West Nile-Innovator Agenda

- “History of West Nile vaccines in US 1999–2011”
- Brief Review of Diseases covered by West Nile-Innovator + EWT
- AAEP Core Vaccine Strategy and West Nile-Innovator combinations
- Fort Dodge to Pfizer Animal Health Label Changes coming in 2012
- Pfizer Animal Health Equine Immunization Support Guarantee
- USDA Label Claim Comparison with Competitive Products
- 2011 AAEP Survey on Equine Vaccines
- Large Combinations introduced with West Nile and Influenza/EHV in 2011
- Key Messages from 2011 Equine Sales Force Effectiveness Study
Before 1999 the U.S. Equine Veterinarian and Horse Owner Did Not Even Know West Nile Virus (WNV) or Flavivirus Encephalitis Existed

1999
Largest Outbreak of Equine Neurologic Disease Caused by a Flavivirus.¹
The Strain was NY ‘99’

2001
First West Nile Vaccine – West Nile-Innovator

2003
West Nile-Innovator Vaccine was Shown to Be 96.7% Effective Against an Outbreak Among Immunologically Naïve Horses²

2004
Recombitek® Equine WNV Vaccine Licensed by Merial

2006
PreveNile® Licensed

¹Reed SM, Bayly WM, Sellon, DC. Flavivirus Encephalitis. Equine Internal Medicine, St Louis 2010 Saunders Elsevier p.628
Despite New Competition in West Nile Category
West Nile-Innovator is Still the Market Leader\(^1\)

### 2009
- **Vetera\(^\text{®}\) EWT** + WNV is Licensed by Boehringer Ingelheim\(^2\)

### 2010
- **Merck Recalls PreveNile\(^\text{®}\)\(^3\)**
- **Pfizer Animal Health Acquires West Nile-Innovator from Fort Dodge**

### 2011
- **Encevac\(^\text{®}\)-T+WNV with Havlogen\(^\text{®}\)** from Merck
- **Introduced to the Market**

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\(^1\)Animalytix Data Nov 2011


Positive Test Results for West Nile Virus Were Widespread in 2003

Cumulative 2003 Data¹

*States and Counties in Yellow Either Did Not Perform Surveillance or Did Not Report Any Positive Test Results from Their Surveillance

Evolution of WNV Strains in North America

- Original WNV strain: NY99 “Eastern” strain
- Displaced by: WN02 “North American” strain (2002-03), a minor genetic variant
- Replacement caused by WN02 “vector competence” – not affinity for birds or horses
- No difference in NY99 or WN02 growth patterns in *in vitro* cell systems

The WN02 Strain

Has a shorter incubation period (by 2-4 days) in mosquitoes compared to the NY99 strain. This allows for more efficient transmission within the mosquito population and selection pressure for the newer strain


Photo: CDC
Non-Functional Genetic Variation Between NY99 and WN02 Strains

- WNV: High degree of genetic stability (differs from equine influenza virus)
- Minimal genetic variation between NY99 and WN02 genomes:
  - 99.7% nucleotide homology¹
  - 99.8% amino acid homology¹
- Minor genetic deviations occur continuously in all WNV strains
- e.g., in 2003, 11 different WN02 variants identified in Harris County, Texas in 2003²

In a 2003 Natural Outbreak, Naïve Horses Were 31 Times Less Likely to Have Disease if Vaccinated with West Nile-Innovator

![Graph showing comparison between vaccinated and non-vaccinated horses with clinical disease.](image)

\[\text{Vaccinated: } N = 527, \text{Clinical Disease} = 9\]

\[\text{Non-vaccinated: } N = 348, \text{Clinical Disease} = 121\]

West Nile-Innovator is credited for helping reduce the number of equine WNV cases by nearly 70% from 2002 to 2003\(^1\)

Despite the emergence of variant WNV strains, equine cases have declined dramatically since widespread vaccination with West Nile-Innovator vaccines began.


