesions
1	NA	46	NA	91	NA	134	H,Sp	179	NA
2	L,K,G	47	NA	92	NA	135	NA	180	NA
3	NA	48	NA	93	H,L	136	H	181	NA
4	L,Sp,K,G	49	NA	94	K	137	H	182	NA
5	NA	50	NA	95	NA	138	H	183	NA
6	NA	51	NA	96	NA	139	H,G	184	NA
7	NA	52	NA	97	NA	140	L,G,K,H, M	185	NA
8	NA	53	H,G,K	98	NA	141	H,K	186	NA
9	NA	54	NA	99	NA	142	H	187	NA
10	NA	55	NA	100	NA	143	Sp,K	188	NA
11	G,K	56	NA	101	NA	144	H, Sp	189	NA
12	NA	57	NA	102	NA	145	L,H,K	190	NA
13	NA	58	H,L,Sp	103	NA	146	H	191	NA
14	NA	59	NA	104	NA	147	H,K,G	192	NA
15	NA	60	NA	105	NA	148	H,Sp	193	NA
16	NA	61	NA	106	NA	149	H,L,Sp, K,G	194	NA
17	NA	62	NA	107	NA	150	H,L	195	NA
18	L,Sp,K,G	63	NA	108	Sp,G,I	151	H,Sp	196	NA
19	NA	64	NA	109	NA	152	H,K	197	NA
20	NA	65	NA	110	NA	153	L,G,K,H	198	NA
21	NA	66	NA	111	NA	154	H,K	199	NA
22	NA	67	NA	112	NA	155	NA	200	NA
23	K	68	NA	113	NA	156	H	201	NA
24	NA	69	NA	114	L	157	H,L,Sp, K,G	202	NA
25	NA	70	NA	115	NA	158	H,L,Sp, K,G	203	NA
26	NA	71	H,L,G	116	NA	159	H,L,Sp, K,G	204	NA
27	K	72	NA	117	L,Sp,G,K	160	K,H	205	NA
28	NA	73	NA	118	H,K,Sp,M	161	H,M	206	NA
29	NA	74	NA	119	NA	162	H,K	207	NA
30	NA	75	NA	120	NA	163	H,Sp	208	NA
31	NA	76	NA	121	NA	164	H,G,K	209	NA
32	NA	77	NA	122	NA	165	H	210	NA
33	NA	78	NA	123	NA	166	H,Sp,K,G	211	NA
34	NA	79	NA	124	NA	167	H,L,Sp,K	212	NA
35	NA	80	NA	125	NA	168	H,Sp,K	213	NA
36	NA	81	L,K,G	126	NA	169	NA	214	NA
37	NA	82	NA	127	L,G,K,Sp	170	H,Sp	215	NA
38	NA	83	NA	128	H	171	H,K,Sp	216	NA
39	G,K,Sp	84	NA	129	NA	172	H,Sp	217	NA
40	NA	85	H,L,K	130	NA	173	H	218	NA
41	NA	86	NA	131	L,K,Sp,G	174	H,K	219	NA
42	NA	87	NA	132	NA	175	H,K	220	NA
43	NA	88	NA	133	K,M,I	176	H,K,G	221	NA
44	NA	89	NA			177	H,L,Sp,K	222	NA
45	NA	90	NA			178	H	223	NA

[1] Tissue with lesion: K=kidney, Sp=spleen, L=liver, H=heart, G=gonad, N=nerves, Sk=skin, E=eye, M=muscle, I=intestines, NA=not applicable (no lesions)

Study Type	Efficacy
Pertaining to	Newcastle Disease Virus (NDV) Texas GB
Study Purpose	To demonstrate effectiveness against NDV Texas GB strain
Product Administration	One dose administered by the in ovo route
Study Animals	30 SPF chicken embryos per treatment group vaccinated at 18 days of incubation
Challenge Description	NDV Texas GB strain at 28 days of age
Interval observed after challenge	Daily observation for 14 days post challenge
Results	A chicken was considered affected by the challenge (positive) if clinical signs of Newcastle disease caused by the NDV Texas GB challenge were present. 3/30 vaccinates, 30/30 positive controls and 0/30 negative controls were affected by the challenge, i.e. 90% of vaccinates were protected against NDV Texas GB. Raw data are shown on the attached page.
USDA Approval Date	February 26, 2016

