

Merck Animal Health Equine Respiratory Update

IN COLLABORATION WITH THE UNIVERSITY OF CALIFORNIA, DAVIS SCHOOL OF VETERINARY MEDICINE

From Outbreak to Vaccine: A True Tale of Equine Influenza Surveillance

An active six-month period for influenza continues to highlight the importance of surveillance and sequencing of recent isolates to understand current circulating strains of the virus

“In a period of three to four weeks, we had as many as 40 to 50 horses ill to the point of requiring monitoring.”

Dr. Jeffrey Powers, owner of Veterinary Clinics North, had his hands full with equine influenza on the small tourist and vacation haven of Mackinac Island, situated between Michigan’s upper and lower peninsulas. Every year, the horse population on the island goes from about 25 to nearly 500 by July 4th. While most of these horses winter in Northern Michigan, a confluence of factors including the stress of shipping and a cold, wet spring, led to an increase in horses developing fevers, nasal discharge and cough—“signs of classic respiratory disease outbreak,” notes Dr. Powers. Most of the horses had an unknown vaccination history.

The frustration of managing a rapidly moving influenza outbreak has likely been shared by many reading this newsletter. There’s often a silver lining in tough situations as this type of frustration serves as inspiration for innovation. What can we learn from the outbreak?

Rewind to 2013, when a substantial equine influenza outbreak hit the Florida HITS show (pun intended). It was an isolate from this outbreak identified through the Biosurveillance Program that became the cornerstone to Merck Animal Health’s introduction of the Florida ‘13 Clade 1 equine influenza strain—the most current Clade 1 strain available in a U.S. commercial inactivated influenza vaccine.¹

But, how do we know—and many of you may have asked this same question—if Florida ‘13 (or any other strain identified, for that matter) is significant and representative of current circulating disease, and thus capable of providing enhanced disease protection? Let’s look to genetic characterization.

What constitutes significant antigenic drift?

It depends not only on the number of amino acid changes that occur in the HA glycoprotein but where those changes are located. Amino acid changes that occur near critical regions on the surface of the HA protein are very significant.

Genetic Characterization of Recent Equine Influenza Outbreaks

Sequencing of the equine influenza virus through a process called *genetic characterization* (comparing genetic sequences of influenza isolates) on an ongoing basis is critical to making informed decisions regarding:

- How equine influenza viruses are ‘related’ to one another
- How equine influenza viruses are evolving
- The genetic variations (mutations) that appear when viruses begin spreading more easily or causing more severe diseases
- How well an equine influenza vaccine might protect against a particular influenza virus

Sequencing of the influenza virus is focused on two gene segments of the influenza A virus—the hemagglutinin (HA) and neuraminidase (NA), which are two glycoproteins found on the surface of the virus. Surface proteins determine important properties of influenza viruses, including the virus’ genetic similarity to influenza vaccine viruses. HA is the most important of the two glycoproteins because it is the target for serum neutralizing antibodies generated by influenza vaccines.

¹Comparison of U.S. commercial inactivated influenza vaccine strains, per respective manufacturer’s label, October 2019.

Sequencing of the HA glycoprotein is an insightful scientific way to compare different strains of EIV. Recent sequencing (2018–2019) of positive equine influenza samples submitted through the Respiratory Biosurveillance Program demonstrated a very high degree of homology (or similarity) to Florida '13.² This validates the relevance of Florida '13 to influenza strains currently circulating throughout the United States and causing disease in the field.

Sample	FL-13 Reference	Outbreak State
FL-13 reference	100.00	Florida
Horse 1	98.50	Pennsylvania
Horse 2	98.69	Missouri
Horse 3	98.88	Ohio
Horse 4	98.88	Arizona
Horse 5	98.69	Tennessee
Horse 6	99.21	Missouri
Horse 7	98.50	Florida
Horse 8	98.67	New York
Horse 9	98.73	Ohio
Horse 10	98.69	Washington
Horse 11	98.99	Texas

Sample submissions collected from equine influenza outbreaks over a 11-month period (April 2018–February 2019). Table shows homology—or similarity—of sample vs. Florida '13, expressed as a percentage. All samples are >98.50% homologous to Florida '13, corresponding to a high degree of similarity. All are Clade 1 viruses.

