Summary of Studies Supporting USDA Product Licensure

Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	1905.24
True Name	Rabies Vaccine, Killed Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Defensor - Zoetis Industria de Produtos Defensor 1 - No distributor specified Defensor 1 - Zoetis Argentina Defensor 1 - Zoetis Colombia S.A.S. Defensor 1 - Zoetis Mexico Defensor 3 - No distributor specified Defensor 3 - SARL Belophram Defensor 3 - Zoetis (Thailand) Limited Defensor 3 - Zoetis Ecuador Cia Ltda. Defensor 3 - Zoetis Hayvan Sagligi Ltd Defensor 3 - Zoetis Korea Defensor 3 - Zoetis Panama Defensor 3 - Zoetis Russia Defensor 3 - Zoetis Schweiz GmbH, Delemont Defensor 3 - Zoetis South Africa Ltd Defensor 3 - Zoetis import Egypt Nobivac 1-Rabies - Intervet, Inc. Nobivac 3 Rabies - Intervet, Inc.
Date of Compilation Summary	February 25, 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>Rabies Virus (RV)</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness and 1 year duration of immunity against rabies disease</td></tr>
<tr><td>Product Administration</td><td>1 dose subcutaneously (SC)</td></tr>
<tr><td>Study Animals</td><td>Forty three ferrets 12 weeks of age, divided into 27 vaccinates and 16 controls</td></tr>
<tr><td>Challenge Description</td><td>Forty three animals (27 vaccinates; 16 controls) were challenged 373 days post-vaccination</td></tr>
<tr><td>Interval observed after challenge</td><td>All challenged animals were observed twice daily up to 90 days or until humane endpoints of clinical signs due to RV were observed</td></tr>
<tr><td>Results</td><td>An animal was classified as affected if it had one or more clinical signs of rabies disease post challenge and/or was positive by direct fluorescent antibody (dFA) in the brain stem tissue.

<u>Table 1. Number of Animals with Rabies Disease</u>

<table>
<tr><th rowspan="3">Treatment</th><th colspan="4">Disease</th><th rowspan="3">Total Animals Challenged Per Group</th></tr>
<tr><th colspan="2">YES</th><th colspan="2">NO</th></tr>
<tr><th>No. of Animals</th><th>%</th><th>No. of Animals</th><th>%</th></tr>
<tr><td>Controls</td><td>16</td><td>100</td><td>0</td><td>0</td><td>16</td></tr>
<tr><td>Vaccinates</td><td>0</td><td>0</td><td>27</td><td>100</td><td>27</td></tr>
</table>

The requirements of 9 CFR 113.209 were met.

The raw data for the control group is shown on the attached pages. There were no clinical signs of rabies disease or positive dFA test results for the vaccinate group.</td></tr>
<tr><td>USDA Approval Date</td><td>01 December 2015</td></tr>
</table>

Table 2: Individual Animal Daily Clinical Signs for Controls

Animal ID	Days post-challenge									
	0 DPC	1 DPC	2 DPC	3 DPC	4 DPC	5 DPC	6 DPC	7 DPC	8 DPC	9 DPC
9052	0	0	0	0	0	0	0	0	0	0
9054	0	0	0	0	0	0	0	0	0	0
9061	0	0	0	0	0	0	0	0	0	0
9062	0	0	0	0	0	0	0	0	0	0
9063	0	0	0	0	0	0	0	0	0	0
9065	0	0	0	0	0	0	0	0	0	0
9066	0	0	0	0	0	0	0	0	0	0
9069	0	0	0	0	0	0	0	0	0	0
9071	0	0	0	0	0	0	0	0	0	0
9080	0	0	0	0	0	0	0	0	0	0
9082	0	0	0	0	0	0	0	0	0	0
9083	0	0	0	0	0	0	0	0	0	0
9096	0	0	0	0	0	0	0	0	0	0
9098	0	0	0	0	0	0	0	0	0	0
9103	0	0	0	0	0	0	0	0	0	0
9104	0	0	0	0	0	0	0	0	0	0

