Summary of Studies Supporting USDA Product Licensure

Establishment Name	Diamond Animal Health, Inc.
USDA Vet Biologics Establishment Number	213
Product Code	9381.D0
True Name	DNA Immunostimulant
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Diamond Animal Health, Inc. Victrio - Bayer HealthCare LLC - Diamond Animal Health, Inc. Victrio - Bayer, Inc., Toronto, Canada Victrio - Bayer, S.A. Victrio - No distributor specified Zelnate - Bayer HealthCare LLC Zelnate - Bayer HealthCare LLC - Diamond Animal Health, Inc. Zelnate - Bayer, Inc., Toronto, Canada Zelnate - Bayer, S.A. Zelnate - Bayer, S.A. - Diamond Animal Health, Inc.
Date of Compilation Summary	October 24, 2018

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>DNA Immunostimulant</td></tr>
<tr><td>Study Purpose</td><td>Efficacy against bovine respiratory disease due to Mannheimia haemolytica</td></tr>
<tr><td>Product Administration</td><td>One dose administered by IM route at 24 hours <u>after</u> the time of challenge. Control group administered diluent only.</td></tr>
<tr><td>Study Animals</td><td>80 Holstein steers of average age 3.7 months; randomized into 2 groups of 40 calves each.</td></tr>
<tr><td>Challenge Description</td><td>All calves challenged with live M. haemolytica</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for 5 days after challenge. Lungs were evaluated on Day 5.</td></tr>
<tr><td>Results</td><td><u>Mortality:</u> The deaths prior to Day 5 were: 1/40 in Treated group; 8/40 in Control group. All deaths were diagnosed as related to fibrinous bronchopneumonia (severe bovine respiratory disease).

<u>Lung scores:</u> The percent of lung mass that was abnormal (consolidated) was calculated/scored for every animal. For animals that died prior to Day 5, the lung score was not included in the analysis.

5-number summary for lung consolidation:
<table>
<tr><th>Treatment</th><th>Minimum</th><th>Q_1</th><th>Median</th><th>Q3</th><th>Maximum</th></tr>
<tr><td>Controls</td><td>1%</td><td>10%</td><td>14%</td><td>29%</td><td>48%</td></tr>
<tr><td>Treated</td><td>1%</td><td>6%</td><td>11%</td><td>22%</td><td>61%</td></tr>
</table>
Raw data shown on attached page. The animals that died prior to Day 5 are marked with an asterisk (*).</td></tr>
<tr><td>USDA Approval Date</td><td>27-Jan-2014</td></tr>
</table>

Lung consolidation scores (%), in order of rank:

Treated	Control
1%	1%
1%	2%
2%	5%
2%	7%
3%	8%
3%	8%
3%	9%
3%	9%
3%	10%
6%	10%
6%	11%
7%	11%
8%	11%
8%	13%
9%	13%
10%	14%
11%	15%
11%	16%
11%	17%
11%	19%
11%	21%
13%	22%
15%	23%
15%	29%
17%	29%
18%	31%
19%	38%
20%	39%
22%	40%
23%	44%
26%	47%
28%	48%
29%	49% *
32%	51% *
33%	52% *
38%	54% *
38%	55% *
46% *	56% *
56%	57% *
61%	80% *

*** death prior to Day 5**

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>DNA Immunostimulant</td></tr>
<tr><td>Study Purpose</td><td>Efficacy against bovine respiratory disease due to Mannheimia haemolytica</td></tr>
<tr><td>Product Administration</td><td>One dose administered by intranasal route at the time of challenge, utilizing mucosal atomization device. Control group administered diluent only via IM route.</td></tr>
<tr><td>Study Animals</td><td>64 Holstein steers of 4-6 months of age; randomized into 2 groups of 32 calves each.</td></tr>
<tr><td>Challenge Description</td><td>All calves challenged with live M. haemolytica</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for 5 days. Lungs were evaluated on day 5.</td></tr>
<tr><td>Results</td><td>The deaths prior to Day 5 were:
1/32 in Treated group
9/32 in Control group
All deaths were diagnosed as related to severe bovine respiratory disease.

The percent of lung mass that was abnormal (consolidated) was calculated/scored for every animal. For animals that died prior to Day 5, the lung score is not included in the 5 number summary.

