Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	1905.D1
True Name	Rabies Vaccine, RNA Particle
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Merck Animal Health Nobivac NXT Canine-1 Rabies - Merck Animal Health Nobivac NXT Feline-1 Rabies - Merck Animal Health Nobivac NXT Feline-1 Rabies - No distributor specified Nobivac NXT Feline-3 Rabies - Merck Animal Health
Date of Compilation Summary	May 10, 2024

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	Rabies virus
Study Purpose	Demonstrate efficacy against Rabies virus 12 months after vaccination to establish a 1-year revaccination interval
Product Administration	One dose, administered subcutaneously
Study Animals	Cats, 12 weeks of age, 28 vaccinates, 13 controls
Challenge Description	Virulent rabies challenge was administered 407 days post-vaccination.
Interval observed after challenge	All cats were observed for 90 days for clinical signs of rabies infection.
Results	Animals displaying clinical signs leading to mortality were considered to be affected by the challenge. Number affected: Vaccinates: 0/27 Controls: 12/13 The study met the criteria described in 9 CFR 113.209 Raw data are shown below only for the days clinical signs or mortality were observed.
USDA Approval Date	June 20, 2019

Table 2: Clinical Signs and Mortality Following Challenge

Cat ID	Treatment Group	Study Day	DPC	Primary Clinical Signs
17EMY1	Control	421	14	Aggression, Incoordination, Euthanized
17EMZ3	Control	417	10	Incoordination, Partial Paralysis, Euthanized
17LMR4	Control	417	10	Incoordination, Convulsions, Euthanized
17LMW6	Control	419	12	Incoordination, Convulsions, Euthanized
17EMX7	Control	420	13	Aggression, Incoordination, Euthanized
17EMV6	Control	421	14	Incoordination, Euthanized
17ENG3	Control	421	14	Aggression, Incoordination, Euthanized
17EMV2	Control	422	15	Aggression, Incoordination, Euthanized
17ENA3	Control	422	15	Death
17LMT1	Control	422	15	Incoordination, Euthanized
17LMT2	Control	424	17	Incoordination, Euthanized
17LNA2	Control	427	20	Incoordination, Euthanized

DPC – Days post challenge

Animals were humanely euthanized based on humane end-points

Study Type	Efficacy
Pertaining to	Rabies virus
Study Purpose	Demonstrate efficacy against Rabies virus 12 months after vaccination to establish a 1-year revaccination interval
Product Administration	One dose, administered subcutaneously
Study Animals	Dogs, 12 weeks of age, 27 vaccinates, 11 controls
Challenge Description	Virulent rabies challenge was administered 392 days post-vaccination.
Interval observed after challenge	All dogs were observed for 90 days for clinical signs of rabies infection.
Results	Animals displaying clinical signs leading to mortality were considered to be affected by the challenge. Number affected: Vaccinates: 0/27 Controls: 9/11 The study met the criteria described in 9 CFR 113.209 Raw data are shown below only for the days clinical signs or mortality were observed.
USDA Approval Date	June 18, 2019

Table 1: Clinical Signs and Mortality Following Challenge

Dog ID	Treatment Group	Study Day	DPC	Primary Clinical Signs
3544908	Control	406	14	Euthanized
3546226	Control	410	18	Aggression, Incoordination, Euthanized
3547435	Control	415	23	Incoordination, Euthanized
3546145	Control	418	26	Partial Paralysis, Coma, Euthanized
3546625	Control	418	26	Coma, Euthanized
3547567	Control	420	28	Incoordination, Euthanized
3548407	Control	420	28	Incoordination, Euthanized
3544011	Control	421	29	Incoordination, Euthanized
3543562	Control	422	30	Incoordination, Euthanized

