Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	1431.5A
True Name	Coccidiosis Vaccine, Live Oocysts
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Coccivac-B52 - Merck Animal Health Coccivac-B52 - No distributor specified Coccivac-D2 - Merck Animal Health Fortegra - Intervet Argentina S.A. Fortegra - Intervet Argentina S.A. - Merck Sharpe and Dohme (MSD) Fortegra - Intervet LLC-Russia - Merck Sharpe and Dohme (MSD) Fortegra - Intervet South Africa (Pty) Ltd. Fortegra - Intervet South Africa (Pty) Ltd. - Merck Sharpe and Dohme (MSD) Fortegra - Intervet Thailand Ltd Fortegra - Intervet Veterinaria Chile Ltda Fortegra - Merck Sharp & Dohme Saude Animal Ltda. Fortegra - No distributor specified Merck Animal Health Merck Sharp & Dohme Saude Animal Ltda.
Date of Compilation Summary	October 12, 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	Eimeria acervulina
Study Purpose	Demonstrate efficacy against Eimeria acervulina
Product Administration	Single dose, administered via spray cabinet
Study Animals	Commercial broilers, one day of age, 28 vaccinates, 27 challenged controls, and 25 non-challenged controls
Challenge Description	Eimeria acervulina, given 21 days after vaccination
Interval observed after challenge	Disease-related intestinal changes (lesions) evaluated 6 days after challenge
Results	Intestines were scored by the following criteria: 0 = No lesions 1 = Petechial hemorrhage in the duodenum 2 = White lesions in the duodenum and upper half of the small intestine 3 = White lesions in the upper half of the small intestine with slight swelling 4 = White lesions, coalescing, sometimes death.

Group	Lesion Score										All
	0		1		2		3		4		
	N	%	N	%	N	%	N	%	N	%	N
Non-challenged Control	22	88.0	3	12.0	0	0	0	0	0	0	25
Challenged Control	8	29.6	2	7.4	0	0	5	18.5	12	44.4	27
Vaccinate	9	32.1	12	42.9	3	10.7	2	7.1	2	7.1	28

*Birds were considered affected by challenge (i.e., positive) if they had a lesion score ≥2.

The above study did not meet expectations of 80% challenged controls positive and 80% vaccinates negative. Therefore 3 product batches (serials) were assessed in a similar manner:

Serial	Vaccinate Lesion Scores	
	0 or 1+	2+, 3+, or 4+
401-09	10/10	0/10
402-09	10/10	0/10
403-09	10/10	0/10

All challenged controls in these studies had scores of ≥2.

Regulatory approval was based on the cumulative results of all the above.

USDA Approval Date	August 4, 2010

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Eimeria maxima</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate efficacy against Eimeria maxima</td></tr>
<tr><td>Product Administration</td><td>Single dose, administered via spray cabinet</td></tr>
<tr><td>Study Animals</td><td>Commercial broilers, one day of age, 28 vaccinates and 29 controls and 25 non-challenged</td></tr>
<tr><td>Challenge Description</td><td>Eimeria maxima given orally 21 days after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Disease-related intestinal changes (lesions) evaluated 6 days after challenge</td></tr>
<tr><td>Results</td><td>Intestines were scored by the following criteria:
0 = No lesions
1 = Petechial hemorrhage in the duodenum
2 = White lesions in the duodenum and upper half of the small intestine
3 = White lesions in the upper half of the small intestine with slight swelling
4 = White lesions, coalescing, sometimes death.

<table>
<tr><th rowspan="2">Group</th><th colspan="10">Lesion Score</th><th rowspan="2">All</th></tr>
<tr><th colspan="2">0</th><th colspan="2">1</th><th colspan="2">2</th><th colspan="2">3</th><th colspan="2">4</th></tr>
<tr><th></th><th>N</th><th>%</th><th>N</th><th>%</th><th>N</th><th>%</th><th>N</th><th>%</th><th>N</th><th>%</th><th>N</th></tr>
<tr><td>Non-challenged Control</td><td>22</td><td>88.0</td><td>1</td><td>4.0</td><td>2</td><td>8.0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>25</td></tr>
<tr><td>Challenged Control</td><td>2</td><td>6.9</td><td>3</td><td>10.3</td><td>5</td><td>17.2</td><td>11</td><td>37.9</td><td>8</td><td>27.6</td><td>29</td></tr>
<tr><td>Vaccinate</td><td>14</td><td>50.0</td><td>5</td><td>17.9</td><td>4</td><td>14.3</td><td>5</td><td>17.9</td><td>0</td><td>0</td><td>28</td></tr>
</table>
*Birds were considered affected by challenge (i.e., positive) if they had a lesion score ≥2.