Animal ID	Days post-challenge					dFA* positive Y/N
	10 DPC	11 DPC	12 DPC	13 DPC	14 DPC	
9052	0	0	NR, HY	PA, NR, DI, OT, ED, HY	-	Y
9054	0	0	NR	PA, NR, HY, DI, ED	-	Y
9061	0	SA, PA, NR, DE, ED	-	-	-	Y
9062	0	SA, PA, NR, HY, OT, ED	-	-	-	Y
9063	0	SA, PA, NR, HY, ED	-	-	-	Y
9065	0	0	DE	SA, PA, OT, NR, HY, DI, ED	-	Y
9066	0	0	-	-	SA, NR, HY, DI, ED	Y
9069	0	PA, DE, OT, ED	-	-	-	Y
9071	0	PA, NR, ED	-	-	-	Y
9080	0	SA, OT, HY, ED	-	-	-	Y
9082	0	0	0	PA, NR, HY, DI, DE, ED	-	Y
9083	0	PA, NR, HY, DE, ED	-	-	-	Y
9096	0	PA, OT, NR, HY, ED	-	-	-	Y
9098	0	PA, NR, DI, ED	-	-	-	Y
9103	0	SA, OT, NR, HY, ED	-	-	-	Y
9104	0	SA, PA, NR, HY, ED	-	-	-	Y

Clinical signs

0	Normal	SA	Salivation
DE	Depression	LB	Labored Breathing
NR	Nervousness / Restless	OT	Other
PA	Paresis	ED	Euthanasia / Death
HY	Hyperresponse		
DI	Disorientation		

***direct fluorescent antibody**

Study Type	Efficacy
Pertaining to	Rabies Virus
Study Purpose	To demonstrate effectiveness and 1 year duration of immunity and 3 year duration of immunity against rabies disease.
Product Administration	Dog: Subcutaneous (SC) Dog: Intramuscular (IM)
Study Animals	Dogs
Challenge Description	
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	15 October 1992

Study Type	Efficacy
Pertaining to	Rabies Virus
Study Purpose	To demonstrate effectiveness and 1 year duration of immunity and 3 year duration of immunity against rabies disease.
Product Administration	Cat: Subcutaneous (SC)
Study Animals	Cats
Challenge Description	
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	15 October 1992

Study Type	Efficacy
Pertaining to	Rabies Virus
Study Purpose	To demonstrate effectiveness and 1 year duration of immunity against rabies disease.
Product Administration	
Study Animals	Cattle and Sheep
Challenge Description	
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	15 October 1992

<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>Demonstrate safety under typical field conditions</td></tr>
<tr><td>Product Administration</td><td>One dose administered subcutaneously (SC)</td></tr>
<tr><td>Study Animals</td><td>Two hundred ferrets (50 between 12 and 13 weeks of age, 150 ≥13 weeks) tested in 3 distinct geographic locations</td></tr>
<tr><td>Challenge Description</td><td>N/A</td></tr>
<tr><td>Interval observed after challenge</td><td>N/A</td></tr>
<tr><td>Results</td><td>Animals were observed for 20 minutes immediately post-vaccination (immediate post-vaccination) and for 10 days post-vaccination (late post-vaccination).

<u>Table 1: Immediate Post-Vaccination Reactions</u>

<table>
<tr><th>Observation</th><th>Study Total</th><th>Minimum Age 12 weeks</th><th>Older ≥13 weeks</th></tr>
<tr><td>Injection Site Self-trauma (scratching)</td><td><u>2/200 (1%)</u></td><td><u>0/50 (0%)</u></td><td><u>2/150 (1.3%)</u></td></tr>
</table>

<u>Table 2: Late Post-Vaccination Reactions[a]</u>

<table>
<tr><th>Observation</th><th>Study Total</th><th>Minimum Age 12 weeks</th><th>Older ≥13 weeks</th></tr>
<tr><td>Depression/Lethargy[b]</td><td>1/200 (0.5%)</td><td>0/50 (0%)</td><td>1/150 (0.7%)</td></tr>
<tr><td>Vomiting[b]</td><td>1/200 (0.5%)</td><td>0/50 (0%)</td><td>1/150 (0.7%)</td></tr>
</table>
[a] Late Post-Vaccination observations reported by owner only if they occurred (by exception)
[b] Both reactions were related to the same animal

No other post-vaccination reactions were noted.</td></tr>
<tr><td>USDA Approval Date</td><td>6 July 2016</td></tr>
</table>

Study Type	Safety
Pertaining to	Rabies Virus
Study Purpose	Demonstrate safety under typical field conditions
Product Administration	
Study Animals	Cattle and Sheep
Challenge Description	
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	15 October 1992

Study Type	Safety
Pertaining to	Rabies Virus
Study Purpose	Demonstrate safety under typical field conditions
Product Administration	
Study Animals	Dogs and Cats
Challenge Description	
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	07 August 1991