DPC – Days post challenge

Animals were humanely euthanized based on humane end-points

Study Type	Efficacy
Pertaining to	Rabies virus
Study Purpose	Demonstrate efficacy against Rabies virus 36 months after vaccination to establish a 3-year revaccination interval
Product Administration	One dose, administered subcutaneously
Study Animals	Cats, 12 weeks of age, 28 vaccinates, 14 controls
Challenge Description	Virulent rabies challenge was administered 1100 days post-vaccination.
Interval observed after challenge	All cats were observed for 90 days for clinical signs of rabies infection.
Results	Animals displaying clinical signs were considered to be affected by the challenge. Number affected: Vaccinates: 0/28 Controls: 14/14 The study met the criteria described in 9 CFR 113.209 Raw data are shown below only for the days clinical signs or mortality were observed.
USDA Approval Date	May 19, 2021

Table 1: Clinical Signs and Mortality Following Challenge

Cat ID	Treatment Group	Study Day	DPC	Primary Clinical Signs
17ENO5	Control	1109	9	Incoordination, Aggression, Excess salivation, Euthanized
17ENL2	Control	1110	10	Incoordination, Aggression, Excess salivation, Euthanized
17LNG3	Control	1111	11	Incoordination, Excess salivation, Euthanized
17LNF5	Control	1112	12	Incoordination, Partial paralysis, Euthanized
17ENM6	Control	1113	13	Incoordination, Euthanized
17LND3	Control	1113	13	Incoordination, Euthanized
17ENM3	Control	1114	14	Incoordination, Aggression, Excess Salivation, Euthanized
17ENO6	Control	1114	14	Incoordination, Aggression, Excess Salivation, Partial paralysis, Euthanized
17LNF3	Control	1114	14	Incoordination, Excess Salivation, Euthanized
17LNC4	Control	1115	15	Incoordination, Aggression, Euthanized
17ENL4	Control	1116	16	Incoordination, Aggression, Excess Salivation, Euthanized
17LNB1	Control	1116	16	Incoordination, Excess Salivation, Euthanized
17LNE4	Control	1116	16	Incoordination, Excess Salivation, Euthanized
17ENJ1	Control	1117	17	Death

DPC – days post challenge
Animals were humanely euthanized based on humane end-points

Study Type	Efficacy
Pertaining to	Rabies virus
Study Purpose	Demonstrate efficacy against Rabies virus 36 months after vaccination to establish a 3-year revaccination interval
Product Administration	One dose, administered subcutaneously
Study Animals	Dogs, 12 weeks of age, 27 vaccinates, 13 controls
Challenge Description	Virulent rabies challenge was administered 1106 days post-vaccination.
Interval observed after challenge	All dogs were observed for 90 days for clinical signs of rabies infection.
Results	Animals displaying clinical signs were considered to be affected by the challenge. Number affected: Vaccinates: 0/27 Controls: 11/13 The study met the criteria described in 9 CFR 113.209 Raw data are shown below only for the days clinical signs were observed.
USDA Approval Date	May 10, 2024

Table 1: Clinical Signs and Mortality Following Challenge

Dog ID	Treatment Group	Primary Clinical Signs
PDO-0	Control	Convulsions, Coma, Death
TAO-0	Control	Incoordination, Euthanized
ROO-0	Control	Incoordination, Convulsions, Euthanized
LJP-0	Control	Death
LRP-0	Control	Incoordination, Euthanized
TUO-0	Control	Incoordination, Euthanized
UEP-0	Control	Euthanized
RHP-0	Control	Death
KZO-0	Control	Death
SLO-0	Control	Incoordination, Euthanized
LUP-0	Control	Incoordination, Euthanized

Animals were humanely euthanized based on humane end-points.