The above study did not meet expectations of 80% challenged controls positive and 80% vaccinates negative. Therefore 3 product batches (serials) were assessed in a similar manner:
<table>
<tr><th rowspan="2">Serial</th><th colspan="2">Vaccinate Lesion Scores</th></tr>
<tr><th>0 or 1+</th><th>1+, 2+, or 3+</th></tr>
<tr><td rowspan="2">401-09</td><td>9/10</td><td>1/10</td></tr>
<tr><td>8/10</td><td>2/10</td></tr>
<tr><td rowspan="2">402-09</td><td>9/10</td><td>1/10</td></tr>
<tr><td>8/10</td><td>2/10</td></tr>
<tr><td>403-09</td><td>10/10</td><td>0/10</td></tr>
</table>
All challenged controls in these studies had scores of ≥2.</td></tr>
</table>

	Regulatory approval was based on the cumulative results of all the above.
USDA Approval Date	August 4, 2010

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Eimeria mivati</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate effectiveness again E. mivati.</td></tr>
<tr><td>Product Administration</td><td>Single dose, administered via spray cabinet</td></tr>
<tr><td>Study Animals</td><td>Commercial broilers, one day of age, 26 vaccinates and 25 controls</td></tr>
<tr><td>Challenge Description</td><td>Eimeria mivati given 21 days after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Disease-related intestinal changes (lesions) evaluated 6 days after challenge.</td></tr>
<tr><td>Results</td><td>Intestinal lesions were scored by the following criteria:
0 = No lesions
1 = Petechial hemorrhage throughout the small intestine, especially the upper half
2 = White lesions throughout the entire small intestine, especially the upper half
3 = While lesions and swelling throughout the entire small intestine, especially upper half
4 = White hemorrhage, lesions, coalescing, sometimes death

<table>
<tr><td rowspan="3">Group</td><td colspan="10">Lesion Score</td><td></td></tr>
<tr><td colspan="2">0</td><td colspan="2">1</td><td colspan="2">2</td><td colspan="2">3</td><td colspan="2">4</td><td>All</td></tr>
<tr><td>N</td><td>%</td><td>N</td><td>%</td><td>N</td><td>%</td><td>N</td><td>%</td><td>N</td><td>%</td><td>N</td></tr>
<tr><td>Challenged Controls</td><td>3</td><td>12</td><td>0</td><td>0</td><td>1</td><td>4</td><td>4</td><td>16</td><td>17</td><td>68</td><td>25</td></tr>
<tr><td>Vaccinates</td><td>20</td><td>76.9</td><td>5</td><td>19.2</td><td>0</td><td>0</td><td>1</td><td>3.8</td><td>0</td><td>0</td><td>26</td></tr>
</table>

*Birds were considered affected by challenge (i.e. positive) if they had a lesion score ≥2. By this criterion:
<table>
<tr><th>Treatment Group</th><th>#Positive*/Total</th></tr>
<tr><td>Vaccinates</td><td>1/26</td></tr>
<tr><td>Controls</td><td>22/25</td></tr>
</table>

Raw data shown on attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>August 4, 2010</td></tr>
</table>

Summary of Gross Lesion Scores

Challenge Controls		Vaccinates	
Bird I.D.	Emi	Bird I.D.	Emi
91	4	511	0
94	3	515	0
606	4	521	0
609	2	523	0
623	4	525	0
625	0	532	0
641	4	536	0
645	4	539	1
656	4	543	1
662	4	548	3
704	4	551	0
709	0	560	0
710	4	576	0
712	0	577	0
713	4	578	0
714	4	585	0
717	3	592	0
721	4	594	1
723	3	598	0
724	4	599	0
732	4	685	1
737	4	687	0
743	4	690	0
754	4	693	0
756	3	695	1
		696	0

