Summary of Studies Supporting USDA Product Licensure

Establishment Name	Zoetis Inc.
USDA Vet Biologics Establishment Number	190
Product Code	1995.20
True Name	West Nile Virus Vaccine, Killed Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	West Nile Innovator - No distributor specified West Nile Innovator - Zoetis Argentina West Nile Innovator - Zoetis Mexico
Date of Compilation Summary	November 22, 2022

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>West Nile Virus (WNV)</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness and duration of immunity against WNV</td></tr>
<tr><td>Product Administration</td><td>Two doses, administered intramuscularly 3 weeks apart</td></tr>
<tr><td>Study Animals</td><td>Thirty-two, 9-11 month (at vaccination) old mixed breed horses that were WNV sero-negative: 19 vaccinates, 11 controls (3 added at challenge)</td></tr>
<tr><td>Challenge Description</td><td>Challenged 12 months after vaccination with WNV</td></tr>
<tr><td>Interval observed after challenge</td><td>After challenge, animals were monitored twice daily for 14 days, and then once daily for an additional week</td></tr>
<tr><td>Results</td><td>The primary outcome was prevention of WNV viremia. Serum samples were collected from each animal twice daily from challenge for 2 weeks, and once thereafter.

Table 1. Virernia detected in vaccinated and control horses after experimental challenge with West Nile Virus

<table>
<tr><th>Treatment group</th><th>Number of viremic horses/horses challenged horses</th></tr>
<tr><td>Vaccinates</td><td>1/19</td></tr>
<tr><td>Controls</td><td>9/11</td></tr>
</table>

The raw data is shown on the attached page.</td></tr>
<tr><td>USDA Approval Date</td><td>August 13, 2002</td></tr>
</table>

Table 2: Number of Viremia incidences detected in vaccinated and control horses after experimental challenge with West Nile virus (WNV)

ID number	Group	Days Post Challenge									
		0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5
4271041A29	Controls	-	-	-	-	-	+	-	+	-	-
4273363D4C		-	-	+	+	-	+	+	+	+	+
422C651E1C		-	-	-	-	-	-	-	-	-	+
524A3B6477/5317501016		-	-	-	-	-	-	-	-	-	+
421B355400/53190B764A		-	-	-	-	-	-	-	-	-	+
42735D5E73		-	-	-	-	-	-	-	-	-	-
421A056A0A		-	-	-	-	-	-	-	-	-	-
421E51781D		-	-	-	-	+	-	+	+	+	-
421E4F723F		-	-	-	-	-	+	-	+	+	+
421B2C3C13		-	-	+	-	-	+	+	+	+	-
421E565A55		-	-	-	-	+	-	+	+	-	-
421A002D66	Vaccinates	-	-	-	-	-	-	-	-	-	-
5308581947		-	-	-	-	-	-	-	-	-	-
422C63576B		-	-	-	-	-	-	-	-	-	-
417B242E4D		-	-	-	-	-	-	-	-	-	-
422C301B30		-	-	-	-	-	-	-	-	-	-
422C643F28		-	-	-	-	-	+	-	-	-	-
421E77405A		-	-	-	-	-	-	-	-	-	-
421E712746		-	-	-	-	-	-	-	-	-	-
421E78465C		-	-	-	-	-	-	-	-	-	-
421E5C0856		-	-	-	-	-	-	-	-	-	-
421E6C706F		-	-	-	-	-	-	-	-	-	-
422C74131B		-	-	-	-	-	-	-	-	-	-
52491F2C40		-	-	-	-	-	-	-	-	-	-
422C63330B		-	-	-	-	-	-	-	-	-	-
421945065E		-	-	-	-	-	-	-	-	-	-
422C5A5E36		-	-	-	-	-	-	-	-	-	-
421E606E22		-	-	-	-	-	-	-	-	-	-
421E5B025B		-	-	-	-	-	-	-	-	-	-
421E6A2314		-	-	-	-	-	-	-	-	-	-

+ Positive for WNV
- Negative for WNV

Table 2 (continued)