\(^2\)USDA APHIS West Nile Surveillance, States with Equine Cases, 1999-2010

# West Nile Vaccine Strains (Killed Virus)

<table>
<thead>
<tr>
<th>Vaccine (Manufacturer)</th>
<th>Date Introduced</th>
<th>WNV Strain</th>
<th>Combinations Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Nile-Innovator (PAH)</td>
<td>2001</td>
<td>NY99</td>
<td>WNV + VEWT</td>
</tr>
<tr>
<td>Vetera® EWT + WNV(BIVI)</td>
<td>2009</td>
<td>WN02</td>
<td>WNV + VEWT</td>
</tr>
<tr>
<td>Encevac®-T+WNV with Havlogen® (Merck)</td>
<td>2011</td>
<td>Killed Flavivirus Chimera</td>
<td>WNV + EWT</td>
</tr>
</tbody>
</table>

PAH = Pfizer Animal Health; BIVI = Boehringer Ingelheim Vetmedica, Inc; VEWT = Venezuelan, Eastern, Western encephalomyelitis vaccine, tetanus toxoid
West Nile Virus Veterinary Disease Map

Cumulative 2003 Data

*States and Counties in Yellow Either Did Not Perform Surveillance or Did Not Report Any Positive Test Results from Their Surveillance

Legend
- Positive Test Results*
- No Positive Test Results**
- Historically Not Found

West Nile Virus Pathogenesis

WNV cycles in nature primarily between Culex mosquitoes and birds, but also infects human, horses, and other vertebrates.\(^1\)

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\(^1\)Virus and Host Determinants of West Nile Virus Pathogenesis. *Diamond M.S. PLoS Pathogens* June 2009 Volume Issue 6 e1000452
Eastern Equine Encephalomyelitis (EEE), Western Equine Encephalomyelitis (WEE) and West Nile Virus

**EEE and WEE, Are Commonly Called Sleeping Sickness**

- All three diseases cause inflammation of the brain and spinal cord (encephalomyelitis)

**Causes Serious Neurological Symptoms and May Resemble**
- Rabies
- Equine Protozoal Myelitis (EPM)
- Equine Herpesvirus Myeloencephalitis (EHV-1)

**Mortality Rates**
- WNV – 30–38% infected horses\(^1\)
  - Increases to 70% if recumbent
- EEE – 75–90% infected horses\(^2\)
- WEE – up to 50% infected horses\(^2\)

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\(^1\) *Equine Internal Medicine*, 3rd Edition, Reed, Bayly and Sellon, Saunders Publishing, Pg 629
West Nile Virus

A Widespread Mosquito-borne, Neurological Disease that Can Kill Approximately One in Three Clinically Affected Horses

- Horses should be vaccinated annually prior to the onset of the mosquito season
- Consider semi-annual vaccination for horses in endemic areas, horses younger than five or older than 15, and horses with compromised immune systems
- The West Nile virus antigen is covered by the Pfizer Animal Health Equine Immunization Support Guarantee

Eastern Encephalomyelitis (EEE)

A Mosquito-borne, Neurological Disease That Can Kill 75 to 90 Percent of Affected Horses

- Horses should be vaccinated annually
- Consider semi-annual vaccination for horses in endemic areas or with compromised immune systems
- The Eastern Encephalomyelitis antigen is covered by the Pfizer Animal Health Equine Immunization Support Guarantee

Western Equine Encephalomyelitis (WEE)

Another Potentially Fatal, Mosquito-borne Disease Found Primarily West of the Mississippi River

- Horses should be vaccinated annually
- Consider semi-annual vaccination for horses in endemic areas or with compromised immune systems
- The Western Equine Encephalomyelitis antigen is covered with the Pfizer Animal Health Equine Immunization Support Guarantee

Venezuelan Equine Encephalomyelitis (VEE)

- Venezuelan Equine Encephalomyelitis virus has a geographical distribution restricted predominantly to Central and South America, although U.S. incursions have occurred, and the risk of introduction persists.\(^1\)

- The Venezuelan Equine Encephalomyelitis antigen is covered with the Pfizer Animal Health Equine Immunization Support Guarantee.