Sequencing Data Reinforces Florida '13 as Highly Relevant Equine Influenza Strain²

1. Demonstrated similarity to isolates from recent outbreaks

- >98.50% sequencing homology
- Spans multiple age groups, breeds and other signalment parameters
- Broad geographic distribution of cases
- Representative of real-life challenge and sick horses

2. Significantly different from Ohio '03 (OIE recommended clade 1 isolate)

- Florida '13 differs from Ohio '03 by seven amino acid mutations
- Five of those mutations occur in clinically significant areas on the surface of the HA glycoprotein—regions associated with antibody binding or receptor binding sites³

As for the horses of Mackinac Island? Fortunately, with diligent management of incoming horses, speedy diagnostics through the Respiratory Biosurveillance Program and a little help from Flu Avert® intranasal modified-live influenza vaccine, the outbreak was curtailed, but not before several horses fell victim to secondary bacterial infections. “Right now (early August), if you come here it would seem as if nothing is going on,” added Dr. Powers. “The horses look good and I would say the respiratory conditions now are probably better than they were a year ago.

Dr. Barnett and Merck Animal Health went above and beyond to help us deal with this problem and we're very grateful for that.”

And just like the 2013 Florida outbreak, who knows how this outbreak may be put to good use, so keep sending in those samples!

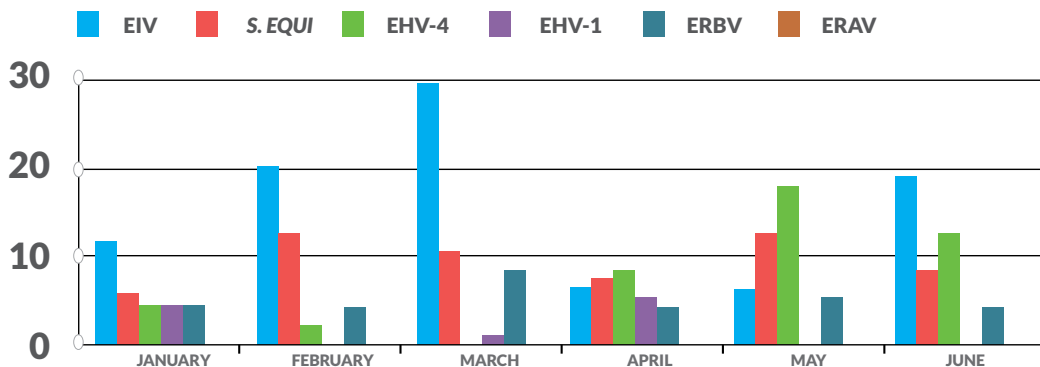


²Data on file. Merck Animal Health

³Singh RK, et al. (2018) A Comprehensive Review on Equine Influenza Virus: Etiology, Epidemiology, Pathobiology, Advances in Developing Diagnostics, Vaccines, and Control Strategies. Front. Microbiol. 9:1941. doi: 10.3389/fmicb.2018.01941

