Tetanus

All horses are at risk of development of tetanus, an often fatal disease caused by a potent neurotoxin elaborated by the anaerobic, spore-forming bacterium, *Clostridium tetani.* Tetanus toxoid is a core equine vaccine and is indicated in the immunization program for all horses.

Clostridium tetani organisms are present in the intestinal tract and feces of horses, other animals and humans, and are abundant as well as ubiquitous in soil. Spores of *Cl. tetani* survive in the environment for many years, resulting in an ever-present risk of exposure of horses and people on equine facilities. Tetanus is not a contagious disease but is the result of *Cl. tetani* infection of puncture wounds (particularly those involving the foot or muscle), open lacerations, surgical incisions, exposed tissues such as the umbilicus of foals and reproductive tract of the postpartum mare (especially in the event of trauma or retained placenta).

Vaccines

Vaccines currently available are formalin-inactivated, adjuvanted toxoids. Tetanus toxoid is a potent antigen that rapidly induces strong serological responses. Circulating antibody is able to mediate complete protection against tetanus. It is generally accepted that tetanus toxoid administered per manufacturer recommendations is both safe and effective.

A 6-month study comparing serologic responses of equids to commercial vaccines demonstrated significant IgG response for the duration of the study. The end point for antibody persistence was not explored and may potentially be longer than the 6 months stated in the study. Extending the revaccination interval beyond the manufacturer's recommendation for annual revaccination is not advisable due to a veterinarian's liability if label recommendations are not followed.

There are no challenge studies that have been published to document the onset or duration of immunity induced by tetanus toxoid products available for use in horses in the USA. Conclusions regarding the efficacy of products used in the USA are based on serologic response in laboratory animals and field experience. This may be accepted as evidence of vaccine efficacy as antibody alone can mediate protection. Tetanus has rarely been documented in vaccinated horses in the USA, illustrating the variability of response of equids to any biologic product. *Note*: Survival of horses with tetanus was strongly associated with previous vaccination.

Vaccination Schedules

Adult horses, previously vaccinated against tetanus: Vaccinate annually. Horses that sustain a wound or undergo surgery 6 or more months after their previous tetanus booster should be revaccinated with tetanus toxoid immediately at the time of injury or surgery. *Note:* The severity of the wound does not predict the risk for development of tetanus. Superficial wounds have resulted in clinical tetanus in horses.

Adult horses, previously unvaccinated against tetanus, or of unknown vaccinal history: Administer a primary 2-dose series of tetanus toxoid with a 4- to 6-week interval between doses. Protective concentrations of immunoglobulin are usually attained within 14 days of the second dose of vaccine. Vaccinate annually thereafter.

Tetanus antitoxin is indicated to provide passive immunity in situations where the horse is at risk of tetanus infection and has not been immunized according to labeled recommendations for tetanus. If the veterinarian determines that administration of tetanus antitoxin is indicated, then it should be administered in one site and the initial dose of a priming series of tetanus toxoid vaccinations in a distant muscular site. The rare, but fatal, risk of Theiler's disease consequent to the use of tetanus antotoxin needs to be taken into consideration when determining if use is indicated.

Pregnant mares previously vaccinated against tetanus: Vaccinate annually 4 to 6 weeks before foaling, both to protect the mare should foaling-induced trauma or retained placenta occur and to enhance concentrations of colostral immunoglobulins.

Pregnant mares uvaccinated against tetanus or of unknown vaccinal history: Administer a 2-dose primary series of tetanus toxoid with a 4- to 6-week interval between doses. Revaccinate 4 to 6 weeks before foaling.

Foals of mares vaccinated against tetanus in the pre-partum period: Administer a primary 3-dose series of tetanus toxoid beginning at 4 to 6 months of age. A 4- to 6-week interval between the first and second doses is recommended. The third dose should be administered at 10 to 12 months of age.