- West Nile-Innovator + VEWT

Tetanus – An Often-fatal Disease Caused by the Bacterium *Clostridium Tetani* Found in Soil and Feces

- All horses should be vaccinated annually
- Tetanus is covered by the Pfizer Animal Health Equine Immunization Support Guarantee

West Nile-Innovator Combinations

- West Nile-Innovator
- West Nile-Innovator + EWT
- West Nile-Innovator + EW
- West Nile-Innovator + VEWT
Equine Vaccines Are Changing to a Pfizer Animal Health Label in 2012

The Vial Caps and Colors Will Remain the Same Only the Oval in the Center Will Be Updated to Pfizer
Equine Immunization Support Guarantee

Pfizer Animal Health Equine Immunization Support Guarantee Provides

Financial Assistance Up to $5,000 for Reasonable Diagnostic and Treatment Costs

Peace of Mind to the Owner and Supports Veterinarians
Immunization Support Guarantee

Equine ISG Program Guidelines Include

- Horse must be vaccinated by a licensed veterinarian with an established client patient relationship

- Horse must have received an age-appropriate initial vaccination series per the vaccine label. A Pfizer Animal Health Vaccine must be the most recent vaccine used in the series

- Veterinarians must submit a copy of medical records pertinent to the case, including vaccine brand, serial number and the date of the vaccination

- At the time of the support request, veterinarians must collaborate with Pfizer Animal Health Veterinary Medical Information and Product Support (VMIPS) in designing an appropriate diagnostic and treatment regime. A diagnosis must be made using criteria predetermined by VMIPS
Peel and Stick Label for Equine Immunization Support Guarantee

Peel and Stick Labels Are Supplied with Vaccine Vials and 12x1s for Easy Record Keeping

Material Number: EQB0611054 Material Name: ISG VACCINE LOG BINDER W/PAD AND MAGNET
USDA Label Claims

Highest Level of Label Indication*

- **Prevention of Infection ++++**
  Prevents All Colonization or Replication of Challenge Organism

- **Prevention of Disease +++**
  Highly Effective in Preventing Clinical Disease

- **Aids in Disease Prevention +++**
  Aids in Preventing Disease by a Clinically Significant Amount

- **Aids in Disease Control ++**
  Aids in Reduction of Disease Severity, Duration or Onset

- **Other Claims**
  Products with Beneficial Effects Other Than Direct Disease Control

Lowest Level of Label Indication*

*Veterinary Services Memorandum No.800.202
## EQUINE CORE VACCINES - WEST NILE
### USDA EQUINE LABEL CLAIM COMPARISON CHART

<table>
<thead>
<tr>
<th>Indications</th>
<th>West Nile-Innovator* +EWT</th>
<th>West Nile-Innovator* +VEWT</th>
<th>Vetera* EWV + NWV</th>
<th>Vetera* EWV + NWV</th>
<th>Recombitek* rWNV-EWT</th>
<th>Encevac* -T+WNV with Havlogen*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core and Risk Claims</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>West Nile viremia</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
</tr>
<tr>
<td>EEE, WEE, Tetanus</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
</tr>
<tr>
<td>VEE*</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
<td>![symbol]</td>
</tr>
<tr>
<td>DURATION OF IMMUNITY</td>
<td>1 year</td>
<td>1 year</td>
<td>1 year</td>
<td>1 year</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Age Restrictions             | No age restrictions       | No age restrictions       | 4 months          | 4 months          | 4 months             | 6 months                     |
| Reconstitution               | no                        | no                        | no                | no                | yes                  | no                            |
| Doses                        | 1 mL                      | 1 mL                      | 1 mL              | 1 mL              | 2 mL                 | 1 mL                          |

### USDA Label Claims
- **PREVENTS INFECTION**
- **PREVENTS DISEASE**
- **AIDS IN PREVENTION**
- **AIDS IN CONTROL OR REDUCTION**

---

1. The vaccine protected 95% of the vaccinated against West Nile virus infection, while 82% of the controls were viremic. Efficacy of the West Nile fraction was demonstrated in horses that received two doses of the vaccine and were challenged one year post-vaccination with West Nile Virus.