ID number	Group	Days Post Challenge									
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0	9.5
4271041A29	Controls	-	-	-	-	-	-	-	-	-	-
4273363D4C		-	-	-	-	-	-	-	-	-	-
422C651E1C		-	-	-	-	-	-	-	-	-	-
524A3B6477/5317501016			+	-	-	-	-	-	-	-	-
421B355400/53190B764A		+	+	-	-	-	-	-	-	-	-
42735D5E73		-	-	-	-	-	-	-	-	-	-
421A056A0A		-	-	-	-	-	-	-	-	-	-
421E51781D		-	-	-	-	-	-	-	-	-	-
421E4F723F		-	+	-	-	-	-	-	-	-	-
421B2C3C13		-	-	-	-	-	-	-	-	-	-
421E565A55		-	-	-	-	-	-	-	-	-	-
421A002D66	Vaccinates	-	-	-	-	-	-	-	-	-	-
5308581947		-	-	-	-	-	-	-	-	-	-
422C63576B		-	-	-	-	-	-	-	-	-	-
417B242E4D		-	-	-	-	-	-	-	-	-	-
422C301B30		-	-	-	-	-	-	-	-	-	-
422C643F28		-	-	-	-	-	-	-	-	-	-
421E77405A		-	-	-	-	-	-	-	-	-	-
421E712746		-	-	-	-	-	-	-	-	-	-
421E78465C		-	-	-	-	-	-	-	-	-	-
421E5C0856		-	-	-	-	-	-	-	-	-	-
421E6C706F		-	-	-	-	-	-	-	-	-	-
422C74131B		-	-	-	-	-	-	-	-	-	-
52491F2C40		-	-	-	-	-	-	-	-	-	-
422C63330B		-	-	-	-	-	-	-	-	-	-
421945065E		-	-	-	-	-	-	-	-	-	-
422C5A5E36		-	-	-	-	-	-	-	-	-	-
421E606E22		-	-	-	-	-	-	-	-	-	-
421E5B025B		-	-	-	-	-	-	-	-	-	-
421E6A2314		-	-	-	-	-	-	-	-	-	-

+ Positive for WNV
- Negative for WNV

Table 2 (continued)

ID number	Group	Days Post Challenge										
		10.0	10.5	11.0	11.5	12.0	12.5	13.0	13.5	14.0	14.5	21.0
4271041A29	Controls	-	-	-	-	-	-	-	-	-	-	-
4273363D4C		-	-	-	-	-	-	-	-	-	-	-
422C651E1C		-	-	-	-	-	-	-	-	-	-	-
524A3B6477/5317501016		-	-	-	-	-	-	-	-	-	-	-
421B355400/53190B764A		-	-	-	-	-	-	-	-	-	-	-
42735D5E73		-	-	-	-	-	-	-	-	-	-	-
421A056A0A		-	-	-	-	-	-	-	-	-	-	-
421E51781D		-	-	-	-	-	-	-	-	-	-	-
421E4F723F		-	-	-	-	-	-	-	-	-	-	-
421B2C3C13		-	-	-	-	-	-	-	-	-	-	-
421E565A55		-	-	-	-	-	-	-	-	-	-	-
421A002D66	Vaccinates	-	-	-	-	-	-	-	-	-	-	-
5308581947		-	-	-	-	-	-	-	-	-	-	-
422C63576B		-	-	-	-	-	-	-	-	-	-	-
417B242E4D		-	-	-	-	-	-	-	-	-	-	-
422C301B30		-	-	-	-	-	-	-	-	-	-	-
422C643F28		-	-	-	-	-	-	-	-	-	-	-
421E77405A		-	-	-	-	-	-	-	-	-	-	-
421E712746		-	-	-	-	-	-	-	-	-	-	-
421E78465C		-	-	-	-	-	-	-	-	-	-	-
421E5C0856		-	-	-	-	-	-	-	-	-	-	-
421E6C706F		-	-	-	-	-	-	-	-	-	-	-
422C74131B		-	-	-	-	-	-	-	-	-	-	-
52491F2C40		-	-	-	-	-	-	-	-	-	-	-
422C63330B		-	-	-	-	-	-	-	-	-	-	-
421945065E		-	-	-	-	-	-	-	-	-	-	-
422C5A5E36		-	-	-	-	-	-	-	-	-	-	-
421E606E22		-	-	-	-	-	-	-	-	-	-	-
421E5B025B		-	-	-	-	-	-	-	-	-	-	-
421E6A2314		-	-	-	-	-	-	-	-	-	-	-