5 number summary for lung consolidation:
<table>
<tr><th>Treatment</th><th>Minimum</th><th>Q_1</th><th>Median</th><th>Q_3</th><th>Maximum</th></tr>
<tr><td>Controls</td><td>9%</td><td>20%</td><td>30%</td><td>41%</td><td>47%</td></tr>
<tr><td>Treated</td><td>9%</td><td>20%</td><td>26%</td><td>31%</td><td>52%</td></tr>
</table>
Raw data shown on attached page. The animals that died prior to Day 5 are marked with an asterisk (*).</td></tr>
<tr><td>USDA Approval Date</td><td>1-Jun-2016</td></tr>
</table>

Lung consolidation scores (%), in order of rank:

Treated	Control
9%	9%
13%	10%
15%	12%
16%	17%
17%	19%
17%	19%
18%	20%
20%	21%
21%	28%
22%	29%
23%	29%
24%	30%
25%	32%
26%	35%
26%	37%
26%	40%
27%	41%
27%	41%
27%	42%
28%	44%
29%	45%
30%	46% *
30%	46%
31%	47%
32%	57% *
32%	58% *
37%	59% *
43%	63% *
45%	65% *
49%	68% *
52%	76% *
73% *	83% *

*** death prior to Day 5**

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Mannheimia haemolytica</td></tr>
<tr><td>Study Purpose</td><td>Efficacy against bovine respiratory disease</td></tr>
<tr><td>Product Administration</td><td>One dose administered by IM route at the time of challenge.
Control group administered diluent only</td></tr>
<tr><td>Study Animals</td><td>64 Holstein steers of 3-4 months of age; randomized into 2 groups of 32 calves each</td></tr>
<tr><td>Challenge Description</td><td>live M. haemolytica inoculum</td></tr>
<tr><td>Interval observed after challenge</td><td>Observed daily for 5 days. Lungs were evaluated 5 days after challenge.</td></tr>
<tr><td>Results</td><td>The percent of lung mass that was abnormal (consolidated) was calculated/scored for every animal. For animals that died prior to Day 5, the necropsy lung score was not included in the analysis.

5 number summary for lung consolidation:
<table>
<tr><th>Treatment</th><th>Minimum</th><th>Q_1</th><th>Median</th><th>Q_3</th><th>Maximum</th></tr>
<tr><td>Controls</td><td>0%</td><td>6%</td><td>10%</td><td>15%</td><td>33%</td></tr>
<tr><td>Treated</td><td>0%</td><td>1%</td><td>4%</td><td>10%</td><td>22%</td></tr>
</table>
Raw data shown on attached page. The animals that died prior to Day 5 are marked with an asterisk (*).

The deaths prior to Day 5 were: 1/32 in Treated group; 1/32 in Control group. Diagnosis was severe peritonitis for calf in Treated group and severe bovine respiratory disease for calf in Control group.</td></tr>
<tr><td>USDA Approval Date</td><td>28-Feb-2013</td></tr>
</table>

Lung consolidation scores (%), in order of rank:

Treated	Control
0%	0%
0%	0%
1%	3%
1%	3%
1%	3%
1%	4%
1%	6%
1%	6%
2%	6%
2%	7%
3%	7%
3%	7%
3% *	8%
4%	8%
4%	10%
4%	10%
4%	10%
5%	10%
5%	10%
6%	11%
8%	13%
9%	14%
10%	15%
10%	15%
10%	18%
11%	18%
12%	21%
13%	23%
13%	27%
15%	29%
18%	33%
22%	34% *

*** death prior to Day 5**

Study Type	Safety
Pertaining to	ALL
Study Purpose	Demonstrate safety of product under field conditions.
Product Administration	One dose administered by IM route.
Study Animals	614 steers and heifers ranging in age from 3 months to greater than 6 months at 4 sites in Nebraska, Indiana (2 sites), and Missouri. Approximately one-third of the population was of the minimum age of 3 months.
Challenge Description	NA
Interval observed after challenge	All animals were observed for 21 days after treatment. The injection site was palpated on day 3 or 4 after treatment.
Results	No injection site lesions were observed. No adverse events were found attributable to the product per the investigators. There were a total of 51 adverse events which occurred at two of the sites, the majority (47/51) of these were determined to be the result of sequelae from Bovine Respiratory Disease on clinical signs. Two additional events were determined to be the result of either abdominal pain (due to bloat) or corneal oedema/blephar-ospasm (due to to corneal injury). In addition, two animals died during the study and necropsy findings indicated the cause of death was tracheal edema/collapse syndrome or fibrinous bronchopneumonia. None of these adverse events were ascribed by the co-operators (investigators) to the experimental product.
USDA Approval Date	24-Apr-2014

Study Type	Safety
Pertaining to	All
Study Purpose	Safety by intranasal route in cattle
Product Administration	
Study Animals	
Challenge Description	
Interval observed after challenge	
Results	Study data are not available