



## Summary of Studies Supporting USDA Product Licensure

Establishment Name	Boehringer Ingelheim Animal Health USA Inc.
USDA Vet Biologics Establishment Number	124
Product Code	9240.D0
True Name	Canine Melanoma Vaccine, DNA
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	
Date of Compilation Summary	April 01, 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.**

<b>Study Type</b>	Efficacy														
<b>Pertaining to</b>	Treatment for oral melanoma														
<b>Study Purpose</b>	Demonstrate efficacy in treatment of oral melanoma														
<b>Product Administration</b>	Intramuscularly in rear leg via transdermal route. Four (4) doses at 2-week intervals as the initial series following surgery. Dogs enrolled in the study for over 6 months received a booster every 6 months until the end of the study period.														
<b>Study Animals</b>	53 client-owned dogs of different breeds ranging in age from 5-16 years with oral melanoma, WHO stage II or III with local disease control. Local disease control is defined as no gross disease of the oral cavity and the absence of regional lymph node involvement and/or pulmonary metastasis. Removal/irradiation of regional lymph nodes or irradiation of the surgical scar may have been performed before the first vaccination to achieve local control.														
<b>Challenge Description</b>	Not applicable														
<b>Interval observed after challenge</b>	The study period for each animal was from the time of surgery to the last physical exam within the data collection period. Following the initial vaccine series, dogs were evaluated monthly. Survival time was calculated from the date of surgery (or histological sample submission) to death or last date of follow-up.														
<b>Results</b>	<p>The primary outcome was defined as survival time from the time of surgery or histological sample submission through death or last date of follow-up during the study period.</p> <p>The median survival time could not be estimated. The 25<sup>th</sup> percentile of the survival time is the time beyond which 75% of the subjects in the population are expected to survive, and is estimated to be 464 days.</p> <p><b>Summary of Outcomes in Melanoma Study Dogs</b></p> <table border="1"> <thead> <tr> <th>Outcome</th> <th># of dogs</th> </tr> </thead> <tbody> <tr> <td>Death due to disease*</td> <td>13</td> </tr> <tr> <td>Death due to unrelated causes</td> <td>9</td> </tr> <tr> <td>Lost to follow up</td> <td>5</td> </tr> <tr> <td>Removed from study</td> <td>7</td> </tr> <tr> <td>Alive at the end of the study</td> <td>19</td> </tr> <tr> <td>Total</td> <td>53</td> </tr> </tbody> </table> <p>*Disease is oral melanoma</p> <p>Raw data on attached page.</p>	Outcome	# of dogs	Death due to disease*	13	Death due to unrelated causes	9	Lost to follow up	5	Removed from study	7	Alive at the end of the study	19	Total	53
Outcome	# of dogs														
Death due to disease*	13														
Death due to unrelated causes	9														
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Removed from study	7														
Alive at the end of the study	19														
Total	53														
<b>USDA Approval Date</b>	October 26, 2009														

**Vaccination dates relative to surgery (defines day of study), survival times in days and outcomes of vaccinated dogs.**

ID Number	Study Day at 1st Admin.	Study Day at 2nd Admin.	Study Day at 3rd Admin.	Study Day at 4th Admin.	1st 6-month Booster	2nd 6-month booster	3rd 6-month booster	<i>Survival Time</i>	Outcome
12361	13	28	42	56	239	378	NA	<b>435</b>	Alive at end of study
11887	15	29	43	57	259	449	NA	<b>723</b>	Alive at end of study
28067	14	29	43	56	255	444	NA	<b>476</b>	Alive at end of study
135382	36	50	64	78	269	NA	NA	<b>332</b>	Alive at end of study
58163	53	67	81	95	300	475	669 <sup>1</sup>	<b>475</b>	Alive at end of study
25239	28	42	56	72	267	437	NA	<b>528</b>	Alive at end of study
12299	25	39	53	67	265	426	NA	<b>426</b>	Alive at end of study
865023	28	42	56	70	288	504	679	<b>679</b>	Alive at end of study
50710	9	23	37	50	240	408 <sup>1</sup>	NA	<b>380</b>	Alive at end of study
3751	38	52	66	79	262	437	NA	<b>437</b>	Alive at end of study
28644	46	60	74	88	271	442	NA	<b>442</b>	Alive at end of study
27254	38	52	66	80	274	449	631 <sup>1</sup>	<b>481</b>	Alive at end of study
11978	20	34	48	62	249	440	NA	<b>685</b>	Alive at end of study
135756	40	54	75	88	304	NA	NA	<b>314</b>	Alive at end of study
3741	63	77	91	105	290	458	801 <sup>1</sup>	<b>633</b>	Alive at end of study