2. Aids in the prevention of viremia and mortality and aids in the reduction of severity of clinical disease caused by West Nile virus.

3. Aids in the prevention of disease, viremia, and encephalitis caused by West Nile virus.

4. Aids in the reduction of disease, encephalitis, and viremia caused by West Nile virus.


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Source: North American Compendium and advertising as of January 2012

25
Newer Licensed Vaccines Used Intrathecal Challenge Which Induced Severe Disease Rather Than Field Infection Ratio of 11:1.1

### West Nile-Innovator License Study Used Mosquito Feeding Challenge Model

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Pfizer</th>
<th>Boehringer</th>
<th>Merial</th>
<th>Merck</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
<td>West Nile-Innovator + EWT</td>
<td>Vetera® EWT + WNV</td>
<td>Recombitek® rWNV-EWT</td>
<td>Encevac®-T + WNV with Havlogen®</td>
</tr>
</tbody>
</table>
| West Nile    | • The vaccine protected 95% of the vaccinates against West Nile virus infection, while 82% of the controls were viremic | • Aids in the prevention of viremia and mortality  
• Aids in the reduction of severity of clinical disease caused by West Nile virus | • Aids in the prevention of disease, viremia, and encephalitis caused by West Nile virus | • Aids in the reduction of disease, encephalitis, and viremia caused by West Nile virus |

\(^1\)Long et al. Comparative efficacies of Three Commercially Available Vaccines against West Nile Virus( WNV) in a Short Duration Challenge Trial Involving an Equine WNV Encephalitis Model. *Clinical and vaccine Immunology* Nov. 2007 p.1465-1471
West Nile-Innovator

Case Criteria/Case Outcome from Long et al.¹

- West Nile-Innovator in study-formalin inactivated killed vaccine

- All vaccinated horses met the criteria for protection against WNV encephalitis. In all groups, irrespective of the vaccine product, the levels of protection were significantly different from those of the control horses ($P \leq 0.0001$)¹

- Company decision not to go back and update label claims with this challenge model

- West Nile-Innovator was the world’s first commercially available West Nile vaccine with more than 30 million doses sold. It is still veterinarians’ #1 choice for mosquito-borne disease protection²

¹Long et al. Comparative efficacies of Three Commercially Available Vaccines against West Nile Virus (WNV) in a Short Duration Challenge Trial Involving an Equine WNV Encephalitis Model. Clinical and vaccine Immunology Nov. 2007 p.1465-1471

²Market Dynamics Inc., July 2011
2011 US Equine Vaccine Survey

Objective
• Understand current trends in vaccine use among equine veterinarians

Methodology
• Postcard mailing containing a link to a web survey conducted from October – November, 2011
  – Participants’ incentive for participation was the opportunity to enter into a raffle for an Apple iPad 2®
  – All were recruited from a list of US veterinarians provided by AAEP (American Association of Equine Practitioners)

Sample: N=306
• All respondents are members of AAEP, and licensed to practice veterinary medicine
• 56% of respondents are practice owners; 38% are associate veterinarians [6% - “Other”]
• On average, 75% of respondents’ practices are devoted to treating horses
• The majority of participants say their practices mostly treat patients in the recreation segment (75%); 68% say they treat horses in the performance space
**Pfizer West Nile Vaccines**

**49%**
...of vets polled **currently use** Pfizer Animal Health’s WNV Vaccine(s)

**17%**
...of veterinarians who switched WNV vaccines (n=88) switched **TO** Pfizer Animal Health (n=15)

- Of those who switched to PAH, the most switched from **Merial**
- The most mentioned reasons veterinarians switched to **PAH’s WNV vaccine(s) are reactions and interactions with a manufacturer** that were either:
  - Negative with their previous WNV manufacturer
  - Positive with Pfizer Animal Health