Foals of unvaccinated mares or mares of unknown vaccinal history: Administer a primary 3-dose series of toxoid beginning at 1 to 4 months of age with 4-week intervals between doses. Serologic data indicates that a 3- dose initial series produces a more consistent anamnestic response in all foals, regardless of the age at which the series is initiated. Tetanus antitoxin is indicated to provide passive immunity in situations where a foal is born to a non-vaccinated mare and is at risk of tetanus infection.(See *Tetanus antitoxin* above.)

Horses having been naturally infected with tetanus and recovered: Revaccinate annually.

Eastern/Western Equine Encephalomyelitis

In the United States, equine encephalitides for which vaccines are available include eastern equine encephalomyelitis (EEE), western equine encephalomyelitis (WEE), Venezuelan equine encephalomyelitis (VEE) and West Nile Virus encephalomyelitis. The distribution of EEE has historically been restricted to the eastern, southeastern and some southern states while outbreaks of WEE have been recorded in the western and mid-western states. Variants of WEE have caused sporadic cases in the northeast and southeast, most notably Florida. VEE occurs in South and Central America but has not been diagnosed in the United States for more than 20 years. The availability of licensed vaccine products combined with an inability to completely eliminate risk of exposure justifies immunization against EEE and WEE as core prophylaxis for all horses residing in or traveling to North America and any other geographic areas where EEE and/or WEE is endemic.

Transmission of EEE/WEE/VEE is by mosquitoes, and infrequently by other bloodsucking insects, to horses from wild birds or rodents, which serve as natural reservoirs for these viruses. Human beings are also susceptible to these diseases when the virus is transmitted to them by infected mosquitoes; however, horse-to-horse or horse-to-human transmission by mosquitoes is highly unlikely, because the amount of virus in the blood of horses affected by EEE or WEE is small. The viremia that occurs with VEE is higher and direct horse-to-horse or horse-to-human transmission is possible. Of these 3 encephalidites, WEE has the lowest mortality (approx. 50%). Eastern equine encephalomyelitis is the most virulent for horses, with mortality approaching 90%. Epidemiological evidence indicates that young horses are particularly susceptible to disease caused by EEE. Venezuelan equine encephalomyelitis can also be lethal, however some horses develop subclinical infections which result in lasting immunity.

The risk of exposure and geographic distribution of EEE and WEE vary from year-to-year with changes in distribution of insect vectors and reservoirs important in the natural ecology of the virus. EEE activity in mosquito and birds, and resultant disease in humans and equids, continues to cause concern along the East Coast and demonstrates northward encroachment. WEE has caused minimal disease in horses in the last two decades; however, the virus continues to be detected in mosquitoes and birds throughout the Western states. In addition, variants that cause clinical disease in equids have been detected in the eastern U.S.

VEE is a reportable foreign animal disease. Epidemics of VEE occur when the virus undergoes genetic change and develops greater virulence in avian and mammalian hosts. These viral variants are able to multiply to high levels in the horse and then the horse becomes a reservoir in these outbreaks. Vaccination against VEE is controversial because:

1) Vaccination against a foreign animal disease may confound testing in the event of an outbreak.

2) Experimental and field data have demonstrated that vaccination with bivalent EEE/WEE provides cross protection against VEE.

3) A conditionally available modified live (MLV) vaccine has been released during previous outbreaks. Should an outbreak occur it is likely that this highly attenuated MLV would be released.

Given this combined data, horses that receive annual EEE/WEE vaccines would be partially to completely protected and vaccination with the highly effective MLV product would induce rapid, complete immunity while allowing for accurate surveillance before VEE specific vaccination. Vaccination of horses with killed VEE vaccine should only be performed in very high risk areas of the U.S. under the guidance of state agriculture officials.

Vaccines:

EEE/WEE vaccines currently available are formalin inactivated adjuvanted whole virus products. Early testing of bivalent (EEE/WEE) vaccines was performed by intracranial challenge with either EEE and WEE; the formalin inactivated preparations demonstrated 100% protection.

Currently, the only available VEE vaccine is a killed product.

