Summary of Studies Supporting USDA Product Licensure

Establishment Name	Ceva Animal Health, LLC
USDA Vet Biologics Establishment Number	368
Product Code	1A91.R1
True Name	Bursal Disease-Marek's Disease-Newcastle Disease Vaccine, Serotypes 1 & 3, Live Virus, Live Marek's Disease Vector
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Ultifend IBD ND + Rispens - No distributor specified
Date of Compilation Summary	July 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 subcutaneous route (SQ)
Study Animals	1. 30 maternal antibody-positive chickens per treatment group vaccinated at day of age by the SQ route 2. 30 maternal antibody-positive chickens placebo-vaccinated as Positive Controls at day of age by the SQ route 3. 30 maternal antibody-positive chickens non-vaccinated and non-challenged as Negative Controls
Challenge Description	IBDV USDA Standard strain at 64 days of age. No challenge was administered to the Negative Controls group.
Interval observed after challenge	Daily observation for 4 days post challenge for clinical signs of IBDV. Tissue examination 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. 1/30 vaccinates, 28/30 Positive Controls and 0/30 Negative Controls were affected by the challenge, IBDV USDA Standard. Raw data are shown on the attached pages.
USDA Approval Date	03/20/17

Vaccinate ID	Infectious Bursal Disease Lesions[1]	Positive Control ID	Infectious Bursal Disease Lesions[1]	Negative Control ID	Infectious Bursal Disease Lesions[1]
1	NA	61	P,E	121	NA
2	NA	62	P,E	122	NA
3	NA	63	P,E	123	NA
4	NA	64	P,E	124	NA
5	NA	65	P,E	125	NA
6	NA	66	P,E	126	NA
7	NA	67	P,E	127	NA
8	NA	68	P,E	128	NA
9	NA	69	P,E,M	129	NA
10	NA	70	P,E	130	NA
11	NA	71	P,E	131	NA
12	NA	72	NA	132	NA
13	NA	73	P,E	133	NA
14	NA	74	P,E,M	134	NA
15	NA	75	P,E,M	135	NA
16	NA	76	P,E	136	NA
17	NA	77	P,E,M	137	NA
18	P,E	78	P,E	138	NA
19	NA	79	P,E,M	139	NA
20	NA	80	P,E	140	NA
21	NA	81	P,E	141	NA
22	NA	82	P,E	142	NA
23	NA	83	P,E,M	143	NA
24	NA	84	P,E	144	NA
25	NA	85	P,E,M	145	NA
26	NA	86	P,E	146	NA
27	NA	87	P,E,M	147	NA
28	NA	88	P,E	148	NA
29	NA	89	NA	149	NA
30	NA	90	P,E	150	NA

[1] Gross lesion: 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)
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 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 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. 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

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]
31	NA	61	Y,P	91	NA
32	NA	62	A,P	92	NA
33	NA	63	Y,P	93	NA
34	NA	64	A,Y,P	94	NA
35	NA	65	A,Y,P	95	NA
36	NA	66	NA	96	NA
37	A,E	67	Y,E	97	NA
38	NA	68	A,Y,P	98	NA
39	NA	69	A,Y	99	NA
40	NA	70	A,Y	100	NA
41	NA	71	A,Y,P	101	NA
42	NA	72	NA	102	NA
43	NA	73	Y,P	103	NA
44	NA	74	A,E	104	NA
45	NA	75	A,E	105	NA
46	NA	76	NA	106	NA
47	NA	77	A,Y,P	107	NA
48	NA	78	A	108	NA
49	Y,E	79	Y,P	109	NA
50	NA	80	Y,P	110	NA
51	NA	81	Y,P	111	NA
52	NA	82	Y,P	112	NA
53	A,Y	83	A,E	113	NA
54	NA	84	A,E	114	NA
55	NA	85	Y,E	115	NA
56	NA	86	A,E	116	NA
57	NA	87	Y,P, M	117	NA
58	NA	88	A,Y,P	118	NA
59	NA	89	A,P	119	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 (MDV) RB1/B strain
Study Purpose	To demonstrate effectiveness against MDV RB1/B
Product Administration	One dose administered by the subcutaneous route (SQ)
Study Animals	1. 45 SPF chickens per treatment group vaccinated at day of age by the SQ route 2. 45 SPF chickens per treatment group HVT Serotype 3 vaccinated controls at day of age by the SQ route 3. 45 SPF chickens per treatment group placebo-vaccinated at day of age by the SQ route as Positive Controls 4. 50 SPF chickens per treatment group placebo-vaccinated at day of age by the SQ route and non-challenged as Negative Controls
Challenge Description	MDV RB1/B strain at five days of age except Negative controls
Interval observed after challenge	Daily observation for 44 days post challenge; tissues examined at 44 days post challenge for MDV
Results	A chicken was considered affected by the challenge (positive) if grossly observable lesions caused by the MDV RB1/B challenge were present. 0/45 vaccinates, 17/45 HVT serotype 3 vaccinate controls, 42/44 Positive Controls and 0/49 Negative Controls were affected by the challenge, MDV RB1/B. Raw data are shown on the attached page.
USDA Approval Date	February 18, 2016