+ Positive for WNV
- Negative for WNV

Study Type	Efficacy
Pertaining to	West Nile Virus (WNV)
Study Purpose	Demonstrate efficacy against West Nile Virus (WNV)
Product Administration	2 doses, administered intramuscularly, 3 weeks apart
Study Animals	30 horses, mixed breeds, male/female, 17-20 months of age. 20 horses in the vaccinated group and 10 horses in the control group.
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	May 13, 2002

Study Type	Safety
Pertaining to	ALL
Study Purpose	Demonstration of safety under field conditions
Product Administration	2 doses, administered intramuscularly, 3 to 4 weeks apart
Study Animals	648 horses
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	April 30, 2002

<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>Determine safety of product in typical field conditions</td></tr>
<tr><td>Product Administration</td><td>2 doses administered intramuscularly 3 to 4 weeks apart</td></tr>
<tr><td>Study Animals</td><td>214 foals approximately 3 months of age were enrolled at 3 different geographical sites</td></tr>
<tr><td>Challenge Description</td><td>N/A</td></tr>
<tr><td>Interval observed after challenge</td><td>Animals were observed for immediate post-vaccination reactions 30 minutes after vaccination, and observed daily for 21 days post-second vaccination</td></tr>
<tr><td>Results</td><td>Two hundred and eleven horses (98.6%) completed the study. Three (3) horses did not complete the study for reasons unrelated to the vaccine. There were no immediate systemic or local reactions using 427 doses of product.

<u>Table 1: Frequency Distribution of Abnormal Health Events in Vaccinates:</u>

<table>
<tr><th>Number of Vaccinations</th><th>Abnormal Health Event</th><th>Number (Percent of Vaccinations)</th></tr>
<tr><td rowspan="11">427 Vaccinations</td><td>Abnormal Breathing</td><td>1 (0.23%)</td></tr>
<tr><td>Death</td><td>3 (0.70%)</td></tr>
<tr><td>Depression</td><td>1 (0.23%)</td></tr>
<tr><td>Diarrhea</td><td>1 (0.23%)</td></tr>
<tr><td>Dyspnea</td><td>1 (0.23%)</td></tr>
<tr><td>Injection Site Swelling (1.5-5.0 cm)</td><td>1 (0.23%)</td></tr>
<tr><td>Lameness</td><td>1 (0.23%)</td></tr>
<tr><td>Loss of Condition</td><td>1 (0.23%)</td></tr>
<tr><td>Joint Pain</td><td>1 (0.23%)</td></tr>
<tr><td>Skin Lesion NOS*</td><td>1 (0.23%)</td></tr>
<tr><td>Weakness</td><td>1 (0.23%)</td></tr>
</table>
*Not otherwise specified

Additional data is provided on the next page.</td></tr>
<tr><td>USDA Approval Date</td><td>July 13, 2015</td></tr>
</table>

Table 2: Abnormal Health Events and Relation to Investigational Veterinary Product (IVP) for Individual Animals

Animal #	Start Day	End Day	Abnormal Health Event	Outcome	Related to IVP[a]
W602	21	21	Skin Lesion NOS	Resolved	No
B061	22	22	Weakness	Removed from Study	No
B061	22	22	Loss of Condition	Removed from Study	No
B061	22	22	Death	Removed from Study	No
B061	13	16	Lameness	Resolved	No
B061	13	18	Abnormal Breathing	Resolved	No
B061	13	18	Dyspnea	Resolved	No
B061	22	22	Depression	Removed from Study	No
B118	31	31	Death	Removed from Study	No
B007	15	17	Joint Pain	Resolved	No
R598	2	3	Injection Site Swelling (1.5 – 5.0 cm)	Resolved	Yes
R599	3	8	Diarrhea	Removed from Study	No
R599	8	8	Death	Removed from Study	No

