Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	19N1.20
True Name	Bovine Coronavirus Vaccine, Modified Live Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Bovilis Coronavirus - Merck Animal Health Bovilis Coronavirus - No distributor specified
Date of Compilation Summary	August 05, 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.

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Bovine Coronavirus (BCV)</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness against enteric disease caused by BCV.</td></tr>
<tr><td>Product Administration</td><td>One dose administered by the intranasal route</td></tr>
<tr><td>Study Animals</td><td>44, 3-5 day old calves in 3 cohorts, distributed equally into vaccinates & controls. Controls received a product-matched placebo. Each cohort was vaccinated at different times based on shipping dates.</td></tr>
<tr><td>Challenge Description</td><td>Calves were challenged on the same day with BCV approximately 4 weeks following the last cohort vaccination (Study Day 36).</td></tr>
<tr><td>Interval observed after challenge</td><td>All calves were observed for signs of enteric disease (diarrhea) for 15 days post-challenge.</td></tr>
<tr><td>Results</td><td>Calves were considered positive for enteric disease if they had a diarrhea score >1 for two or more consecutive days post-challenge.

Number of vaccinates and controls (out of the total) that are positive for enteric disease.
<table>
<tr><th>Cohort</th><th>Product Administration</th><th>Challenge in Days after Product Administration</th><th>Vaccinates*</th><th>Controls**</th></tr>
<tr><td>1</td><td>SD*** 0</td><td>33</td><td>5/8</td><td>4/7</td></tr>
<tr><td>2</td><td>SD 3</td><td>29</td><td>2/8</td><td>8/10</td></tr>
<tr><td>3</td><td>SD 7</td><td>26</td><td>1/4</td><td>4/5</td></tr>
<tr><td>Total</td><td></td><td></td><td>8/20</td><td>16/22</td></tr>
</table>
* 2 vaccinates were excluded from the study prior to challenge due to unrelated causes.
** 2 controls died 12 days post-challenge due to enteritis with mild to moderate immunohistochemical staining to BCV on colon tissue.
***SD is Study Day</td></tr>
<tr><td>USDA Approval Date</td><td>02/17/2015</td></tr>
</table>

Enteric disease in calves post challenge with BCV.

Animal ID	Treatment	Cohort	Diarrhea Scores* on Days Post Challenge with BCV																	
			-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
378	Control	1						2	1	3	1									
379	Control	1							3	3	2	3	3							
380	Control	1												1						
381	Control	1					1	3	3	3		3		2	2					
382	Control	1						2	2	2	3	3		3		2	2			
383	Control	1						1	2	2	2									
384	Control	1					2	1			2			2		1				
393	Control	2							2	3	3		3	3	2	2				
394	Control	2						3	3	3	1			2	2		1			
395	Control	2								3	1	2	2							
396	Control	2						3	3	3	3		3	1	2	2	1	3	3	1
397	Control	2					1	3	2	3	3	3	3	1	1					
398	Control	2																		
399	Control	2						2	1	3	3	2		1			3			
400	Control	2							1	2							2			
401	Control	2					3	3	3	3	2		3	3	1					
402	Control	2						3			2	1	3	3	2		1	1		
412	Control	3						ns		3	3	1	3	3		2	2		1	
413	Control	3						3	2	3		3		1	3		1			
414	Control	3					2	2	3	2	3	3	1			3	2			
415	Control	3						2	3	3	1	3	2	3	2	2				
416	Control	3											2				3			
385	Vac	1		1	1		2					1	2	1		2	1	1	1	1
386	Vac	1						3	3	3			2	1						
387	Vac	1																		
388	Vac	1						3	3	3	3	1	3	3	1	1	1	3		
389	Vac	1						3	3	3	3				1					
390	Vac	1						2	2		1		1			1				
391	Vac	1								2	1	2		1						
392	Vac	1						2			2	3	2	1			1			
403	Vac	2					1	3		3				2		1	1	1		
404	Vac	2						2									1			
405	Vac	2								2				3						
407	Vac	2						2	3	3	3									
408	Vac	2						2							1		1			
409	Vac	2					1	1												
410	Vac	2									2	2	1	1	1					
411	Vac	2							ns			3		3				1		
417	Vac	3					1				3									
419	Vac	3									2	2								
420	Vac	3																		
421	Vac	3											1	1			1			

*(Mild, 1)=more runny than normal but still some semisolid form, (Moderate, 2)=very little solid material, (Severe, 3)=primarily watery, little to no solid material

<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>To demonstrate safety under typical field conditions</td></tr>
<tr><td>Product Administration</td><td>One dose administered by the intranasal route</td></tr>
<tr><td>Study Animals</td><td>930 calves (619 vaccinates & 311 controls) ranging in age from 1 day to 4 months, located at 3 different sites. 1/3 of calves were of minimum ages recommended for product administration.</td></tr>
<tr><td>Challenge Description</td><td>N/A</td></tr>
<tr><td>Interval observed after challenge</td><td>No challenge. All calves were observed once between 1- and 4-hours following vaccination and then daily through 21 days post-vaccination.</td></tr>
<tr><td>Results</td><td><u>Adverse Event (AE) Summary</u>
<table>
<tr><th rowspan="2">Group</th><th rowspan="2">Age (days)</th><th rowspan="2"># Calves Enrolled</th><th colspan="4"># of Calves with AE's</th></tr>
<tr><th>Respiratory*</th><th>Enteric**</th><th>Other¥</th><th>Mortality†</th></tr>
<tr><td rowspan="2">Vaccinates</td><td>≤ 7</td><td>233</td><td>65</td><td>156</td><td>0</td><td>17</td></tr>
<tr><td>> 7</td><td>386</td><td>21</td><td>1</td><td>1</td><td>2</td></tr>
<tr><td rowspan="2">Controls (Placebo)</td><td>≤ 7</td><td>119</td><td>30</td><td>70</td><td>2</td><td>8</td></tr>
<tr><td>> 7</td><td>192</td><td>7</td><td>1</td><td>0</td><td>0</td></tr>
</table>
*Respiratory disease was due to Bovine Coronavirus, Histophilus somni, Infectious Bovine Rhinotracheitis, Pasteurella multocida, or Mycoplasma bovis. Pathogens may have been detected prior to vaccination and at the time of the adverse event.
**Enteric disease was due to Bovine Coronavirus, Bovine Rotavirus, Cryptococcus sp, and E. coli. Pathogens may have been detected prior to vaccination and at the time of the adverse event.
¥ Other included bloating, lameness, and not eating and affirmed by licensee to not be related to administration of the vaccine.
†Mortality was not related to vaccine administration as affirmed by the licensee.</td></tr>
<tr><td>USDA Approval Date</td><td>03/08/2016</td></tr>
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