ID Number	Study Day at 1st Admin.	Study Day at 2nd Admin.	Study Day at 3rd Admin.	Study Day at 4th Admin.	1st 6-month Booster	2nd 6-month booster	3rd 6-month booster	<i>Survival Time</i>	Outcome
24239	207	221	235	249	425	593	NA	<b>736</b>	Alive at end of study
26189	18	32	46	63	257	455	NA	<b>455</b>	Alive at end of study
3740	38	52	66	86	276	445	625	<b>625</b>	Alive at end of study
136371	15	29	43	62	259	NA	NA	<b>267</b>	Alive at end of study
874398	7	21	38	53	NA	NA	NA	<b>235</b>	Death due to disease
3739	22	36	50	64	NA	NA	NA	<b>100</b>	Death due to disease
3742	32	47	NA	NA	NA	NA	NA	<b>52</b>	Death due to disease
28077	41	53	67	81	291	NA	NA	<b>464</b>	Death due to disease
12158	71	85	98	112	314	NA	NA	<b>320</b>	Death due to disease
27134	9	23	37	51	240	416	NA	<b>475</b>	Death due to disease
28018	40	53	67	81	NA	NA	NA	<b>199</b>	Death due to disease
57456	45	59	73	87	NA	NA	NA	<b>177</b>	Death due to disease
12285	380	394	408	422	NA	NA	NA	<b>583</b>	Death due to disease
3748	115	129	143	157	NA	NA	NA	<b>181</b>	Death due to disease
3749	81	96	110	124	265	NA	NA	<b>290</b>	Death due to disease

ID Number	Study Day at 1st Admin.	Study Day at 2nd Admin.	Study Day at 3rd Admin.	Study Day at 4th Admin.	1st 6-month Booster	2nd 6-month booster	3rd 6-month booster	<i>Survival Time</i>	Outcome
133349	48	61	75	89	NA	NA	NA	<b>293</b>	Death due to disease
26456	62	76	94	108	NA	NA	NA	<b>165</b>	Death due to disease
26105	22	36	49	64	260	414	NA	<b>550</b>	Death due to unrelated cause
861225	37	51	65	79	NA	NA	NA	<b>267</b>	Death due to unrelated cause
860776	41	57	69	84	NA	NA	NA	<b>293</b>	Death due to unrelated cause
20872	38	53	67	81	262	NA	NA	<b>470</b>	Death due to unrelated cause
25403	51	65	79	NA	NA	NA	NA	<b>87</b>	Death due to unrelated cause
12157	26	41	50	NA	NA	NA	NA	<b>62</b>	Death due to unrelated cause
864280	4	20	33	48	245	NA	NA	<b>307</b>	Death due to unrelated cause
132409	15	29	43	57	NA	NA	NA	<b>274</b>	Death due to unrelated cause
27190	107	121	135	149	NA	NA	NA	<b>304</b>	Death due to unrelated cause
864332	20	34	48	62	NA	NA	NA	<b>62</b>	Lost to follow-up

ID Number	Study Day at 1st Admin.	Study Day at 2nd Admin.	Study Day at 3rd Admin.	Study Day at 4th Admin.	1st 6-month Booster	2nd 6-month booster	3rd 6-month booster	<i>Survival Time</i>	Outcome
3746	40	53	67	81	NA	NA	NA	<b>139</b>	Lost to follow-up
3750	47	61	75	105	NA	NA	NA	<b>200</b>	Lost to follow-up
12310	150	164	178	192	388	NA	NA	<b>557</b>	Lost to follow-up
3747	33	44	58	72	NA	NA	NA	<b>245</b>	Lost to follow-up
857655	0	14	28	42	189	NA	NA	<b>280</b>	Removed
11989	61	76	90	104	301	488	NA	<b>525</b>	Removed
3743	35	48	63	77	273	465	NA	<b>510</b>	Removed
28036	36	50	64	78	NA	NA	NA	<b>178</b>	Removed
58070	13	27	41	53	250	NA	NA	<b>411</b>	Removed
102674	29	43	NA	NA	NA	NA	NA	<b>57</b>	Removed
3745	14	29	42	56	NA	NA	NA	<b>84</b>	Removed

<sup>1</sup>Dogs' vaccine booster dates continued to be recorded past the end of the data collection period for statistical analysis of survival time.

Vaccinated dogs removed from the study:

- Six (6) dogs were removed by owner/veterinarian to pursue an alternative treatment option for melanoma.
- One (1) dog was removed by owner/veterinarian due to a primary lung nodule.