Vaccinate ID	Clinical Signs of Newcastle Disease[1]	Positive Control ID	Clinical Signs of Newcastle Disease	Negative Control ID	Clinical Signs of Newcastle Disease
1	Neg	31	Pos	61	Neg
2	Neg	32	Pos	62	Neg
3	Neg	33	Pos	63	Neg
4	Neg	34	Pos	64	Neg
5	Neg	35	Pos	65	Neg
6	Neg	36	Pos	66	Neg
7	Pos	37	Pos	67	Neg
8	Pos	38	Pos	68	Neg
9	Neg	39	Pos	69	Neg
10	Neg	40	Pos	70	Neg
11	Neg	41	Pos	71	Neg
12	Neg	42	Pos	72	Neg
13	Neg	43	Pos	73	Neg
14	Neg	44	Pos	74	Neg
15	Neg	45	Pos	75	Neg
16	Neg	46	Pos	76	Neg
17	Neg	47	Pos	77	Neg
18	Neg	48	Pos	78	Neg
19	Pos	49	Pos	79	Neg
20	Neg	50	Pos	80	Neg
21	Neg	51	Pos	81	Neg
22	Neg	52	Pos	82	Neg
23	Neg	53	Pos	83	Neg
24	Neg	54	Pos	84	Neg
25	Neg	55	Pos	85	Neg
26	Neg	56	Pos	86	Neg
27	Neg	57	Pos	87	Neg
28	Neg	58	Pos	88	Neg
29	Neg	59	Pos	89	Neg
30	Neg	60	Pos	90	Neg

[1] Clinical Signs: Pos=death, Neg=negative for clinical signs, including death

<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>Field Safety</td></tr>
<tr><td>Product Administration</td><td>One dose administered via the in ovo route.</td></tr>
<tr><td>Study Animals</td><td>Broiler chickens at 18 or 19 days of embryonation. Two independent study sites.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>Animals were observed daily for mortality through 21 days after vaccination.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><th>Location</th><th>Treatment</th><th>% Hatchability</th><th>Total Chicks Placed</th><th>21 Day Mortality</th><th>% Mortality</th><th>% Condemnation</th></tr>
<tr><td>1</td><td>Product Code 1A91.R0</td><td>88.09</td><td>33,300</td><td>578</td><td>1.74</td><td>0.034</td></tr>
<tr><td>1</td><td>Control</td><td>84.05</td><td>34,500</td><td>406</td><td>1.18</td><td>0.033</td></tr>
<tr><td>2</td><td>Product Code 1A91.R0</td><td>89.69</td><td>28,700</td><td>544</td><td>1.90</td><td>0.13</td></tr>
<tr><td>2</td><td>Control</td><td>88.00</td><td>28,700</td><td>462</td><td>1.61</td><td>0.18</td></tr>
</table>
No adverse reactions attributable to the vaccine were recorded.
</td></tr>
<tr><td>USDA Approval Date</td><td>August 1, 2017</td></tr>
</table>

<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>One dose administered via the subcutaneous route.</td></tr>
<tr><td>Study Animals</td><td>Commercial chickens at day of age. Chickens were observed daily for 22 days after vaccination.</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 rowspan="2">Location</th><th rowspan="2">Vaccine Serial No./Treatment Group</th><th rowspan="2">No. of Chickens Vaccinated</th><th rowspan="2">No. of Birds Placed</th><th colspan="2">Mortality</th><th rowspan="2">Observations</th></tr>
<tr><th>Total No. of Deaths</th><th>Percent</th></tr>
<tr><td rowspan="2">PA</td><td>377-001</td><td>20,000</td><td>20,000</td><td>208</td><td>1.04%</td><td>No adverse reactions</td></tr>
<tr><td>control</td><td>19,998</td><td>19,998</td><td>155</td><td>0.77%</td><td>No adverse reactions</td></tr>
<tr><td rowspan="2">MD</td><td>377-002</td><td>86,500</td><td>86,500</td><td>534</td><td>0.62%</td><td>No adverse reactions</td></tr>
<tr><td>control</td><td>86,600</td><td>86,600</td><td>512</td><td>0.59%</td><td>No adverse reactions</td></tr>
</table>

No adverse reactions attributable to the vaccine were recorded.</td></tr>
<tr><td>USDA Approval Date</td><td>October 4, 2017</td></tr>
</table>