Vaccination Schedules EEE/WEE:

Adult horses previously vaccinated against EEE/WEE Annual revaccination must be completed prior to vector season in the spring. In animals of high risk or with limited immunity, more frequent vaccination or appropriately timed vaccination is recommended in order to induce protective immunity during periods of likely exposure. In areas where mosquitoes are active year-round, many veterinarians elect to vaccinate horses at 6-month intervals to ensure uniform protection throughout the year, although this practice is not specifically recommended by manufacturers of vaccines.

Adult horses, previously unvaccinated against EEE/WEE or of unknown vaccinal history Administer a primary series of 2 doses with a 4 to 6 week interval between doses. Revaccinate prior to the onset of the next vector season and annually thereafter.

Pregnant mares, previously vaccinated against EEE/WEE Vaccinate 4 to 6 weeks before foaling.

Pregnant mares, unvaccinated or having unknown vaccinal history Immediately begin a 2-dose primary series with a 4-week interval between doses. Booster at 4 to 6 weeks before foaling or prior to the onset of the next vector season—whichever occurs first.

Foals of mares vaccinated against EEE/WEE in the pre-partum period Administer a primary three-dose series beginning at 4 to 6 months of age. A 4- to 6-week interval between the first and second doses is recommended. The third dose should be administered at 10 to12 months of age prior to the onset of the next mosquito season.

In the southeastern U.S., due to earlier seasonal disease risk, vaccination may be started at 2 to 3 months of age. When initiating vaccinations in younger foals, a series of 4 primary doses should be administered, with a 4-week interval between the first and second doses and a 4-week interval between the second and third doses. The fourth dose should be administered at 10 to 12 months of age prior to the onset of the next mosquito season.

Foals of unvaccinated mares or having unknown vaccinal history Administer a primary 3-dose series beginning at 3 to 4 months of age. A 4-week interval between the first and second doses is recommended. The third dose should be administered at 10 to 12 months of age before the onset of the next mosquito season.

Horses having been naturally infected and recovered: Recovered horses likely develop lifelong immunity. Consider revaccination only if the immune status of the animal changes the risk for susceptibility to infection. Examples of these conditions would include the long term use of corticosteroids and pituitary adenoma.

West Nile Virus

West Nile virus (WNV) is the leading cause of arbovirus encephalitis in horses and humans in the United States. Since 1999, over 24,000 cases of WNV encephalitis have been reported in U.S. horses, with 1,069 cases reported in

2006. In 2006, there was a 14% increase in human cases and new expansion of WNV into 52 U.S. counties. The occurrence of over 2,500 human cases in 2007 indicates widespread viral activity in the environment. 1,086 equine cases were reported in the U.S. in 2006. As of October 2007, 250 equine cases were reported. This decline likely reflects both vaccination and naturally acquired immunity. Nonetheless, horses represent 96.9% of all non-human mammalian cases of WNV disease.

This virus has been identified in all of the continental United States, most of Canada and Mexico. Several Central and South American countries have also identified WNV within their borders. The virus is transmitted from avian reservoir hosts by mosquitoes (and infrequently by other bloodsucking insects) to horses, humans and a number of other mammals. West Nile virus is transmitted by many different mosquito species and this varies geographically. The virus and mosquito host interactions result in regional change in virulence of the virus and no prediction can be made regarding future trends in local activity of the viruses. Horses and humans are considered to be dead-end hosts for WNV; the virus is not directly contagious from horse to horse or horse to human. Indirect transmission via mosquitoes from infected horses is highly unlikely as these horses do not circulate a significant amount of virus in their blood.

The case fatality rate for horses exhibiting clinical signs of WNV infection is approximately 33%. Data have supported that 40% of horses that survive the acute illness caused by WNV still exhibit residual effects, such as gait and behavioral abnormalities, 6 months post-diagnosis.

There are three challenge models that have been used to license currently available vaccines. The mosquito and needle challenge were the two models used in early studies. These challenge models result in 90% of nonvaccinated control horses developing viremia, while only 10% of these horses demonstrated clinical disease. More recently, the intrathecal (infection in the atlanto-occipital space) challenge model has been employed. In this model, 70 to 90% of nonvaccinated control horses become viremic and 90 to 100% develop grave signs of encephalomyelitis.

