David Mathieson, a senior vet with Donnington Grove Veterinary Group in Great Britain, displays flu vaccines required for every racehorse

Staying a Step Ahead

INFORMATION ON **EQUINE INFLUENZA** STRAINS KEY IN VACCINES

By **AMANDA DUCKWORTH**
Photos by **EDWARD WHITAKER/RACING POST**

THERE ARE TWO main tiers when it comes to vaccinating horses: core vaccines and risk-based vaccines.

The first set is strongly recommended for any horse, anywhere; no matter their lifestyle. The second set, as the name suggests, varies depending on risk level to a specific horse, which is determined from many factors that include geography and use. Core vaccines are just that, but deciding which at-risk vaccines a horse may or may not need is more complex.

Within the list of potentially needed vaccines is the one concerning equine influenza virus. A lot of current research has examined this particular issue.

It is important to remember that the American Association of Equine Practitioners provides clear vaccination guidelines. It reminds everyone that there is no single standard for a vaccination program. Each individual horse and situation can require something different.

According to the AAEP, the standard criteria for creating a vaccination program includes: risk of infection (anticipated exposure, environmental factors, geographic factors, age, breed, use, and sex of the horse); consequences of the disease (morbidity/mortality, zoonotic potential); anticipated effectiveness of the selected product(s); potential for severe adverse reactions to a vaccine(s); and cost of immunization (time, labor, and vaccine costs) vs. potential cost of disease (time out of competition; impact of movement restrictions imposed in order to control an outbreak of contagious disease; cost of treatment, or loss of life).

When it comes to equine health, working closely with a trusted veterinarian is key to making a vaccination plan. In terms of the risk-based vaccines, the Equine Disease Communication Center describes thusly:

"At-risk vaccines are recommended by a veterinarian after they have considered the risks and benefits for your horse based on the horse's history, the group of horses it lives among, its occupation and the amount of associated commingling with other horses, and/or the region the horse lives in. Owners, trainers, barn managers, and event organizers are encouraged to consult with their veterinarian when assessing disease-risk and the appropriate immunization protocol for their horses and/or facility. Risk-based vaccines include those that protect horses against equine influenza virus, equine herpesvirus 1&4, strangles, Potomac horse fever, anthrax, botulism, leptospirosis, and equine viral arteritis."

When it comes to EIV, it is important to know that it is endemic in the equine population both in the United States and throughout the world. New Zealand, Australia, and Iceland are the rare and notable exceptions.

"Equine influenza, caused by the orthomyxovirus equine influenza A type 2 H3N8 subtype, is one of the most common infectious diseases of the respiratory tract of horses," explains the AAEP. "Equine influenza is highly contagious, and the virus spreads rapidly through groups of horses in aerosolized droplets dispersed by coughing or

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through fomite transmission. The majority of the clinical signs are respiratory and may also include fever, edema, and enlarged lymph nodes."

Much like the human flu has different strains, so does EIV. The OIE Expert Influenza Surveillance panel reviews currently circulating strains and makes recommendations for strain inclusion in the vaccine products. There are two types of EIV vaccine currently marketed: inactivated (killed) vaccines for intramuscular administration and modified-live vaccine for intranasal administration.

Understanding how and where EIV is spreading can play a valuable role in determining a horse's risk factors. In June 2024, Frontiers in Veterinary Science published "Spatiotemporal pattern and suitable areas analysis of equine influenza in global scale (2005-2022)."

"Equine influenza is a severe infectious disease that causes huge economic losses to the horse industry," explained researchers. "Spatial epidemiology technology can explore the spatiotemporal distribution characteristics and occurrence risks of infectious diseases. It has played an important role in the prevention and control of major infectious diseases in humans and animals. For the first time, this study conducted a systematic analysis of the spatiotemporal distribution of EI using SaTScan software and investigated the important environmental variables and suitable areas for EI occurrence using the Maxent model."

During the study, a total of 517 occurrences of equine influenza from 2005-22 were evaluated, and 14 significant spatiotemporal clusters were identified by researchers.

"The results indicated that annual average ultraviolet radiation, horse density, and precipitation of the coldest quarter were the three most important environmental variables affecting EI occurrence," researchers concluded. "The suitable areas for EI occurrence are widely distributed across all continents, especially in Asia (India, Mongolia, and China) and the Americas (Brazil, Uruguay, USA, and Mexico). In the future, these suitable areas will expand and move eastward. The largest expansion is predicted under SSP126 scenarios, while the opposite trend will be observed under SSP585 scenarios.