**60%**
...of veterinarians who switched WNV vaccines (n=88) switched **FROM** Pfizer Animal Health (n=53)

- Of the veterinarians who switched from Pfizer, Animal Health the most switched to **Boehringer Ingelheim**
- The most mentioned reason veterinarians switched from Pfizer Animal Health’s WNV vaccine(s) is because West Nile EWT was on backorder in Spring 2011 and this introduced the opportunity to try the new **combination vaccine**

**FACT**
62% of Veterinarians Who Currently Use PAH’s WNV Vaccine(s) Still Refer to PAH as Fort Dodge
### Large Combo Antigen Chart

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>WN (Core)</th>
<th>WEE/EEE (Core)</th>
<th>Tetanus (Core)</th>
<th>Flu (Risk)</th>
<th>Rhino (Risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Nile-Innovator EWT</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Fluvac Innovator EHV 4/1</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Vetera Gold</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PRESTIGE® V + WNV WITH HAVLOGEN®</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

“Big Combos” Do Not Allow Risk/Benefit Analysis for AAEP Guidelines Regarding Core vs. Risk Antigens

“Big Combos” Add More Inventory for a Practice to Cover as the Large Combo is Not Needed in the Fall
The study was conducted using an Internet-based self-administered survey. Using the PAH called-on target list, respondents were contacted by email, fax or letter, and invited to a password-protected web site, and passed a series of screening questions. Qualified respondents are those who:

- Are licensed veterinarians, owners or partners, in practice for at least 2 years
- Spend at least 50% of their professional time devoted to equine
- Have been detailed on at least two of the following PAH brands in the past three months: FLUVAC INNOVATOR®, WEST NILE-INNOVATOR®, DORMOSEDAN®/DORMOSEDAN® GEL, EXCEDE®, QUEST® / QUEST® Plus and STRONGID® C / STRONGID® C 2X™
- Met a sales rep from another animal health company to discuss an equine product in the past three months
- Are not affiliated with any advertising agencies, FDA/USDA/EPA other drug regulatory agencies, market research companies, pharmaceutical consulting companies, pharmaceutical manufacturers, or PR agencies

The sample size consists of 105 PAH called-on veterinarians
West Nile-Innovator – The More Often Reps Ask Veterinarians to Purchase or Increase Usage, the More Likely Veterinarians Are to Take Action\(^1\)

\(N=64\)

<table>
<thead>
<tr>
<th>Action Requested By Rep</th>
<th>Action Taken by Veterinarian</th>
</tr>
</thead>
<tbody>
<tr>
<td>66% of veterinarians asked to purchase/increase usage</td>
<td>52% of veterinarians who purchased/increased usage</td>
</tr>
</tbody>
</table>

\(^1\)2011 PAH Equine Sales Force Effectiveness Survey
Most Important Messages to Veterinarians Regarding West Nile-Innovator

N=64

**DOI**

- West Nile-Innovator has a one year labeled duration of immunity

**ISG**

- West Nile-Innovator is guaranteed by an Equine Immunization Support Guarantee which means Pfizer Animal Health will provide up to $5,000 to cover diagnostics and treatment costs for horses vaccinated with West Nile-Innovator who subsequently contract disease

1 2011 PAH Equine Sales Force Effectiveness Survey
Equine Veterinary Operations Team
Supporting PAH Equine Vaccines

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ARVAC®, EQUILOID INNOVATOR®, EQUIVAC® INNOVATOR, FLUVAC INNOVATOR®, PINNACLE® I.N., PNEUMABORT-K® +1b, ROTAVIRUS, TETANUS ANTITOXIN, TETANUS TOXOID, TRIPLE-E T INNOVATOR®, WEST NILE-INNOVATOR®, ZYLEXIS®

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