

Merck Animal Health Equine Respiratory Update

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

SPECIAL ANNIVERSARY ISSUE

Equine Respiratory Biosurveillance Program: 10 Years Later

Important learnings from a decade of data

Infectious respiratory disease outbreaks have played an often too visible role in the horse industry and the costs have been staggering. From influenza and equine herpesvirus to strangles, we've faced the best and worst of days as an industry. The challenging and elusive properties of these diseases continue to keep the industry on its toes, which is why experts have long-recognized the importance of ongoing surveillance to monitor emerging trends, manage disease cases and improve preventive strategies.

The Equine Respiratory Biosurveillance Program idea began to take shape more than 15 years ago during collaborative conversations between D. Paul Lunn, BVSc, MS, PhD, MRCVS, Dipl. ACVIM, now dean of veterinary medicine at North Carolina State University, and D. Craig Barnett, DVM, director of equine veterinary professional services at Merck Animal Health. In March 2008, it came to fruition as the Infectious Upper Respiratory Disease Study.

The goals of the study were four-fold:

1. Provide participating veterinarians with a valuable diagnostic tool to assist them in providing an accurate and timely diagnosis so they can treat and manage infectious respiratory disease accordingly.
2. Provide the industry with a better understanding of the prevalence and epidemiology of common respiratory pathogens.
3. Identify and monitor the current circulating strains of major equine respiratory pathogens.
4. Evaluate the efficacy of current vaccination protocols.

Due to Merck Animal Health's unwavering support for this program, the largest cumulative equine

infectious upper respiratory biosurveillance data set exists; and with it, we've gained powerful learnings.

“Credit goes to Dr. Paul Lunn for the vision of the program,” says Dr. Barnett. “Without his foresight, the program would not be what it is today.”

In addition to Dr. Lunn, there were several other folks integral to the program's design and implementation, including Drs. Wendy Vaala, Josie Traub-Dargatz, Nicola Pusterla and others.

In late 2007, a partnership was born with the team at University of California, Davis School of Veterinary Medicine (UC Davis), led by Nicola Pusterla, DVM, Dipl. ACVIM, to serve as the real-time PCR laboratory for sample submissions.

“Our partnership with Dr. Pusterla and UC Davis is invaluable,” Dr. Barnett said. “He provided critical input at the beginning and was instrumental in helping with the logistics and final study design. Dr. Pusterla's expertise and assistance have been unprecedented. Samantha Barnum in the lab at UC Davis has been an incredible resource and has provided exceptional customer service throughout the course of this study.”

“When we started this program, we didn't know how much we would gain over this period,” Dr. Pusterla said.

“What Merck Animal Health has done is and will remain an unmatched service to the entire U.S. equine community.”

Dr. Pusterla highlights four contributions of the program:

- Increased awareness of respiratory pathogens in the veterinary community.
- Invaluable epidemiological information pertaining to common and less characterized respiratory pathogens.
- Demonstration of how the industry adds value to the equine community by pursuing diagnostic testing and disseminating that information.
- Sequencing of equine influenza virus (EIV) isolates to monitor how the virus is changing in the field and to evaluate and improve the efficacy of vaccines.

“The program has changed the way we look at equine respiratory pathogens and helped evolve the way the industry manages these costly diseases, not only through timely and accurate diagnostic services, but also with improved vaccination solutions and disease management measures, bringing the program full-circle to our original vision,” Dr. Barnett said. “Few things in my professional career have provided more satisfaction, and I'm so proud to work with the team responsible for making it happen every day. **But without you, the participating clinic, this surveillance program would not be possible. Thank you to the many veterinarians across the country who have contributed samples and played a part in developing this powerful data set.** I can't wait to see what else is in store as the program continues.”

A Decade of Notable Findings

On this special anniversary occasion, we've compiled 10 highlights of the program:

- Breadth and depth of information** is unparalleled and, today, the Merck Animal Health Equine Respiratory Biosurveillance Program is recognized as **the largest equine infectious upper respiratory biosurveillance data set ever created**, with more than 8,200 samples collected over 10-plus years, including a large collection of equine influenza isolates that has provided valuable insight to this changing virus.
- Five published research papers and ten abstracts presented at four national and six international conferences** have resulted from the study, spanning comprehensive data collected on all the major respiratory pathogens surveilled, as well as in-depth papers on influenza, EHV-1, EHV-2 and EHV-5, with more in the works.

- Identification of important antigenic drift and isolation of a new influenza strain (Florida '13) responsible for a significant disease outbreak in well-vaccinated horses.**

The study confirmed that EIV is an ongoing

significant threat to the equine industry and is the **second most commonly diagnosed infectious upper respiratory**

disease pathogen, representing 28% of all positive samples, just behind EHV-4.¹ Prior to the implementation of this study, veterinarians would commonly report that they weren't seeing much influenza in horses.