Six-Month Disease Trends January to June 2019⁴

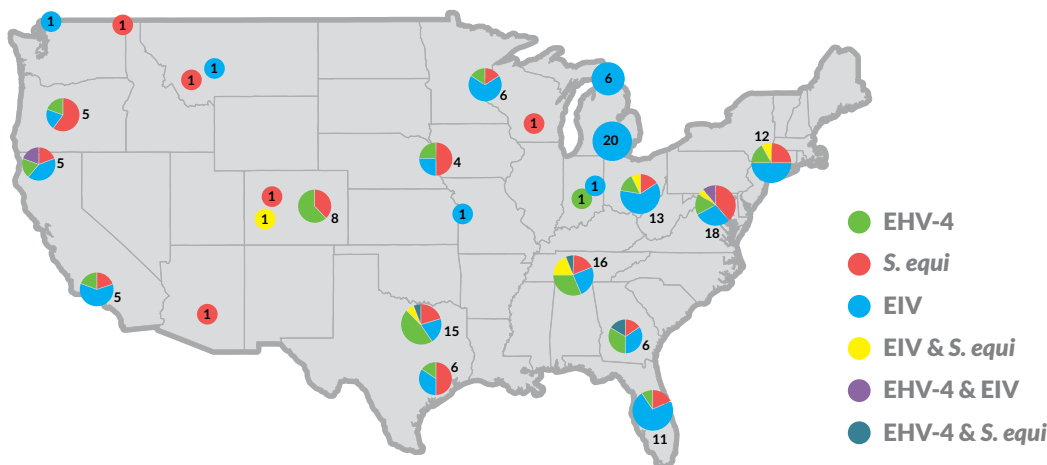
A total of 421 samples were submitted from January to June 2019. Overall, 53% of total samples submitted tested positive for one of the six primary pathogens (*S. equi*, EHV-4, EIV, ERBV, EHV-1, ERAV).



The most recent six months of data (January–June 2019) show that EIV was the most prevalent infectious upper respiratory disease reported, representing 39% of total positive samples, followed by *S. equi* (24%) and EHV-4 (19%).

Demographic Summary	EIV (88 Cases)	<i>S. equi</i> (54 cases)	EHV-4 (43 Cases)
Median Age	6 years Range: 8 months – 27 years	7 years Range: 1 – 34 years	6 years Range: 1 month – 25 years
Predominant Breed(s)	Warmblood; other	Quarter Horse	Quarter Horse; Thoroughbred
Travel	No 37% Yes 31% Unknown 32%	No 65% Yes 22% Unknown 13%	No 72% Yes 19% Unknown 9%
Primary Discipline	Show 41% Pleasure 27% Other/Unknown 32%	Pleasure 52% Show 24% Other/Unknown 24%	Pleasure 40% Show 35% Other/Unknown 25%

Summary of primary demographic parameters for the three major pathogens (January–June 2019).⁴



Geographic representation of the top three pathogens January–June 2019.⁴ Pie represents the proportion of total positive EIV, EHV-4 and *S. equi* cases in an area, including areas of disease overlap (e.g., EIV and *S. equi* positive cases in a given area).

⁴Merck Animal Health and University of California, Davis School of Veterinary Medicine (Nicola Pusterla). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008-present.

Practice Tips

We Want to Hear from You

Within the next two weeks, you will receive a survey requesting your input on the Respiratory Biosurveillance Program. We're eager to hear what you like about the program, areas we can enhance and new ideas to help you better manage equine infectious upper respiratory disease. Thank you, in advance, for providing valuable feedback on the Respiratory Biosurveillance Program. Results from the survey will be shared in the next newsletter.

Your feedback is always welcome by contacting the **Merck Animal Health Equine Veterinary Professional Services team** at **(866) 349-3497**.

Quick Tips For Clients

Disease Education for Clients

Click to download and share the following influenza quick facts infographic on your clinic Facebook page or your website.



 [Click to download](#)

Respiratory Biosurveillance Program in the News

Earlier this year, in honor of the Respiratory Biosurveillance Program's 10th anniversary, we publicly shared some of the insights and data from the program as a result of your participation and partnership. Here are a few highlights.