"This study presents the spatial epidemiological characteristics of EI

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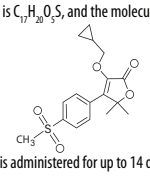
CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: EquiCoxib™ (firocoxib) belongs to the coxib class of non-narcotic, non-steroidal anti-inflammatory drugs (NSAIDs). Firocoxib is a white crystalline compound described chemically as 3-(cyclopropylmethoxy)-4-(4-(methylsulfonyl)phenyl)-5,5-dimethylfuranone. The empirical formula is $C_{17}H_{20}O_5S$, and the molecular weight is 336.4. The structural formula is shown below:



Indications: EquiCoxib Oral Solution is administered for up to 14 days for the control of pain and inflammation associated with osteoarthritis in horses.

Dosage and Administration: Always provide the Client Information Sheet with the prescription. The recommended dosage of EquiCoxib (firocoxib) for oral administration in horses is 0.045 mg/lb (0.1 mg/kg) of body weight once daily for up to 14 days. In target animal safety studies, toxicity was seen at the recommended dose when the duration of treatment exceeded 30 days. **Only administer EquiCoxib with the provided dosing syringe.**

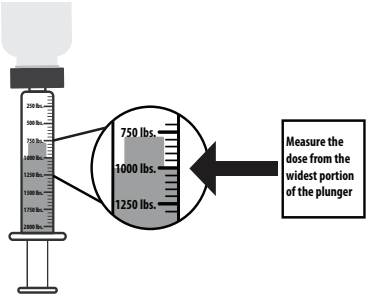
Each 1.25 mL volume will treat 250 pounds of body weight and each additional 0.25 mL volume corresponds to approximately a 50 lb weight increment. The provided dosing syringe is calibrated so that each line corresponds to a 50 lb weight increment. To deliver the correct dose, round the horse's body weight up to the nearest 50 pound increment (if the body weight is an exact 50 pound increment, do not round up).

FOR ORAL USE ONLY. DO NOT INJECT EQUICOXIB.
ONLY ADMINISTER WITH THE PROVIDED DOSING SYRINGE.

EquiCoxib Oral Dosing Guide

Body Weight (lb)	Dose Volume (mL)
250	1.25 mL
500	2.5 mL
750	3.75 mL
1000	5 mL
1250	6.25 mL

1) Remove draw-off cap. Peel off the foil-backed seal from the bottle.
2) Screw the draw-off cap tightly back on the bottle.
3) Remove the seal from the top of the cap exposing the cross-hatched opening in the center of the silicone liner.
4) Remove the provided oral dosing syringe from its plastic cover.
5) Insert the oral dosing syringe firmly into the cross-hatched opening of the cap's silicone liner.
6) Turn the bottle with attached syringe upside down. Pull back the syringe plunger until the widest portion of the plunger lines up with the line that corresponds with the animal's weight. Each line between the 250 lb increments corresponds to 50 lb.



7) Turn the bottle with attached syringe right side up and separate the dosing syringe from the bottle.
8) Give orally according to your veterinarian's instructions. DO NOT INJECT.

Contraindications: Horses with hypersensitivity to firocoxib should not receive EquiCoxib Oral Solution.

Warnings:
For oral use in horses only. Do not use in horses intended for human consumption.

Human Warnings: Not for use in humans. Keep this and all medications out of the reach of children. Wash hands with soap and water after use. Consult a physician in case of accidental ingestion by humans.

Animal Safety: Clients should be advised to observe for signs of potential drug toxicity and be given a Client Information Sheet with each prescription.

Keep EquiCoxib in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Aurora Pharmaceutical at 1-888-215-1256 or www.aurorapharmaceutical.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

Precautions:
Horses should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests should be conducted to establish hematological and serum biochemical baseline data before and periodically during administration of any NSAID. Clients should be advised to observe for signs of potential drug toxicity and be given a Client Information Sheet with each prescription. See **Information for Owner or Person Treating Horse** section of this package insert.