- Greater understanding of the demographic and signalment parameters** associated with common upper respiratory disease infections in horses, including recognition that age does not define susceptibility to certain infectious respiratory pathogens. For example, the broad distribution of demographics in positive EIV cases, showing wide age ranges, and representation from a variety of disciplines, breeds and travel patterns reinforces any horse is at risk.

- New insights on strangles**, including a high-frequency of *S. equi* in non-traveling pleasure horses, higher median age than in horses with other upper respiratory diseases (strangles is the most commonly diagnosed upper respiratory disease in horses 6-10 years of age²), and the propensity for co-infection with EHV-4.
- EHV-4 is a predominant virus** associated with upper airway infection and a major infectious upper respiratory disease threat, particularly in young horses. EHV-4 is the most commonly diagnosed disease, representing 33% of all positive cases since program inception³.
- New understandings of the lesser known herpesviruses – EHV-2 and EHV-5**, which are often a source of co-infection with the major respiratory pathogens — likely due to these viruses' ability to downregulate the immune system, making the horse more susceptible to other viral and bacterial infections.
- Unprecedented 24-hour diagnostic turnaround** for sample submissions thanks to the UC Davis Equine Infectious Disease Research Laboratory. This rapid turnaround time allows veterinarians to fine tune their management strategies and biosecurity recommendations, even when dealing with contagious diseases that have short incubation periods.
- Reinforced biosecurity practices**, including importance of isolation and daily monitoring post-travel and the need for isolation and daily monitoring of new arrivals to the stable/farm/ranch.
- Responsive and evolving nature of the program provides an inroad to detecting pathogens on the horizon.** We added the equine rhinitis viruses (A/B) to the program in 2012 and have established a surveillance platform that facilitates our ability to identify and monitor emerging respiratory disease threats.

Spotlight:

Perhaps the most notable accomplishment of the ongoing Respiratory Biosurveillance Program is the identification of a new influenza strain, representative of a current circulating strain responsible for an outbreak in a large number of well-vaccinated horses.

Sequencing work revealed Florida '13 differs from OH '03 (OIE recommended clade 1 isolate) by seven amino acid changes, and five of those mutations occur on the surface of the HA glycoprotein and are in or near regions associated with antibody binding or receptor binding sites⁴ — making them critically significant.

"Incessant surveillance programs will aid in opting a better control strategy for this virus (EIV) by updating the circulating vaccine strains. ... Antigenic drift at the HA gene (a major protein of influenza A virus) led to vaccine failure in various parts of the world... To deal with this problem, continuous checks and monitoring through surveillance programs and updating vaccines with recent strains remains the best and effective way in prevention and control of this disease."

- Excerpts from "A Comprehensive Review of Equine Influenza Virus: Etiology, Epidemiology, Pathobiology, Advances in Developing Diagnostics, Vaccines and Control Strategies," from the Sept. 6, 2018 issue of *Frontiers in Microbiology*, authored by Singh RK, et al.

¹Merck Animal Health and University of California, Davis School of Veterinary Medicine (Nicola Pusterla). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008-present.

²Surveillance programme for important equine infectious respiratory pathogens in the USA. N. Pusterla, P.H. Kass, S. Mapes, C. Johnson, D.C. Barnett, W. Vaala, et al. *Vet Rec* 2011.

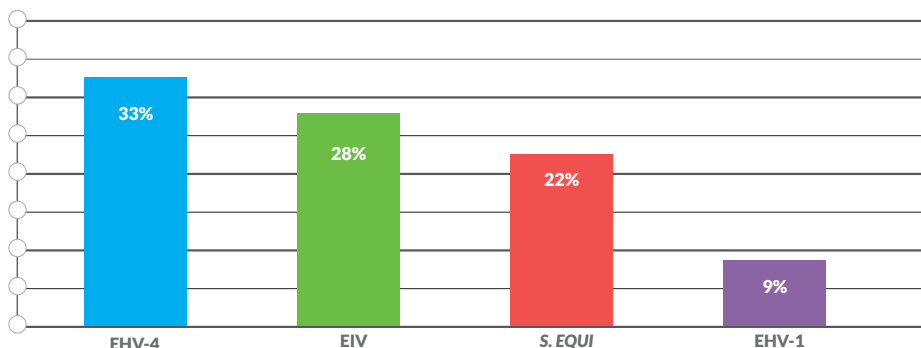
³Merck Animal Health and University of California, Davis School of Veterinary Medicine (Nicola Pusterla). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008-present.

⁴Data on file, Merck Animal Health.