<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 in cats under field conditions</td></tr>
<tr><td>Product Administration</td><td>One dose administered subcutaneously</td></tr>
<tr><td>Study Animals</td><td>665 cats represented 10 sites in three geographic locations. 200 cats were 12 weeks of age, which is the recommended minimum age, 64 cats ranged in age from 13 weeks to 1 year and 401 cats ranged in age from 1 year to 21 years.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>Cats were observed daily for 14 days post-vaccination for any adverse events.</td></tr>
<tr><td>Results</td><td>
<u>Summary of Adverse Events:</u>
<table>
<tr><th>VeDDRA Code for Adverse Events Related to the Test Vaccine</th><th>Number of Adverse Events in 665 doses</th></tr>
<tr><td>Injection site pruritis*</td><td>14 (2.1%)</td></tr>
<tr><td>Lethargy</td><td>9 (1.4%)</td></tr>
<tr><td>Anorexia</td><td>2 (0.3%)</td></tr>
<tr><td>Emesis</td><td>2 (0.3%)</td></tr>
<tr><td>Injection site edema*</td><td>2 (0.3%)</td></tr>
<tr><td>Sneezing</td><td>2 (0.3%)</td></tr>
<tr><td>Abnormal behavior</td><td>1 (0.2%)</td></tr>
<tr><td>Aggression</td><td>1 (0.2%)</td></tr>
<tr><td>Diarrhea</td><td>1 (0.2%)</td></tr>
<tr><td>Gastroenteritis</td><td>1 (0.2%)</td></tr>
<tr><td>Hyperactivity</td><td>1 (0.2%)</td></tr>
<tr><td>Injection site pain*</td><td>1 (0.2%)</td></tr>
<tr><td>Injection site complication*</td><td>1 (0.2%)</td></tr>
<tr><td>Joint Pain NOS</td><td>1 (0.2%)</td></tr>
<tr><td>Neurological disorder NOS</td><td>1 (0.2%)</td></tr>
<tr><td>Total</td><td>40 (6.0%)</td></tr>
</table>
*Resolved within 24 hours
<table>
<tr><th>Vaccination Location</th><th>Total number of animals vaccinated per location</th><th>Local Adverse Event Reaction</th><th>Systemic Adverse Event Reaction</th><th>Total</th></tr>
<tr><td>Hind Leg (Flank)</td><td>544</td><td>17</td><td>22</td><td>39</td></tr>
<tr><td>Suprascapular</td><td>121</td><td>1</td><td>0</td><td>1</td></tr>
<tr><td>Total</td><td>665</td><td>18</td><td>22</td><td>40</td></tr>
</table>
</td></tr>
</table>

	<table><tr><th>VeDDRA Code for Adverse Events Not Related to the Test Vaccine</th><th>Number of Adverse Events in 665 doses</th></tr><tr><td>Emesis</td><td>9 (1.3%)</td></tr><tr><td>No sign (extra affectionate, missing cat)</td><td>5 (0.7%)</td></tr><tr><td>Lethargy</td><td>3 (0.4%)</td></tr><tr><td>Injection site pruritis</td><td>2 (0.3%)</td></tr><tr><td>Gastritis</td><td>2 (0.3%)</td></tr><tr><td>Sneezing</td><td>2 (0.3%)</td></tr><tr><td>Anorexia</td><td>2 (0.3%)</td></tr><tr><td>Inappropriate urination</td><td>2 (0.3%)</td></tr><tr><td>Urinary tract infection</td><td>2 (0.3%)</td></tr><tr><td>Gingival disorder</td><td>1 (0.1%)</td></tr><tr><td>Otitis externa</td><td>1 (0.1%)</td></tr><tr><td>Ataxia</td><td>1 (0.1%)</td></tr><tr><td>Urinary incontinence</td><td>1 (0.1%)</td></tr><tr><td>Respiratory tract infection NOS</td><td>1 (0.1%)</td></tr><tr><td>Rhinitis</td><td>1 (0.1%)</td></tr><tr><td>Dermatitis and eczema</td><td>1 (0.1%)</td></tr><tr><td>Trauma NOS</td><td>1 (0.1%)</td></tr><tr><td>Conjunctivitis</td><td>1 (0.1%)</td></tr><tr><td>Aggression</td><td>1 (0.1%)</td></tr><tr><td>Diarrhea</td><td>1 (0.1%)</td></tr><tr><td>Retching</td><td>1 (0.1%)</td></tr><tr><td>Anxiety</td><td>1 (0.1%)</td></tr><tr><td>Digestive tract disorder</td><td>1 (0.1%)</td></tr><tr><td>Anxiety disorder</td><td>1 (0.1%)</td></tr><tr><td>Bacterial skin infection</td><td>1 (0.1%)</td></tr><tr><td>Total</td><td>45 (6.8%)</td></tr></table>
USDA Approval Date	October 3, 2022