West Nile virus vaccines are licensed either as 1) an aid in protection against viremia or 2) protective against viremia and clinical disease. The basis for labeling reflects the route of virulent challenge performed at the time of licensure. Recent literature indicates that all licensed vaccines demonstrate approximately 95% efficacy when horses undergo intrathecal challenge 28 days post-vaccination. These studies support the epidemiological studies that have demonstrated high efficacy for vaccination. Thus vaccination for West Nile virus is recommended as a core vaccine and is an essential standard of care for all horses in North America.

Vaccines:

Three licensed vaccines are currently available:

Inactivated whole virus vaccine with an adjuvant. Label instructions call for an initial series of two intramuscular injections administered 3 to 6 weeks apart followed by a 12-month revaccination interval.

- This vaccine was tested in a needle challenge model and 95% of vaccinated horses were considered protected based on their failure to develop viremia when challenged 12 months post-vaccination. The product is labeled as an aid in protection against WNV viremia.
- Severe encephalitis was not observed in horses challenged intrathecally 28-days after vaccination.

Recombinant vector vaccine with protective antigens expressed in a canary pox vector which does not replicate in the horse. The vaccine contains an adjuvant.Label instructions call for an initial series of two intramuscular injections administered 3 to 6 weeks apart followed by a 12 month revaccination interval. The product is labeled as an aid in protection against WNV viremia.

Additional studies with canary pox vector vaccine have been performed and have demonstrated:

- Initial efficacy studies utilized the mosquito challenge model and 90% of horses were protected against viremia for a duration of 12 months.
- For horses previously vaccinated with another product, revaccination with a single dose of this product induced an antibody response. Vaccines can be interchanged without repeating primary inoculation.
- Naïve horses, having received a single dose of the vaccine, and subsequently challenged 28 days post- vaccination were protected from viremia.
- 90% of vaccinated horses were protected when challenged by the intrathecal model 2 weeks after vaccination.

- Severe encephalitis was not observed in horses challenged intrathecally 28 days after vaccination.

Modified live chimera vaccine having the protective proteins of WNV expressed in a flavivirus vector. The vaccine does not contain an adjuvant. Label instructions are for a single injection followed by revaccination at a 12 month interval.

Efficacy testing for licensing used the intrathecal challenge model in which disease, in addition to viremia, was produced. Severe encephalitis was not observed in horses challenged intrathecally 28 days after vaccination with 1 dose of vaccine. Therefore, this product is labelled for the prevention of disease. Additional intrathecal challenge tests demonstrated:

- 12-month duration of immunity against clinical disease and an aid to prevention against viremia in 90% of horses.
- Severe encephalitis was not observed in horses challenged intrathecally 12 months after vaccination with 1 dose of vaccine.
- Severe encephalitis was not observed 5/6 in horses challenged intrathecally 10 days after vaccination with 1 dose of vaccine.

Vaccination Schedules:

Adult horses previously vaccinated Vaccinate annually in the spring, prior to the onset of the insect vector season.

For animals at high risk or with limited immunity, more frequent vaccination or appropriately timed revaccination is recommended in order to induce protective immunity during periods of likely exposure. For instance, juvenile horses (<5 years of age) appear to be more susceptible than adult horses that have likely been vaccinated and/or had subclinical exposure. Geriatric horses (>15 years of age) have been demonstrated to have enhanced susceptibility to WNV disease. Therefore, more frequent vaccination is recommended to meet the vaccination needs of these horses.

Booster vaccinations are warranted according to local disease or exposure risk. Only the modified live chimera WNV vaccine has been tested for protection against signs of clinical disease but protection against disease for 12 months is likely with all WNV vaccines. However, m ore frequent vaccination may be indicated with any of these products depending on risk assessment.

Adult horses previously unvaccinated or having unknown vaccinal history

Inactivated whole virus vaccine: A primary series of 2 doses is administered to naïve horses. A 4- to 6-week interval between doses is recommended. The label recommended revaccination interval is 12 months.