Biosurveillance Program Disease Incidence: March 2008–December 2018¹

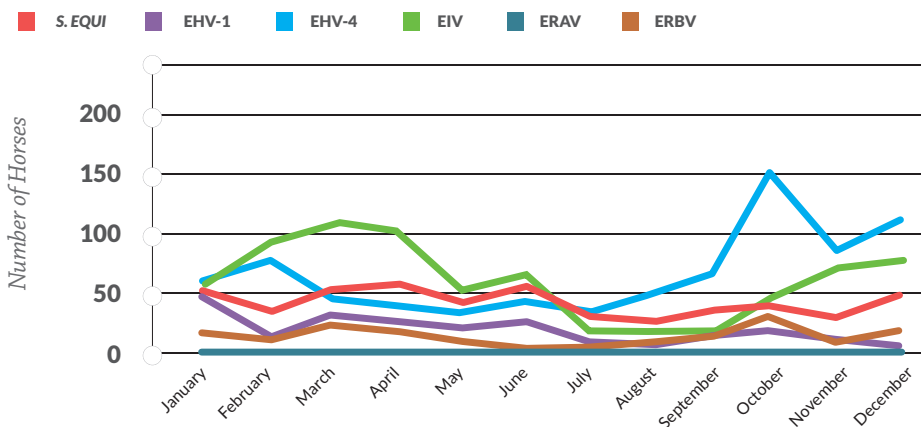
More than 8,200 samples have been collected since the biosurveillance program began more than 10 years ago. Of those, 30% have returned positive for one of six pathogens tracked, including equine herpesvirus types 1 and 4 (EHV-1, EHV-4), equine influenza virus (EIV) and *Streptococcus equi*, which have been tracked from the inception of the program, and ERAV and ERBV, which were added in 2012.

Disease Incidence 2008–2018¹ (As a percentage of total positive samples)



Through December 2018, equine herpesvirus type 4 (EHV-4) was the most commonly diagnosed infectious upper respiratory disease, comprising 33% of all positive samples, followed closely by equine influenza virus at 28% and then *Streptococcus equi* at 22%.

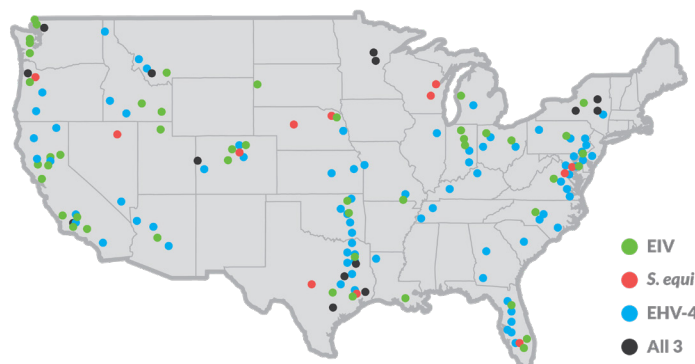
Biosurveillance Results Monthly Cumulative 2008–2018¹



The monthly cumulative depicts the seasonal effect of respiratory pathogens spanning 130 months of surveillance. EHV-4 continues to be more prevalent in the fall months, in contrast to the other respiratory pathogens (especially EIV) that are more prevalent in the winter and spring months.

Geographic representation of the top three pathogens since program inception, including cases of EHV-4, EIV and *S. equi* (March 2008–December 2018).¹

NOTE: Pins represent the origin of more than 2,064 positive cases of EHV-4, EIV and *S. equi*, not the actual quantity of cases.

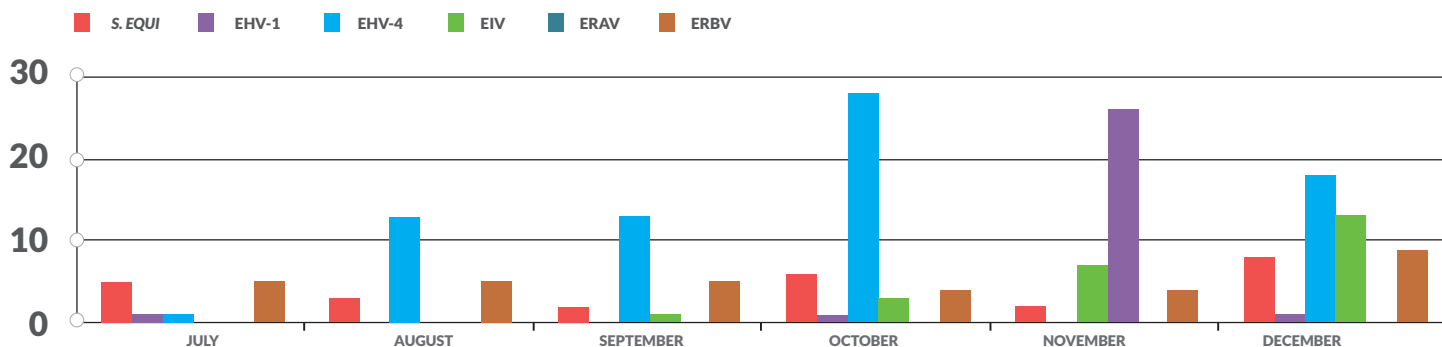


¹Merck Animal Health and University of California, Davis School of Veterinary Medicine (Nicola Pusterla). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008–present.