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

2 This chicken died at 15 days of age, death not attributable to vaccination

3 This chicken died at 9 days of age, death not attributable to vaccination

Study Type	Efficacy
Pertaining to	Newcastle disease virus (NDV) Texas GB strain
Study Purpose	The objective of this study was to demonstrate (i) Subcutaneous (SQ) efficacy in Mab-positive chickens challenged with NDV Texas GB strain, and (ii) the Rispens fraction does not interfere with protection against NDV Texas GB challenge.
Product Administration	One 0.2 mL SQ dose was administered at day of age.
Study Animals	Day-old chicks were divided into 5 groups Group 1. 30 vaccinated NDV-challenged. Group 2. 30 placebo-vaccinated NDV-challenged positive control. Group 3. 30 placebo-vaccinated non-challenged negative control. Group 4. 10 maternal antibody-positive chickens, non-vaccinated, NDV-challenged to show presence of maternal antibodies. Group 5. 10 SPF chickens, non-vaccinated, NDV-challenged to show susceptibility to NDV challenge.
Challenge Description	NDV Texas GB challenge strain
Interval observed after challenge	Daily for 14 days post challenge.
Results	Vaccinates and controls were evaluated for the presence or absence of clinical signs and mortality consistent with Newcastle disease (ND). Clinical signs associated with ND include respiratory signs such as increased respiration rate and depth, nasal exudate, and swelling of eyes and head; neurologic signs such as tremors, loss of coordination and paralysis, viscerotropic signs such as listlessness, weakness, diarrhea, and prostration; and mortality. Birds with ND clinical signs Group 1: 0/30 Group 2: 30/30 Group 3: 0/30 Group 4: 0/10 Group 5: 10/10 Raw Data is as follows on the pages below. The absence or presence of ND clinical signs are defined as the following: Neg is Negative or absent for clinical signs. Pos is Positive or clinical signs were present.

Tag No.	Group ID	NDV Clinical Signs
541	1	Neg
544	1	Neg
547	1	Neg
549	1	Neg
550	1	Neg
552	1	Neg
554	1	Neg
555	1	Neg
561	1	Neg
572	1	Neg
581	1	Neg
583	1	Neg
587	1	Neg
590	1	Neg
592	1	Neg
596	1	Neg
599	1	Neg
603	1	Neg
611	1	Neg
620	1	Neg
624	1	Neg
630	1	Neg
632	1	Neg
638	1	Neg
650	1	Neg
663	1	Neg
665	1	Neg
670	1	Neg
671	1	Neg
672	1	Neg

Tag No.	Group ID	NDV Clinical Signs
543	2	Pos
545	2	Pos
558	2	Pos
567	2	Pos
574	2	Pos
578	2	Pos
579	2	Pos
586	2	Pos
588	2	Pos
593	2	Pos
598	2	Pos
605	2	Pos
609	2	Pos
613	2	Pos
627	2	Pos
631	2	Pos
634	2	Pos
635	2	Pos
637	2	Pos
643	2	Pos
644	2	Pos
645	2	Pos
651	2	Pos
652	2	Pos
653	2	Pos
656	2	Pos
658	2	Pos
662	2	Pos
664	2	Pos
674	2	Pos

Tag No.	Group ID	NDV Clinical Signs
542	3	Neg
557	3	Neg
559	3	Neg
563	3	Neg
564	3	Neg
568	3	Neg
570	3	Neg
571	3	Neg
585	3	Neg
594	3	Neg
600	3	Neg
602	3	Neg
607	3	Neg
612	3	Neg
614	3	Neg
617	3	Neg
622	3	Neg
628	3	Neg
629	3	Neg
646	3	Neg
647	3	Neg
648	3	Neg
655	3	Neg
659	3	Neg
661	3	Neg
666	3	Neg
667	3	Neg
668	3	Neg
669	3	Neg
675	3	Neg

Tag No.	Group ID	NDV Clinical Signs
546	4	Neg
553	4	Neg
575	4	Neg
582	4	Neg
608	4	Neg
621	4	Neg
626	4	Neg
641	4	Neg
642	4	Neg
673	4	Neg

Tag No.	Group ID	NDV Clinical Signs
556	5	Pos
565	5	Pos
573	5	Pos
580	5	Pos
604	5	Pos
606	5	Pos
615	5	Pos
633	5	Pos
640	5	Pos
657	5	Pos

USDA Approval Date	March 22, 2017

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>Demonstrate safety of the product under typical use conditions.</td></tr>
<tr><td>Product Administration</td><td>Single dose administered by the subcutaneous route.</td></tr>
<tr><td>Study Animals</td><td>Commercial chickens served as vaccinates and controls. Animals were observed daily for mortality through 21 days after vaccination.
Studies were performed at three independent study sites.</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">Treatment Group</th><th rowspan="2">No. of Chickens Vaccinated</th><th rowspan="2">No. of Chickens Placed</th><th colspan="2">21 Day Mortality</th></tr>
<tr><th>Total No. of Deaths</th><th>Percent (%)</th></tr>
<tr><td rowspan="2">Site 1</td><td>Vaccinates</td><td>80,766</td><td>80,766</td><td>1,232</td><td>1.53</td></tr>
<tr><td>Control</td><td>78,834</td><td>78,834</td><td>744</td><td>0.94</td></tr>
<tr><td rowspan="2">Site 2</td><td>Vaccinates</td><td>64,854</td><td>64,854</td><td>648</td><td>1.00</td></tr>
<tr><td>Control</td><td>45,943</td><td>32,090</td><td>483</td><td>1.51</td></tr>
<tr><td rowspan="2">Site 3</td><td>Vaccinates</td><td>97,829</td><td>97,829</td><td>1,132</td><td>1.16</td></tr>
<tr><td>Control</td><td>89,260</td><td>86,460</td><td>1,467</td><td>1.70</td></tr>
</table>

No adverse reactions attributable to the vaccine were recorded.
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<tr><td>USDA Approval Date</td><td>March 12, 2021</td></tr>
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