Recombinant canary pox vector vaccine: A primary series of 2 doses is administered to naïve horses with a 4- to 6-week interval between doses. The label recommended revaccination interval is 12 months.

Modified live flavivirus chimera vaccine: Primary immunization is by a single dose administered to horses 5 or more months of age. The label recommended revaccination interval is 12 months.

Pregnant mares
Limited studies have been performed that examine vaccinal protection against WNV disease in pregnant mares. While none of the licensed vaccines are specifically labeled for administration to pregnant mares at this time, practitioners have vaccinated pregnant mares due to the risk of natural infection. It is an accepted practice by many veterinarians to administer WNV vaccines to pregnant mares as the risk of adverse consequences of WNV infection outweighs any reported adverse effects of use of vaccine.

Pregnant mare previously vaccinated
Vaccinate at 4 to 6 weeks before foaling.

Pregnant mares previously unvaccinated
Initiate a primary vaccination series (see *Adult horses previously unvaccinated*) immediately. Limited antibody response was demonstrated in pregnant mares vaccinated for the first time with the killed vaccine. It is unknown if this is true for the other products. Vaccination of naïve mares while open is a preferred strategy.

Foals

Limited studies have been performed examining maternal antibody inference and inhibition of protection against WNV disease. The only data currently available is for the inactivated product in which foals were demonstrated to produce antibody in response to vaccination despite the presence of maternal antibody. No studies have been performed evaluating protection from disease in foals vaccinated in the face of maternal immunity.

Foals of vaccinated mares

Inactivated vaccine: Administer a primary 3-dose series beginning at 4 to 6 months of age. A 4- to 6-week interval between the first and second doses is recommended. The third dose should be administered at 10 to 12 months of age prior to the onset of the next mosquito season.

Data indicates that maternal antibodies do not interfere with this product; however protection from clinical disease has not been provocatively tested in foals.

Animals may be vaccinated more frequently with this product if risk assessment warrants.

Recombinant canary pox vector vaccine: No data are available for the vaccination of foals.

Administration of a 3-dose primary vaccination series beginning at 5 to 6 months of age is based on the assumption that foals of that age respond to vaccination similarly to adults. There should be a 4-week interval between the first and second doses. The third dose should be administered at 10 to 12 months of age prior to the onset of the next mosquito season.

There is no data for this product regarding maternal antibody interference. Protection from clinical disease has not been provocatively tested in foals. Animals may be vaccinated more frequently with this product if risk assessment warrants.

Modified live flavivirus chimera vaccine: This vaccine is labeled for the administration of a single dose to foals 5 months of age or older. A second dose is recommended at 10 to 12 months of age prior to the onset of the next vector season.

There is no data regarding administration of this product to younger foals. It is recommended that the above described schedule be followed to completion should this vaccine be administered to increased-risk foals < 5 months of age. Animals may be vaccinated more frequently with the product if risk assessment warrants.

Foals of unvaccinated mares

The primary series of vaccinations should be initiated at 3 - 4 months of age and, where possible, be completed prior to the onset of the high-risk insect vector season.

Inactivated vaccine: Administer a primary series of 3 doses with a 30-day interval between the first and second doses and a 60-day interval between the second and third doses. If the primary series is initiated during the mosquito vector season, an interval of 3-4 weeks between the second and third doses is preferable to the above described interval of 8 weeks.

Recombinant canary pox vaccine: No data are available for the vaccination of foals and scheduling of the administration of the primary vaccination is based on the assumption that foals at 5 to 6 months of age respond to vaccination similarly to adults. A second dose, given at a 3-4 week interval after the first dose, may be warranted to ensure protective immunity. Animals may be vaccinated more frequently with this product if risk assessment warrants.

Modified live flavivirus chimera vaccine: There is no data regarding administration of this product to foals younger than 5 months of age. Due to presence of vectors and risk of disease, vaccination is warranted at earlier than 5 months of age and the use of this product is likely more appropriate for revaccination of older juveniles having already been administered a primary series.