Treatment with EquiCoxib should be terminated if signs such as inappetance, colic, abnormal feces, or lethargy are observed. As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Horses that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Patients at greatest risk for adverse events are those that are dehydrated, on diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached or avoided. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since many NSAIDs possess the potential to produce gastrointestinal ulcerations and/or gastrointestinal perforation, concomitant use of EquiCoxib Oral Solution with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. The concomitant use of protein bound drugs with EquiCoxib Oral Solution has not been studied in horses. The influence of concomitant drugs that may inhibit the metabolism of EquiCoxib Oral Solution has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy. The safe use of EquiCoxib Oral Solution in horses less than one year in age, horses used for breeding, or in pregnant or lactating mares has not been evaluated. Consider appropriate washout times when switching from one NSAID to another NSAID or corticosteroid.

Adverse Reactions: In controlled field studies, 127 horses (ages 3 to 37 years) were evaluated for safety when given firocoxib at a dose of 0.045 mg/lb (0.1 mg/kg) orally once daily for up to 14 days. The following adverse reactions were observed. Horses may have experienced more than one of the observed adverse reactions during the study.

Adverse Reactions Seen in U.S. Field Studies Firocoxib was safely used concomitantly with other therapies, including vaccines, anthelmintics, and antibiotics, during the field studies. The safety data sheet (SDS) contains more detailed occupational safety information.

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Aurora Pharmaceutical Inc. at 1-888-215-1256 or www.aurorapharmaceutical.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or online at www.fda.gov/reportanimalae.

Adverse Reactions	Firocoxib n=127	Active Control n=125
Abdominal pain	0	1
Diarrhea	2	0
Excitation	1	0
Lethargy	0	1
Loose stool	1	0
Polydipsia	0	1
Urticaria	0	1

Information for Owner or Person Treating Horse: You should give a Client Information Sheet to the person treating the horse and advise them of the potential for adverse reactions and the clinical signs associated with NSAID intolerance. Adverse reactions may include erosions and ulcers of the gums, tongue, lips and face, weight loss, colic, diarrhea, or icterus. Serious adverse reactions associated with this drug class can occur without warning and, in some situations, result in death. Clients should be advised to discontinue NSAID therapy and contact their veterinarian immediately if any of these signs of intolerance are observed. The majority of patients with drug-related adverse reactions recover when the signs are recognized, drug administration is stopped, and veterinary care is initiated.

Clinical Pharmacokinetics / Pharmacodynamics: Pharmacokinetics: When administered as a 0.045 mg/lb (0.1 mg/kg) dose in oral paste to adult horses with normal access to roughage, feed, and water, the absolute bioavailability of firocoxib from oral paste is approximately 79%. Following oral administration, drug peak concentration (Cmax) of 0.08 mcg/mL can be reached at 4 hours (Tmax) post-dosing. However, in some animals, up to 12 hours may be needed before significant plasma concentrations are observed. Little drug amount distributes into blood cells. The major metabolism mechanism of firocoxib in the horse is decyclopropyl-methylation followed by glucuronidation of that metabolite. Based upon radiolabel studies, the majority of firocoxib is eliminated in the urine as the decyclopropylmethylated metabolite. Despite a high rate of plasma protein binding (98%), firocoxib exhibits a large volume of distribution (mean Vd(ss) = 1652 mL/kg). The terminal elimination half-life ($T_{1/2}$) in plasma averages 30-40 hours after IV or oral paste dosing. Therefore, drug accumulation occurs with repeated dose administrations and steady state concentrations are achieved beyond 6-8 daily oral doses in the horse. Dose linearity exists from 1X-2X of 0.1 mg/kg/day.

Mode of action: EquiCoxib (firocoxib) is a cyclooxygenase-inhibiting (coxib) class, non-narcotic, non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic activity[1] in animal models. Based on in vitro horse data, firocoxib is a selective inhibitor of prostaglandin biosynthesis through inhibition of inducible cyclooxygenase-2-isoenzyme (COX-2)[2]. Firocoxib selectivity for the constitutive isoenzyme, cyclooxygenase-1 (COX-1) is relatively low. However, the clinical significance of these in vitro selectivity findings has not been established.

Effectiveness: Two hundred fifty-three client-owned horses of various breeds, ranging in age from 2 to 37 years and weighing from 595 to 1638 lbs, were randomly administered firocoxib oral paste or an active control drug in multi-center field studies. Two hundred forty horses were evaluated for effectiveness and 252 horses were evaluated for safety. Horses were assessed for lameness, pain on manipulation, range of motion, joint swelling, and overall clinical improvement in a non-inferiority evaluation of firocoxib oral paste compared to an active control. At study's end, 84.4% of horses treated with firocoxib oral paste were judged improved on veterinarians' clinical assessment, and 73.8% were also rated improved by owners. Horses treated with firocoxib oral paste showed improvement in veterinarian-assessed lameness, pain on manipulation, range of motion, and joint swelling that was comparable to the active control.