Emi is Eimeria score

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Eimeria tenella</td></tr>
<tr><td>Study Purpose</td><td>Demonstrate effectiveness again E. tenella.</td></tr>
<tr><td>Product Administration</td><td>Single dose, administered via spray cabinet</td></tr>
<tr><td>Study Animals</td><td>Commercial broilers, one day of age, 19 vaccinates and 28 controls</td></tr>
<tr><td>Challenge Description</td><td>Eimeria tenella given 21 days after vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>Disease-related intestinal changes (lesions) evaluated 6 days after challenge.</td></tr>
<tr><td>Results</td><td>Intestinal lesions were scored by the following criteria:
0 = No lesions
1 = Few petechial hemorrhages
2 = Petechial hemorrhages in the ceca, ceca walls thickened
3 = Slightly bloody ceca
4 = Cecal walls extended with blood or cores, +/- death

<table>
<tr><th rowspan="3">Group</th><th colspan="10">Lesion Score</th><th></th></tr>
<tr><th colspan="2">0</th><th colspan="2">1</th><th colspan="2">2</th><th colspan="2">3</th><th colspan="2">4</th><th>All</th></tr>
<tr><th>N</th><th>%</th><th>N</th><th>%</th><th>N</th><th>%</th><th>N</th><th>%</th><th>N</th><th>%</th><th>N</th></tr>
<tr><td>Challenged Controls</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>28</td><td>100</td><td>28</td></tr>
<tr><td>Vaccinates</td><td>19</td><td>100</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>19</td></tr>
</table>

*Birds were considered affected by challenge (i.e. positive) if they had a lesion score ≥2. By this criterion:
<table>
<tr><th>Treatment Group</th><th>#Positive*/Total</th></tr>
<tr><td>Vaccinates</td><td>0/19</td></tr>
<tr><td>Controls</td><td>28/28</td></tr>
</table>

Raw data shown on attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>August 4, 2010</td></tr>
</table>

Summary of Gross Lesion Scores

Challenge Controls

Tag No.	Gross Lesion Score
691*	4
696	4
701*	4
706	4
711*	4
716*	4
721	4
726	4
731	4
736*	4
741	4
746*	4
751**	4
756	4
761*	4
771	4
776*	4
781*	4
786	4
791	4
901*	4
906	4
911*	4
916*	4
921	4
926*	4
931*	4
936*	4

Vaccinates

Tag No.	Gross Lesion Score
429	0
437	0
505	0
513	0
521	0
529	0
537	0
545	0
553	0
569	0
801	0
809	0
825	0
833	0
841	0
865	0
881	0
889	0
897	0

<table>
<tr><td>Study Type</td><td>Safety</td></tr>
<tr><td>Pertaining to</td><td>All fractions</td></tr>
<tr><td>Study Purpose</td><td>Field Safety</td></tr>
<tr><td>Product Administration</td><td>Single dose, administered via spray cabinet</td></tr>
<tr><td>Study Animals</td><td>Commercial Broilers at one day of age. 4 independent study sites.</td></tr>
<tr><td>Challenge Description</td><td>NA</td></tr>
<tr><td>Interval observed after challenge</td><td>Chicks were followed through grow-out to slaughter.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><th rowspan="2">Site</th><th rowspan="2">Number of chickens</th><th colspan="2">Mortality (%)</th><th colspan="2">Condemnation (%)</th></tr>
<tr><th>Vaccinates</th><th>Controls</th><th>Vaccinates</th><th>Controls</th></tr>
<tr><td>1</td><td>43,119</td><td>4.78</td><td>3.23</td><td>0.27</td><td>0.07</td></tr>
<tr><td>2</td><td>44,600</td><td>4.14</td><td>4.66</td><td>0.20</td><td>0.37</td></tr>
<tr><td>3</td><td>43,400</td><td>5.40</td><td>5.02</td><td>0.34</td><td>0.27</td></tr>
<tr><td>4</td><td>90,437</td><td>1.17</td><td>1.78</td><td>0.09</td><td>0.13</td></tr>
</table>
*Mortality and condemnation rates were within normal limits for each site
</td></tr>
<tr><td>USDA Approval Date</td><td>November 23, 2010</td></tr>
</table>