Journal of the American Veterinary Medical Association: [Ongoing Merck Equine Study Reveals 10 Years of Data](#)



The Horse: [10 Years of Upper Respiratory Disease in Horses](#)



EquiManagement: [Key Respiratory Findings Released from Merck Biosurveillance Research](#)



Modern Equine Vet: [Equine Surveillance Changes Understanding of Common Respiratory Diseases](#)



Animal Pharm: [Merck Biosurveillance Data Reveals New Insights into Equine Respiratory Disease](#)



Paulick Report: [Merck Animal Health Equine Biosurveillance Program Delivers Unprecedented 10 Years of Data](#)

About the Newsletter

This bi-annual newsletter is being sent as a value-added service to clinics enrolled in the biosurveillance program. Merck Animal Health is passionate about this program and is providing this newsletter to customer veterinarians to help them stay up-to-date on the latest trends and historical information the study has yielded to date. Technical veterinary advice, interpretation and case management support will be provided by Merck Equine Veterinary Professional Services (Drs. Barnett, Vaala, Gaughan, Craig, Bain and Chappell) and Nicola Pusterla, D.V.M., Department of Medicine and Epidemiology, UC Davis.

If you have questions about the program, please call our professional services team at (866) 349-3497, or email one of the professional services veterinarians at the addresses listed below.

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Relevant Supporting Research

For more information on the latest respiratory disease published research from Merck Animal Health, click on the links below.

- 1) [“Prevalence Factors Associated with EHV-2/5 Among Equines with Signs of Upper Respiratory Infection in the US.”](#)
James, K., Vaala, W., Chappell, D., Barnett, D.C., Gaughan, E., Craig, B., Bain, F., Pusterla, N. ACVIM 2017 Abstract.
- 2) [“Prevalence factors associated with equine herpesvirus type 1 infection in equids with upper respiratory tract infection and/or acute onset of neurological signs from 2008 to 2014.”](#)
Pusterla, N., Mapes, S., Akana, N., Barnett, D.C., Mackenzie, C., Gaughan, E., Craig, B., Chappell, D., Vaala, W. *Vet Rec.* 2015; doi: 10.1136/vr.103424.
- 3) [“Voluntary Surveillance Program for Equine influenza Virus in the United States from 2010 to 2013”](#)
Pusterla, N., Kass, P.H., Mapes, S., Wademan, C., Akana, N., Barnett, D.C., Mackenzie, C., Vaala, W. *J Vet Intern Med* 2015; 29:417-422
- 4) [“Surveillance programme for important equine infectious respiratory pathogens in the USA”](#)
Pusterla, N., Kass, P.H., Mapes, S., Johnson, C., Barnett, D.C., Vaala, W., et. al. *Vet Rec.* 2011 July 2;169(1):12. doi: 0.1136/vr.d2157.
- 5) [“Voluntary surveillance program for important equine infectious respiratory pathogens in the United States”](#)
Pusterla, N., Kass, P.H., Mapes, S., Johnson, C., Barnett, D.C., Vaala, W., Gutierrez, C., et. al. AAEP Proceedings 2010.

About the Program

Since March of 2008, Merck Animal Health has been conducting an ongoing, voluntary equine biosurveillance program to study the prevalence and epidemiology of relevant viral and bacterial respiratory pathogens. More than 8,700 samples from U.S. equids of all ages, genders and breeds presenting with fever and signs of acute upper respiratory disease and/or acute neurological disease have been collected since the study began. Samples are submitted by participating Merck Animal Health customer clinics and tested via quantitative PCR at the University of California, Davis School of Veterinary Medicine (UC Davis). **To be eligible for testing, horses must have an unexplained fever (T ≥ 101.5°F) AND one or more of the following signs: depression, nasal discharge, cough and/or acute onset of neurologic disease.** The results are then returned to the Merck Animal Health customer within 24 hours and provide invaluable diagnostic and treatment information.

Four-Fold Purpose:

- 1) To provide a valuable diagnostic tool to participating Merck Animal Health customers to assist in obtaining an accurate and timely diagnosis during an acute respiratory disease outbreak so they can provide optimal treatment, quarantine and vaccination strategies to their clients and patients.
- 2) To provide the horse industry with a better understanding of the prevalence and epidemiology of these respiratory pathogens.
- 3) To identify and monitor the current circulating strains of major equine respiratory pathogens.
- 4) To evaluate the efficacy of current vaccination protocols.



The Science of
Healthier Animals