Animal Safety: In a target animal safety study, firocoxib was administered orally to healthy adult horses (two male castrates and four females per group) at 0, 0.1, 0.3 and 0.5 mg firocoxib/kg body weight (1, 3 and 5X the recommended dose) for 30 days. Administration of firocoxib at 0.3 and 0.5 mg/kg body weight was associated with an increased incidence of oral ulcers as compared to the control group but, no oral ulcers were noted with 0.1 mg/kg. There were no other drug-related adverse findings in this study.

In another target animal safety study, firocoxib was administered orally to healthy adult horses (four males or male castrates and four females per group) at 0, 0.1, 0.3 and 0.5 mg firocoxib/kg body weight (1, 3 and 5X the recommended dose) for 42 days. Administration of firocoxib at 0.1, 0.3 and 0.5 mg/kg body weight was associated with delayed healing of pre-existing oral (lip, tongue, gingival) ulcers. In addition, the incidence of oral ulcers was higher in all treated groups as compared to the control group.

Clinical chemistry and coagulation abnormalities were seen in several horses in the 0.5 mg/kg (5X) group. One 5X male horse developed a mildly elevated BUN and creatinine over the course of the study, prolonged buccal mucosal bleeding time (BMBT), and a dilated pelvis of the right kidney. Another 5X male had a similar mild increase in creatinine during the study but did not have any gross abnormal findings. One female in the 5X group had a prolonged BMBT, bilateral tubulointerstitial nephropathy and bilateral papillary necrosis. Tubulointerstitial nephropathy occurred in one 3X female, two 3X male horses, and the 5X female horse discussed above with the prolonged BMBT. Papillary necrosis was present in one 1X male horse and the 5X female horse discussed above. Despite the gross and microscopic renal lesions, all of the horses were clinically healthy and had normal hematology, clinical chemistry and urinalysis values.

In another target animal safety study, firocoxib was administered orally to healthy adult horses (three females, two male castrates and one male per group) at 0, 0.25 mg/kg, 0.75 mg/kg and 1.25 mg/kg (2.5, 7.5 and 12.5X the recommended dose of 0.1 mg/kg) for 92 days. An additional group of three females, two male castrates and one male per group, was dosed at 1.25 mg/kg for 92 days but was monitored until Days 147-149. There were treatment-related adverse events in all treated groups. These consisted of ulcers of the lips, gingiva and tongue and erosions of the skin of the mandible and head. Gross and microscopic lesions of the kidneys consistent with tubulointerstitial nephropathy were seen in all treated groups. Papillary necrosis was seen in the 2.5X and 12.5X groups. In addition, several 12.5X horses had elevated liver enzymes (GGT, SDH, AST and ALT). One 2.5X horse had increased urine GGT and urine protein levels which was due to renal hemorrhage and nephropathy. Gastric ulcers of the margo plicatus and glandular area were more prevalent in the 2.5X and 7.5X groups, but not seen in the 12.5X group. The group of horses that were monitored until Days 147-149 showed partial to full recovery from oral and skin ulcers, but no recovery from tubulointerstitial nephropathy.

Storage Information: Store below 77°F (25°C). Brief excursions up to 104°F (40°C) are permitted.

How Supplied: EquiCoxib is available in bottles containing 90 mL of EquiCoxib Oral Solution, sufficient to treat a 1250 lb. horse for up to 14 days.

References: [1]McCann ME, Rickes EL, Hora DF, Cunningham PK et al. In vitro effects and in vivo efficacy of a novel cyclooxygenase-2 inhibitor in cats with lipopolysaccharide-induced pyrexia. Am J Vet Res. 2005 Jul;66 (7):1278-84

[2]McCann ME, Anderson DR, Brideau C et al. In vitro activity and in vivo efficacy of a novel COX-2 inhibitor in the horse. Proceedings of the Academy of Veterinary Internal Medicine. 2002. Abstract 114, p.789.

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for the first time. The results could provide valuable scientific insights that can effectively inform prevention and control strategies in regions at risk of EI worldwide."