Horses having been naturally infected and recovered

Recovered horses likely develop life-long immunity. Consider revaccination only if the immune status of the animal changes the risk for susceptibility to infection. Examples of these conditions would include the long term use of corticosteroids and pituitary adenoma.

Rabies

These guidelines were updated April 2009.

Rabies is an infrequently encountered neurologic disease of equids. While the incidence of rabies in horses is low, the disease is invariably fatal and has considerable public health significance. It is recommended that rabies vaccine be a core vaccine for all equids.

Exposure occurs through the bite of an infected (rabid) animal, typically a wildlife source such as raccoon, fox, skunk, or bat. Bites to horses occur most often on the muzzle, face, and lower limbs. The virus migrates via nerves to the brain where it initiates rapidly progressive, invariably fatal encephalitis.

Vaccines:

Three vaccines are licensed for rabies prophylaxis in horses. All are inactivated tissue culture derived products. The vaccines are given by intramuscular injection and appear to be safe. Rabies is an excellent immunogen and these vaccines induce a strong serologic response after a single dose.

Challenge studies demonstrating efficacy are required for licensing of all rabies vaccines (including those labeled for use in equids in the USA), however published results are not available. The challenge studies are conducted by the vaccine manufacturers as outlined in the Code of Federal Regulations (CFR) from the United States Department of Agriculture.

Vaccination Schedules:

(Veterinarians should read the label for each specific product recommendation.)

Adult horses previously vaccinated against rabies: Annual revaccination.

Adult horses previously unvaccinated against rabies or having unknown vaccinal history: Administer a single primary dose. Revaccinate annually.

Pregnant mares, previously vaccinated against rabies: Vaccinate 4 to 6 weeks before foaling. Alternatively, veterinarians may recommend that mares be vaccinated with rabies vaccine before breeding. Duration of immunity is such that antibodies to rabies virus are maintained at sufficient levels in mares vaccinated prior to breeding as to provide passive immunity through colostrum to the foal. Administration of rabies vaccine prior to breeding of the mare reduces the number and type of vaccines given in the period prior to foaling.

Pregnant mares, previously unvaccinated or of unknown vaccinal history: Vaccinate 4 to 6 weeks before foaling.

Foals of mares vaccinated against rabies: Administer a primary series. The first dose of vaccine should be administered no earlier than 6 months of age. The second dose should be given 4 to 6 weeks later. Revaccinate annually thereafter. This schedule avoids maternally-derived antibody (MDA) interference with induction of a serologic response in the foal.

Foals of mares NOT vaccinated against rabies: Administer according to label directions. The first dose of vaccine should be administered at 3 to 4 months of age. Revaccinate annually thereafter.

Foals of mares of unknown vaccinal history - Follow one of two rational options:

1. Assume the mare to be antibody-positive and follow the above recommendations for foals from mares known to be vaccinated against rabies, i.e. the first dose starting at 6 months of age followed by second dose 4 - 6 weeks later. Revaccinate annually thereafter.
2. Document the rabies antibody status of the foal by testing serum collected from the foal at 24 hours of age or older, or from the dam during the peri-parturient period.* If the foal of mare is rabies antibody-negative, follow the above recommendations for foals of mares known not to be vaccinated against rabies. If the foal or mare is rabies antibody-positive, follow recommendations for foals of mares known to be vaccinated against rabies.

*Testing for rabies antibodies using the rapid fluorescence focus inhibition test (RFFIT) is available through the Kansas State Veterinary Diagnostic Laboratory, Mosier Hall O-245, 1800 Denison Avenue, Manhattan, KS 66506-5601. Further information is available at www.vet.k-state.edu/depts/dmp/service/rabies/guideline.htm.

Horses exposed to confirmed rabid animal*

Horse currently vaccinated against rabies with one of the USDA-approved rabies vaccines: Immediate revaccination by a licensed veterinarian and observation (as directed by public health officials) for 45 days for development of clinical signs of rabies.