<b>Study Type</b>	Safety
<b>Pertaining to</b>	ALL
<b>Study Purpose</b>	Demonstrate safety under field conditions
<b>Product Administration</b>	Intramuscularly into rear leg via transdermal route Four (4) doses at 2-week intervals
<b>Study Animals</b>	60 dogs with oral melanoma
<b>Challenge Description</b>	Not applicable
<b>Interval observed after challenge</b>	Animals were monitored for at least 30 minutes after vaccination by a veterinarian. Vaccination sites were examined 2 weeks after vaccination by a veterinarian. Owners observed dogs and recorded observations daily for 2 weeks after each vaccination.
<b>Results</b>	Four dogs received at least two vaccinations but did not complete the series.  See next page for data summary.
<b>USDA Approval Date</b>	March 18, 2009

**Table 1: Number of Acute Local Reactions or any Bruising/Hematoma in 234 vaccinations of 60 dogs.**

Injection Site Pain		Injection Site Wheal		Injection Site Leakage		Injection Site Bleeding <sup>a</sup>	
Mild	Moderate	Acute <sup>b</sup>	Subacute <sup>b</sup>	Droplet <sup>c</sup>	Wet <sup>c</sup>	Bruising alone	Hematoma <sup>d</sup>
73	12	3	5	117	11	13	3

<sup>a</sup>All but one case of bruising resolved within 2 weeks.

<sup>b</sup>Acute: arose and resolved within 30 minutes; Subacute: still present after 30 minutes. Wheals typically resolved within 1 hour.

<sup>c</sup>Droplet: a drop of fluid or blood at entry site. Wet: flow of fluid or blood from entry site. Occurred and resolved at time of injection.

<sup>d</sup>Reports of hematoma could also include bruising. Hematomas resolved within the first few days after vaccination.

**Table 2: Post – vaccination veterinarian reported events.**

Clinical Sign	Number of events in 234 vaccinations of 60 dogs
Anemia	1
Anorexia	2
Anxiety	1
Diarrhea	1
Injection site crust	2
Injection site itching	3
Injection site pain	5
Injection site rash	1
Injection site swelling	1
Fever	1
Lethargy	2
Limb weakness	1
Pyoderma	1
Sneezing	1
Vomiting	3



**Table 3: Post- vaccination owner reported observations. Events are only reported once per vaccination, even if they were reported on multiple days. Events duplicated in the veterinarian reports are reported in Table 2.**

Clinical Sign	Number of events in 234 vaccinations of 60 dogs
Abdominal pain	1
Aggression	1
Anxiety	2
Behavioral disorder Non-specific	2
Bloodshot eye	5
Confusion	1
Cough	4
Decreased activity	2
Decreased appetite/Not eating	21
Depression	33
Diarrhea	8
Difficulty breathing	1
Difficulty standing	6
Difficulty walking	4
Disoriented	1
Enlarged lymph node	1
Erythema	1
Erythematous rash	1
Eye discharge	5
Fever	4
Glazed eye	3
Groaning	1
Hair loss	1
Hiccup	1
Hypersalivation	1
Increased appetite	13
Increased drinking	4
Increased temperature	4
Increased thirst	3
Injection site lump	1
Injection site pain	12
Injection site reddening	12
Injection site self-trauma	1
Injection site swelling <sup>a</sup>	13
Injection site warmth	14
Itchy	6
Jaw disorder	1
Lameness	7
Lethargy	3

Clinical Sign	Number of events in 234 vaccinations of 60 dogs
Loose stool	2
Lump	2
Malaise	2
Nasal bleeding	1
Neurological abnormality Non-specific	1
Not eating	2
Oral bleeding	3
Oral pain	1
Others <sup>b</sup>	18
Pacing	1
Pain	1
Pain on palpation	14
Red eye	1
Reddening of the skin	1
Retching	2
Scratching	5
Self-trauma	1
Skin disorder	1
Skin infection	1
Sleep disorder Non-specific	2
Sneezing	5
Stiffness	4
Swollen eye	1
Tiredness	19
Tongue protrusion	1
Vocalization	1
Vomiting	8
Weight loss	1

<sup>a</sup>Swelling typically reported for 1-3 days.

<sup>b</sup>Includes arthritis, deaths (heart mass, metastatic melanoma, anaplastic sarcoma), ear infection, forgetful, gastric dilatation/volvulus, inappropriate defecation, incontinence, licking, lipoma, paw tumor, pica, primary lung tumor, surgical site self-trauma, voice alteration, whipworms