<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 in dogs under field conditions</td></tr>
<tr><td>Product Administration</td><td>One dose administered subcutaneously</td></tr>
<tr><td>Study Animals</td><td>622 dogs represented 7 sites. 206 dogs were 12 weeks of age, which is the recommended minimum age, 21 dogs ranged in age from 13 weeks to 1 year and 395 dogs ranged in age from 1 year to 16 years.</td></tr>
<tr><td>Challenge Description</td><td>Not applicable</td></tr>
<tr><td>Interval observed after challenge</td><td>Dogs were observed daily for 14 days post-vaccination for any adverse events.</td></tr>
<tr><td>Results</td><td><u>Summary of Adverse Events:</u>

<table>
<tr><th>VeDDRA Code for Adverse Events Related to the Test Vaccine</th><th>Number of Adverse Events in 622 doses</th></tr>
<tr><td>Lethargy</td><td>16 (2.6%)</td></tr>
<tr><td>Anorexia</td><td>8 (1.3%)</td></tr>
<tr><td>Emesis</td><td>7 (1.1%)</td></tr>
<tr><td>Diarrhea</td><td>4 (0.6%)</td></tr>
<tr><td>Injection site pain*</td><td>4 (0.6%)</td></tr>
<tr><td>Nausea</td><td>3 (0.5%)</td></tr>
<tr><td>Aggression</td><td>2 (0.3%)</td></tr>
<tr><td>Hyperaesthesia</td><td>2 (0.3%)</td></tr>
<tr><td>Injection site edema*</td><td>2 (0.3%)</td></tr>
<tr><td>Lameness</td><td>2 (0.3%)</td></tr>
<tr><td>Abnormal behavior</td><td>1 (0.2%)</td></tr>
<tr><td>Anxiety disorder</td><td>1 (0.2%)</td></tr>
<tr><td>Application site self trauma</td><td>1 (0.2%)</td></tr>
<tr><td>Enteritis</td><td>1 (0.2%)</td></tr>
<tr><td>Injection site inflammation*</td><td>1 (0.2%)</td></tr>
<tr><td>Injection site pruritis*</td><td>1 (0.2%)</td></tr>
<tr><td>Injection site stiffness*</td><td>1 (0.2%)</td></tr>
<tr><td>Total</td><td>57 (9.2%)</td></tr>
</table>
* Resolved within 1-5 days</td></tr>
</table>

Vaccination Location	Total number of animals vaccinated per location	Local Adverse Event Reaction	Systemic Adverse Event Reaction	Total
Suprascapular	360	0	10	10
Hind Leg (Flank)	258	10	37	47
Shoulder	2	0	0	0
Right Front	2	0	0	0
Total	**662**	**10**	**47**	**57**

VeDDRA Code for Adverse Events Not Related to the Test Vaccine*	Number of Adverse Events in 622 doses
Diarrhea	9 (1.4%)
Emesis	9 (1.4%)
Lethargy	5 (0.8%)
Aggression	2 (0.3%)
Anorexia	2 (0.3%)
Dermatitis and eczema	1 (0.2%)
Edema NOS	1 (0.2%)
Hyperactivity	1 (0.2%)
Muscle pain	1 (0.2%)
Nausea	1 (0.2%)
Otitis externa	1 (0.2%)
Pruritus	1 (0.2%)
Trauma NOS	1 (0.2%)
Total	**35 (5.6%)**

*As affirmed by licensee

USDA Approval Date	October 19, 2022