Being informed on the latest strains of EIV is a crucial part of any vaccination program. In February 2022 the Journal of Equine Veterinary Science published "Antibody Responses to a Reverse Genetics-Derived Bivalent Inactivated Equine Influenza Vaccine in Thoroughbred Horses."

"Updating vaccine strains is important to control equine influenza," explained researchers. "Previously, we reported that a monovalent inactivated EI vaccine derived from a virus generated by reverse genetics elicited immunogenicity in horses. In the present study, we compared antibody responses to a bivalent inactivated EI vaccine generated by RG and a commercially available bivalent inactivated EI vaccine derived from wild-type equine influenza viruses in Thoroughbred horses."

During the study, 16 unvaccinated yearlings received two doses of a primary vaccination course four weeks apart. From that group, seven received the RG vaccine and nine got the CO vaccine. Additionally, 32 vaccinated adult horses received a single dose of a booster vaccination. Of that population, 18 made up the RG-vaccinated group and 14 were CO-vaccinated.

"The patterns of hemagglutination inhibition antibody response to the primary and booster vaccinations were similar for the RG and CO groups in unvaccinated yearlings and vaccinated adult horses," researchers concluded. "These results suggest that a bivalent vaccine derived from RG viruses elicits equivalent immunogenicity to that elicited by a CO vaccine derived from wild-type viruses. RG viruses can, therefore, be used in multivalent as well as monovalent vaccines for horses."

As the above study indicates, the age of the horse in question does impact its vaccination schedule.

"Individual horses will vary in their response to vaccination," explained the EDCC. "The immune response to vaccination can be negatively impacted by age. In young foals, high levels of maternally derived colostral antibodies may diminish their immune response to initial vaccination; the guidelines

“VACCINES AGAINST EQUINE INFLUENZA ARE AVAILABLE, AND VACCINATION IS MANDATORY FOR HORSES THAT PARTICIPATE IN AFFILIATED COMPETITIONS, BUT THIS GROUP FORMS A SMALL PROPORTION OF THE TOTAL HORSE POPULATION.”

—RESEARCHERS IN A JULY 2020 ISSUE OF PREVENTIVE VETERINARY MEDICINE

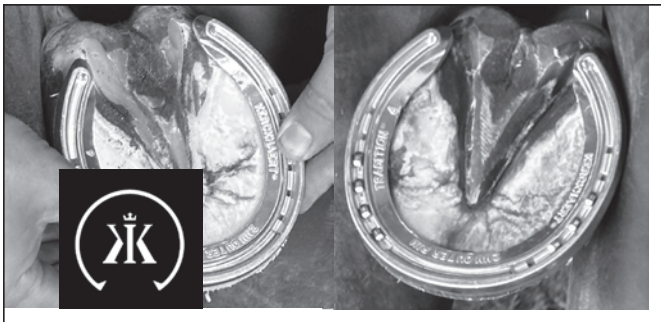
provide specifics related to when to first vaccinate foals based on the vaccination history of their dams.”

Keeping foals healthy is a multifaceted process, and vaccinations are a central component. In April 2021 the Journal of Equine Veterinary Science published “An Evaluation of Three Different Primary Equine Influenza Vaccination Intervals in Foals.”

For the study, 21 unvaccinated Thoroughbred foals were separated into three groups of seven and then vaccinated at three different intervals of primary immunization. There were one-, two-, or three-month intervals between the first and second vaccine. Following that, the antibody response was measured for up to a year after the third immunization, which was administered six months after the second.

“All weanlings had seroconverted and exceeded the clinical protection threshold two weeks after V2 and one month after V3 until the end of the study,” researchers concluded. “Significant differences were measured at the peak of immunity after V2 and for the duration of the immunity gap between V2 and V3.

“The group with one-month primary



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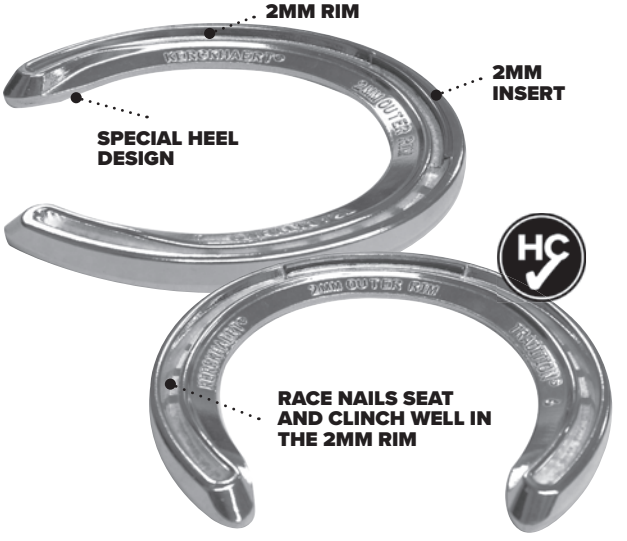

