Summary of Studies Supporting USDA Product Licensure

Establishment Name	Ceva Animal Health, LLC
USDA Vet Biologics Establishment Number	368
Product Code	1A89.R0
True Name	Bursal Disease-Marek's Disease-Newcastle Disease Vaccine, Serotype 3, Live Marek's Disease Vector
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Biomune Company Ultifend IBD ND - Biomune Company
Date of Compilation Summary	June 08, 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)

Study Type	Efficacy
Pertaining to	Infectious Bursal Disease Virus (IBDV) USDA Standard
Study Purpose	To demonstrate effectiveness against IBDV USDA Standard strain
Product Administration	1. One dose administered by the subcutaneous route (SQ) 2. One dose administered by the *in ovo* route
Study Animals	1. 30 SPF chickens per treatment group vaccinated at day of age by the SQ route 2. 30 SPF chicken embryos per treatment group vaccinated at 18 days of incubation by the *in ovo* route 3. 30 SPF chicken embryos per treatment group placebo-vaccinated at 18 days of incubation by the *in ovo* route as Positive Controls 4. 30 SPF chickens per treatment group placebo-vaccinated at day of age by the SQ route and non-challenged as Negative Controls
Challenge Description	IBDV USDA Standard strain at 35 days of age, except the Negative Control group
Interval observed after challenge	Daily observation for 4 days post challenge; tissues examined at 4 days post challenge for IBDV.
Results	A chicken was considered affected by the challenge (positive) if grossly observable lesions caused by the IBDV USDA Standard challenge were present. *In ovo* vaccination: 3/30 vaccinates were affected by the challenge. SQ vaccination: 3/30 vaccinates were affected by the challenge. Controls: 27/30 Positive Controls and 0/30 Negative Controls were affected by the challenge. Raw data are shown on the attached page.
USDA Approval Date	February 12, 2016

In ovo Vaccinate ID	Infectious Bursal Disease Lesions[1]	SQ[2] Vaccinate ID	Infectious Bursal Disease Lesions[1]	Positive Control ID	Infectious Bursal Disease Lesions[1]	Negative Control ID	Infectious Bursal Disease Lesions[1]
1	E,Y	31	NA	61	Y,P	91	NA
2	NA	32	NA	62	A,P	92	NA
3	NA	33	NA	63	Y,P	93	NA
4	NA	34	NA	64	A,Y,P	94	NA
5	NA	35	NA	65	A,Y,P	95	NA
6	NA	36	NA	66	NA	96	NA
7	A,P	37	A,E	67	Y,E	97	NA
8	NA	38	NA	68	A,Y,P	98	NA
9	A,E	39	NA	69	A,Y	99	NA
10	NA	40	NA	70	A,Y	100	NA
11	NA	41	NA	71	A,Y,P	101	NA
12	NA	42	NA	72	NA	102	NA
13	NA	43	NA	73	Y,P	103	NA
14	NA	44	NA	74	A,E	104	NA
15	NA	45	NA	75	A,E	105	NA
16	NA	46	NA	76	NA	106	NA
17	NA	47	NA	77	A,Y,P	107	NA
18	NA	48	NA	78	A	108	NA
19	NA	49	Y,E	79	Y,P	109	NA
20	NA	50	NA	80	Y,P	110	NA
21	NA	51	NA	81	Y,P	111	NA
22	NA	52	NA	82	Y,P	112	NA
23	NA	53	A,Y	83	A,E	113	NA
24	NA	54	NA	84	A,E	114	NA
25	NA	55	NA	85	Y,E	115	NA
26	NA	56	NA	86	A,E	116	NA
27	NA	57	NA	87	Y,P, M	117	NA
28	NA	58	NA	88	A,Y,P	118	NA
29	NA	59	NA	89	A,P	119	NA
30	NA	60	NA	90	A	120	NA

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

[2] = Subcutaneous

Study Type	Efficacy
Pertaining to	Marek's Disease Virus
Study Purpose	To demonstrate effectiveness against Marek's Disease Virus (MDV)
Product Administration	1. One dose administered by the *in ovo* route 2. One dose administered by the subcutaneous route (SQ)
Study Animals	1. 45 SPF chicken embryos per treatment group vaccinated at 18 days of incubation with product (*in ovo* vaccinate) 2. 45 SPF chickens per treatment group vaccinated at day of age with product (SQ vaccinate) 3. 45 SPF chickens per treatment group vaccinated at at 18 days of incubation with placebo-matched vaccine (positive control) 4. 45 SPF chickens per treatment group vaccinated at day of age with placebo-matched vaccine (negative control)
Challenge Description	Marek's Disease Virus GA strain at five days of age for all except the negative control group
Interval observed after challenge	Daily observation for 45 days post challenge; Tissues examined at 45 days post challenge
Results	A chicken was considered affected by the challenge (positive) if grossly observable lesions caused by the MDV GA challenge were present. *In ovo* vaccination: 9/45 (20%) vaccinates were affected by the challenge. SQ vaccination: 6/45 (13%) vaccinates were affected by the challenge. Controls: 37/45 (82%) positive controls were affected by the challenge. 0/45 (0%) negative controls were affected by the challenge. Raw data are shown on the attached page.
USDA Approval Date	February 2, 2016

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

[1] Tissue with lesion: K=kidney, Sp=spleen, L=liver, H=heart, G=gonad, N=nerves, Sk=skin, E=eye, M=muscle, 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

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 subcutaneous route (SQ)
Study Animals	1. 30 SPF chickens per treatment group vaccinated at day of age by the SQ route 2. 30 SPF chickens embryos per treatment group placebo-vaccinated at 18 days of incubation by the *in ovo* route as Positive Controls 3. 30 SPF chickens per treatment group placebo-vaccinated at day of age by the SQ route non-challenged as Negative Controls
Challenge Description	NDV Texas GB Standard strain at 28 days of age, except the Negative Control group
Interval observed after challenge	Daily observation for 14 days post challenge for clinical signs of NDV
Results	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 0/30 Negative Controls were affected by the challenge, NDV Texas GB. Raw data are shown on the attached page.
USDA Approval Date	April 28, 2016

Vaccinate ID	Clinical Signs of Newcastle Disease[1]	Positive Control ID	Clinical Signs of Newcastle Disease[1]	Negative Control ID	Clinical Signs of Newcastle Disease[1]
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	Neg	37	Pos	67	Neg
8	Neg	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	Neg	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.
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<tr><td>USDA Approval Date</td><td>August 1, 2017</td></tr>
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<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>
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