Unvaccinated horse: Euthanatize immediately. If the owner is unwilling to have this done then horse should be closely monitored under veterinary supervision for 6 months. Public health officials may establish requirements and conditions for monitoring of exposed, unvaccinated animals.

*Rabies exposure and transmission occur only when the virus is introduced into bite wounds, into open cuts in skin, or onto mucous membranes from saliva or other potentially infectious material such as neural tissue.

Equine herpesvirus type 1 **(**EHV-1) and equine herpesvirus type 4 **(**EHV-4) can each infect the respiratory tract, causing disease that varies in severity from sub-clinical to severe and is characterized by fever, lethargy, anorexia, nasal discharge, and cough. Infection of the respiratory tract with EHV-1 and EHV-4 typically first occurs in foals in the first weeks or months of life, but recurrent or recrudescent clinically apparent infections are seen in weanlings, yearlings, and young horses entering training, especially when horses from different sources are commingled. Equine herpesvirus type 1 causes epidemic abortion in mares, the birth of weak nonviable foals, or a sporadic paralytic neurologic disease (myeloencephalopathy) secondary to vasculitis of the spinal cord and brain.

Both EHV-1 and EHV-4 spread via aerosolized secretions from infected coughing horses, by direct and indirect (fomite) contact with nasal secretions, and, in the case of EHV-1, contact with aborted fetuses, fetal fluids, and placentae associated with abortions. Like herpesviruses in other species, these viruses establish latent infection in the majority of horses, which do not show clinical signs but may experience reactivation of infection and shedding of the virus when stressed. Those epidemiologic factors seriously compromise efforts to control these diseases and explain why outbreaks of EHV-1 or EHV-4 can occur in closed populations of horses.

Because both viruses are endemic in most equine populations, most mature horses have developed some immunity through repeated natural exposure; thus, most mature horses do not develop serious respiratory disease when they become infected but may be a source of exposure for other susceptible horses. In contrast, horses are not protected against the abortigenic or neurologic forms of the disease, even after repeated exposure, and mature horses are in fact more commonly affected by the neurologic form of the disease than are juvenile animals.

Recently, a genetic variant of EHV-1 has been described (defined by a single point mutation in the DNA polymerase [DNApol] gene) that is more commonly associated with neurologic disease. This mutation results in the presence of either aspartic acid (D) or an asparagine (N) residue at position 752. The D_{752} form is associated with neurological disease, and the N_{752} is not. Molecular diagnostic techniques can identify EHV-1 isolates carrying these genetic markers, although currently the implications of this finding for management of EHV-1 outbreaks, or individual horses actively or latently infected with these isolates, are uncertain. It is important to understand that both isolates can and do cause neurological disease, it is just more common for the D_{752} isolates to do so (it is estimated that 80-90% of neurological disease is caused by D_{752} isolates, and 10-20% by N_{752} isolates). Experts do not currently advise any specific management procedures for horses based on which isolate they are latently infected with, and it is possible that 5-10% of all horses normally carry the D_{752} form (this estimate is based on limited studies at this time). In the face of an active outbreak of EHV-1 disease, identification of an D_{752} isolate may be grounds for some increased concern about the risk of development of neurological disease.

Primary indications for use of equine herpesvirus vaccines include prevention of EHV-1-induced abortion in pregnant mares, and reduction of signs and spread respiratory tract disease (rhinopneumonitis) in foals, weanlings, yearlings, young performance and show horses that are at high risk for exposure. Many horses do produce post-vaccinal antibodies against EHV, ***but the presence of those antibodies does not ensure complete protection***. Consistent vaccination appears to reduce the frequency and severity of

disease and limit the occurrence of abortion storms but unambiguously compelling evidence is lacking. Management of pregnant mares is of primary importance for control of abortion caused by EHV-1.