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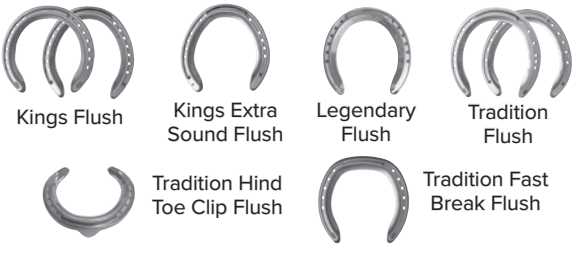

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vaccination interval had a lower immunity peak after V2 and a wider immunity gap between V2 and V3 when compared with other groups. The advantage observed in the group with one-month primary vaccination interval, which induces an earlier protective immunity, is counterbalanced with a lower peak of immunity and a wider immunity gap after V2, when compared with foals vaccinated with two- and three-month intervals."

Although equine influenza is widespread, it is not something everyone vaccinates against. In July 2020 Preventive Veterinary Medicine examined some reasons why owners do or do not take advantage of equine influenza vaccines in "Equine influenza vaccination as reported by horse owners and factors influencing their decision to vaccinate or not."

"Equine influenza virus is a highly contagious respiratory pathogen that causes pyrexia, anorexia, lethargy, and coughing in immunologically naïve horses," said researchers. "Vaccines against equine influenza are available, and vaccination is mandatory for horses that participate in affiliated competitions, but this group forms a small proportion of the total horse population.

"The aims of this study were to identify the equine influenza vaccination rate as reported in 2016 by horse owners in the United Kingdom; examine the demographics of owners and horses which were associated with significantly lower influenza vaccination rates; and explore factors that influence horse owners' decisions around influenza vaccine uptake."

For the study, responses submitted by 4,837 horse owners with a total of 10,501 horses in their care were examined. Researchers found 80% of the horses were vaccinated for equine influenza. Owner demographics and horse age played key roles in those who were not vaccinated.

"Several owner demographic characteristics were associated with significantly lower reported equine influenza vaccination rates including: some geographical locations, increasing horse owner age, annual household income of less than £15,000, and owning more than one horse," concluded researchers. "Horse-related features which were associated with significantly lower reported equine influenza vaccination rates included age ranges of <4 years and >20 years, use as a companion or breeding animal, or leaving their home premises either never or at most once a year.

Newmarket Equine Hospital vet Stuart Williamson inserts a swab and then cuts the end of the swab into a test tube for testing for equine influenza

"The most common reasons cited for failing to vaccinate horses was no competition activity, lack of exposure to influenza, and expense of vaccines. In contrast, the most common underlying reasons given by horse owners who vaccinated their horse were protection of the individual horse against disease, veterinary advice, and to protect the national herd. Owners of vaccinated horses had less previous experience of an influenza outbreak or adverse reaction to vaccination compared with owners of unvaccinated horses."

For those wanting to understand more about the history of equine influenza and how it has spread globally, Vaccines (Basel) published the review "Equine Influenza Virus: An Old Known Enemy in the Americas" in October 2022.

"Certain factors related to the disease, such as an outdated vaccination plan, age, training, and close contact with other animals, favor the presentation of equine influenza," explained researchers. "This review focuses on the molecular, pathophysiological, and epidemiological characteristics of EIV in the Americas to present updated information to achieve prevention and control of the virus. We also discuss the need for monitoring the disease, the use of vaccines, and the appropriate application of those biologicals, among other biosecurity measures that are important for the control of the virus.

"The equine influenza virus is primarily caused by the H3N8 subtype, both in the Americas and worldwide. It is one of the equine diseases with greater clinical and economic implications; the latter is associated with the cancellation of training, veterinary treatments, and equestrian events."

When it comes to risk-based vaccines, it is important to work with veterinarians to understand what is the best course of action for an individual horse. However, oftentimes vaccination is a cornerstone to good herd health. BH

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