[a] Investigational Veterinary Product

<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 pregnant mares in the third trimester under field conditions.</td></tr>
<tr><td>Product Administration</td><td>Single dose administered intramuscularly during the third trimester of pregnancy.</td></tr>
<tr><td>Study Animals</td><td>A total of 282 healthy pregnant mares in their third trimester were enrolled in one of two treatment groups in two distinct geographical locations. The animals were distributed as follows: Controls, n = 57, Vaccinated, n = 225.</td></tr>
<tr><td>Challenge Description</td><td>N/A</td></tr>
<tr><td>Interval observed after last treatment</td><td>Clinical observations were performed on all mares for at least 30 minutes following vaccination. Pregnant mares were also observed at least once daily for general health for 21 days following vaccination and at least once weekly until foaling.

Mares were observed during foaling and foals were observed at least once weekly for general health until they were at least 21 days of age.</td></tr>
<tr><td>Results</td><td>
Mare Abnormal Health Events
<table>
<tr><th colspan="2">Number of Mares</th><th rowspan="2">Mares with no AE* (%)</th><th rowspan="2">Mares with AE* (%)</th></tr>
<tr><th>Total Enrolled</th><td>282</td></tr>
<tr><td>Controls</td><td>57</td><td>54 (94.7%)</td><td>3 (5.3%)</td></tr>
<tr><td>Vaccinated</td><td>225</td><td>214 (95.1%)</td><td>11 (4.9%)</td></tr>
</table>
*AE= Adverse Events
<table>
<tr><th>Treatment / Number of Vaccinations</th><th>Mare Abnormal Health Events</th><th>Number of Mares / Percent of Vaccinations</th></tr>
<tr><td rowspan="4">Controls (57 animals)</td><td>Agalactia</td><td>1 / 1.75%</td></tr>
<tr><td>Death[1]</td><td>1 / 1.75%</td></tr>
<tr><td>Dystocia</td><td>1 / 1.75%</td></tr>
<tr><td>Fracture</td><td>1 / 1.75%</td></tr>
<tr><td rowspan="11">Vaccinated (Product Code 48R5.20; 225 animals)</td><td>Abdominal Pain</td><td>1 / 0.44%</td></tr>
<tr><td>Decreased Appetite</td><td>1 / 0.44%</td></tr>
<tr><td>Dystocia</td><td>3 / 1.33%</td></tr>
<tr><td>Fracture</td><td>1 / 0.44%</td></tr>
<tr><td>Injection Site Swelling</td><td>1 / 0.44%</td></tr>
<tr><td>Laceration</td><td>1 / 0.44%</td></tr>
<tr><td>Lameness</td><td>2 / 0.89%</td></tr>
<tr><td>Nasal Discharge</td><td>1 / 0.44%</td></tr>
<tr><td>Placental Abnormality</td><td>1 / 0.44%</td></tr>
<tr><td>Retained Placenta</td><td>1 / 0.44%</td></tr>
</table>
[1] Mare died due to septic shock as a result of a difficult foaling.
</td></tr>
</table>

<table>
<tr><td></td><td>There was only one adverse event that was attributable to IVP which was an injection site reaction in a vaccinate that was observed the day after vaccination and resolved the following day.

Birth Outcome Summary from Vaccinated Mares
<table>
<tr><th colspan="2">Number of Foals</th><th>Live Foals</th><th>Foal died during or immediately post-parturition</th></tr>
<tr><td>Total Foals</td><td>280[1]</td><td>273 (97.50%)</td><td>7 (2.50%)</td></tr>
<tr><td>Controls</td><td>56</td><td>53 (94.64%)</td><td>3 (5.36%)</td></tr>
<tr><td>Vaccinated</td><td>224</td><td>220 (98.21%)</td><td>4 (1.79%)</td></tr>
</table>
[1] Two mares (one vaccinate and one control) were removed prior to foaling due to fractured legs.</td></tr>
<tr><td>USDA Approval Date</td><td>March 02, 2022</td></tr>
</table>