Most Recent Six-Month Disease Trends (July to December) 2018¹

A total of 427 samples were submitted from July to December 2018.

Overall, 43% 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 (July to December 2018) show that EHV-4 was the most prevalent infectious upper respiratory disease reported, followed by EIV and *S. equi*.

Demographic Summary	EHV-4 (80 Cases)	EIV (43 Cases)	<i>S. equi</i> (26 cases)
Median Age	4 years Range: 4 months – 32 years	4 years Range: 6 months – 19 years	5 years Range: 6 months – 19 years
Predominant Breed(s)	Quarter Horse, Thoroughbred	Quarter Horse	Quarter Horse, other
Travel	Yes 25% No 75%	Yes 33% No 58% Unknown 9%	Yes 46% No 31% Unknown 23%
Primary Discipline	Show/performance; racing	Show and pleasure	Show/performance; racing

The table provides a summary of primary demographic parameters for the three major pathogens during the most recent six months (July–December 2018).¹

¹Merck 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

Please Report Influenza Cases to EDCC

The American Horse Council Health & Regulatory Committee has taken note of the increased incidence of equine influenza (EI) and the need to recommend more vaccination. The committee would like to encourage clinicians to report more EI cases to the Equine Disease Communication Center (EDCC). You have a leg up because of your participation in the biosurveillance program. Please report positive EI cases to the EDCC, using the [EDCC Alert Request Form](#).

As a reminder, Merck Animal Health currently reports biosurveillance results to the EDCC on a biweekly basis. This is included on the [EDCC news page](#). Clearly the industry is asking for more help getting the word out about equine influenza. Your support in reporting positive EI disease cases is appreciated.

The submitting veterinarian's name and contact information is strictly confidential. Veterinarians can also see and download disease information, owner fact sheets and venue specific biosecurity protocols available on the EDCC website (<http://equinediseasecc.org/disease-information> and <http://equinediseasecc.org/biosecurity>).

Quick Tips For Clients

Disease Education for Clients

To reinforce your recommendations regarding risk-based vaccination, click to download and share the following visual and disease education on your clinic Facebook page or website.

Most Common Culprits of Contagious Equine Disease Outbreaks

EHV-1 and EHV-4 ("rhino"): After initial infection, herpesvirus remains dormant (latent) in the horse; stress can reactivate the virus, and viral shedding can occur without symptoms.

- EHV-1 can cause respiratory disease, late-term abortions, early foal deaths, neurologic disease
- EHV-4 is typically associated with upper respiratory disease in younger horses.

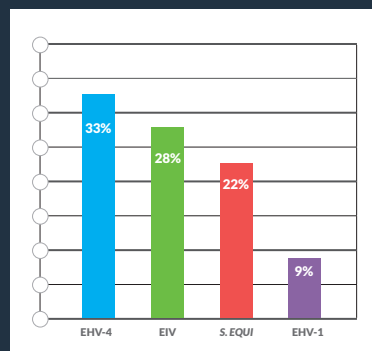
EIV: Equine flu is perhaps the most contagious and quick to spread.

- Can spread up to 50 yards from a coughing horse
- Destroys the cells lining the airways, requiring significant recovery time.

S. equi: Strangles or "distemper"—abscess-forming bacteria that often appears as enlarged, swollen and tender lymph nodes around the horse's head.

Disease Incidence 2008–2018¹

(As a percentage of total positive samples)



[Click to download](#)

Also, be sure to ask your Merck Animal Health sales representative about our disease infographics available to support client education, including:

- Equine Influenza (EIV)
- Equine Herpesvirus Type 1 (EHV-1)
- Equine Herpesvirus Type 4 (EHV-4)
- Equine Herpesvirus Myeloencephalopathy (EHM)
- Eastern/Western Equine Encephalomyelitis (EEE/WEE)
- Streptococcus equi (strangles)
- West Nile Virus (WNV)

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.
- 6) ["Equine Viral Respiratory Pathogen Surveillance at Horse Shows and Sales."](#)
Carlson JK, Traub-Dargatz JL, Lunn DP, Morley PS, Kohler A, Kasper K, Landolt GA, Barnett DC, Lunn KF. *Journal of Equine Veterinary Science*. 33 (2013) 229-237.

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 8,200 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.



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