



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Elanco US Inc.
USDA Vet Biologics Establishment Number	196
Product Code	7906.R0
True Name	Mannheimia Haemolytica Bacterial Extract-Toxoid
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Nuplura PH - Elanco US Inc.
Date of Compilation Summary	February 20, 2020

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	<i>Mannheimia haemolytica</i>																		
Study Purpose	To demonstrate the efficacy in calves against <i>M. haemolytica</i>																		
Product Administration	1 dose, given subcutaneously																		
Study Animals	30 calves, ≤ 3 months of age. 20 vaccinates and 10 controls.																		
Challenge Description	<i>M. Haemolytica</i> , administered on 10 days after vaccination.																		
Interval observed after challenge	Lungs evaluated 4 days after challenge																		
Results	<p>The percent of the lung mass that was abnormal (consolidated) was calculated for every animal.</p> <p>5-number summary for lung consolidation (%)</p> <table border="1"> <thead> <tr> <th><i>Treatment</i></th> <th><i>Minimum</i></th> <th><i>Q1</i></th> <th><i>Median</i></th> <th><i>Q3</i></th> <th><i>Maximum</i></th> </tr> </thead> <tbody> <tr> <td><i>Controls</i></td> <td>4.6</td> <td>20.6</td> <td>23</td> <td>52.3</td> <td>57.8</td> </tr> <tr> <td><i>Vaccinates</i></td> <td>1.0</td> <td>6.5</td> <td>9.9</td> <td>14.7</td> <td>41.3</td> </tr> </tbody> </table> <p>Raw data shown on attached page.</p>	<i>Treatment</i>	<i>Minimum</i>	<i>Q1</i>	<i>Median</i>	<i>Q3</i>	<i>Maximum</i>	<i>Controls</i>	4.6	20.6	23	52.3	57.8	<i>Vaccinates</i>	1.0	6.5	9.9	14.7	41.3
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USDA Approval Date	June 5, 2009																		

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

Vaccinate	Control
0.97	4.61
1.69	13.35
3.66	20.63
4.45	20.65
5.95	20.66
7.13	25.4
7.2	26.35
7.25	52.25
7.35	55.85
9.48	57.75
10.25	
10.93	
11.21	
12.26	
12.86	
16.45	
16.59	
20.4	
38.25	
41.3	

Study Type	Safety																																																																									
Pertaining to	All																																																																									
Study Purpose	To demonstrate safety under typical field conditions																																																																									
Product Administration	Calves were administered a single dose subcutaneously.																																																																									
Study Animals	A total of 626 calves in 3 separate geographical sites were used in this study. 208 calves were 5-28 days of age; other calves were 4-12 months of age.																																																																									
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Interval observed after challenge	Animals were observed for 2 hours following vaccination. On days 1, 2, 7, 14, and 21 calves were observed under normal housing conditions for overall health status. On days 7 and 21, injection site location on each calf was palpated and recorded. If the injection site reaction was larger than a walnut on day 21, the animal was palpated on Day 35.																																																																									
Results	<p>The only adverse reactions observed were transient injection site reactions.</p> <p style="text-align: center;">Number of Animals with Swelling Observed</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: center;">Observation Day Site 1</th> <th style="text-align: center;">No palpable swelling</th> <th style="text-align: center;">Palpable swelling ≤ pea size</th> <th style="text-align: center;">Palpable swelling > pea and < walnut size</th> <th style="text-align: center;">Palpable swelling > walnut size</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">Day 7*</td> <td style="text-align: center;">17</td> <td style="text-align: center;">1</td> <td style="text-align: center;">72</td> <td style="text-align: center;">117</td> </tr> <tr> <td style="text-align: center;">Day 21**</td> <td style="text-align: center;">64</td> <td style="text-align: center;">50</td> <td style="text-align: center;">93</td> <td style="text-align: center;">0</td> </tr> <tr> <th style="text-align: center;">Observation Day Site 2</th> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">Day 1</td> <td style="text-align: center;">20</td> <td style="text-align: center;">30</td> <td style="text-align: center;">18</td> <td style="text-align: center;">138</td> </tr> <tr> <td style="text-align: center;">Day 2</td> <td style="text-align: center;">49</td> <td style="text-align: center;">23</td> <td style="text-align: center;">33</td> <td style="text-align: center;">103</td> </tr> <tr> <td style="text-align: center;">Day 7</td> <td style="text-align: center;">74</td> <td style="text-align: center;">31</td> <td style="text-align: center;">80</td> <td style="text-align: center;">23</td> </tr> <tr> <td style="text-align: center;">Day 21**</td> <td style="text-align: center;">118</td> <td style="text-align: center;">51</td> <td style="text-align: center;">34</td> <td style="text-align: center;">4</td> </tr> <tr> <th style="text-align: center;">Observation Day Site 3</th> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td style="text-align: center;">Day 1</td> <td style="text-align: center;">47</td> <td style="text-align: center;">46</td> <td style="text-align: center;">78</td> <td style="text-align: center;">246</td> </tr> <tr> <td style="text-align: center;">Day 2</td> <td style="text-align: center;">64</td> <td style="text-align: center;">30</td> <td style="text-align: center;">143</td> <td style="text-align: center;">181</td> </tr> <tr> <td style="text-align: center;">Day 7</td> <td style="text-align: center;">113</td> <td style="text-align: center;">53</td> <td style="text-align: center;">305</td> <td style="text-align: center;">155</td> </tr> <tr> <td style="text-align: center;">Day 21</td> <td style="text-align: center;">222</td> <td style="text-align: center;">126</td> <td style="text-align: center;">261</td> <td style="text-align: center;">15</td> </tr> <tr> <td style="text-align: center;">Day 35</td> <td style="text-align: center;">2</td> <td style="text-align: center;">5</td> <td style="text-align: center;">8</td> <td style="text-align: center;">0</td> </tr> </tbody> </table> <p>*Palpation not performed on Day 1 or Day 2 **No palpation required on Day 35</p>				Observation Day Site 1	No palpable swelling	Palpable swelling ≤ pea size	Palpable swelling > pea and < walnut size	Palpable swelling > walnut size	Day 7*	17	1	72	117	Day 21**	64	50	93	0	Observation Day Site 2					Day 1	20	30	18	138	Day 2	49	23	33	103	Day 7	74	31	80	23	Day 21**	118	51	34	4	Observation Day Site 3					Day 1	47	46	78	246	Day 2	64	30	143	181	Day 7	113	53	305	155	Day 21	222	126	261	15	Day 35	2	5	8	0
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