Vaccines:

Inactivated vaccines

A variety of inactivated vaccines are available, including those licensed only for protection against respiratory disease, which currently all contain a low antigen load, and two that are licensed for protection against both respiratory disease and abortion which contain a high antigen load. Performance of the inactivated low antigen load respiratory vaccines is variable, with some vaccines outperforming others. Performance of the inactivated high antigen load respiratory/abortion vaccines is superior, resulting in higher antibody responses and some evidence of cellular responses to vaccination. This factor may provide good reason to choose the high antigen load respiratory/abortion vaccines when the slightly higher cost is not a decision factor.

Modified live vaccine

A single manufacturer provides a licensed modified live EHV-1 vaccine, which has never been directly compared to high antigen-load respiratory/abortion vaccines. This modified live vaccine has been shown to offer superior clinical protection and reduce viral shedding in a comparison with a single inactivated low antigen-load respiratory vaccine.

Available vaccines make no label claim to prevent the myeloencephalitic form of EHV-1 infection.

Vaccination against either EHV-1 or EHV-4 can provide partial protection against the heterologous strain; vaccines containing EHV-1 may be superior in this regard.

Vaccination schedules:

Adult, non-breeding, horses previously vaccinated against EHV : Frequent vaccination of non-pregnant mature horses with EHV vaccines is generally not indicated as clinical respiratory disease is infrequent in horses over 4 years of age. In younger/juvenile horses, immunity following vaccination appears to be short-lived. It is recommended that the following horses be revaccinated at 6-month intervals:

- Horses less than 5 years of age.
- Horses on breeding farms or in contact with pregnant mares.
- Horses housed at facilities with frequent equine movement on and off the premises, thus resulting in an increased risk of exposure.
- Performance or show horses in high-risk areas, such as racetracks, more frequent vaccination may be required as a criterion for entry to the facility.

Adult, non-breeding horses unvaccinated or having unknown vaccinal history: Administer a primary series of 3 doses of inactivated EHV-1/EHV-4 vaccine or modified-live EHV-1 vaccine. A 4- to 6-week interval between doses is recommended.

Pregnant mares: Vaccinate during the fifth, seventh, and ninth months of gestation using an inactivated EHV-1 vaccine licensed for prevention of abortion. Many veterinarians also recommend a dose during the third month of gestation and some recommend a dose at the time of breeding.

Vaccination of mares with an inactivated EHV-1/EHV-4 vaccine 4 to 6 weeks before foaling is commonly practiced to enhance concentrations of colostral immunoglobulins for transfer to the foal. Maternal antibody passively transferred to foals from vaccinated mares may decrease the incidence of respiratory disease in foals, but disease can still occur in those foals and infection is common.

Barren mares at breeding facilities: Vaccinate before the start of the breeding season and thereafter based on risk of exposure.

Stallions and teasers: Vaccinate before the start of the breeding season and thereafter based on risk of exposure.

Foals: Administer a primary series of 3 doses of inactivated EHV-1/EHV-4 vaccine or modified-live EHV-1 vaccine, beginning at 4 to 6 months of age and with a 4- to 6-week interval between the first and second doses. Administer the third dose at 10 to 12 months of age.

Immunity following vaccination appears to be short-lived and it is recommended that foals and young horses be revaccinated at 6-month intervals.

The benefit of intensive vaccination programs directed against EHV-1 and EHV-4 in foals and young horses is not clearly defined because, despite frequent vaccination, infection and clinical disease continue to occur.

Outbreak mitigation: In the face of an outbreak, horses at high risk of exposure, and consequent transmission of infection, may be revaccinated. Administration of a booster vaccination is likely to be of some value if there is a history of vaccination. The simplest approach is to vaccinate all horses in the exposure area—independent of their vaccination history. If horses are known to be unvaccinated, the single dose may still produce some protection.

There remain concerns that heavily vaccinated horses may be more susceptible to developing neurological disease caused by EHV-1. This possibility is unsubstantiated and a subject of active investigation. To date, the use of a single vaccine immediately before exposure has not shown any association with an increased incidence of neurological disease.

Horses having been naturally infected and recovered: Horses with a history of EHV infection and disease, including neurological disease, are likely to have immunity consequent to the infection that can be expected to last for 3 to 6 months (longer in older horses). Booster vaccination can be resumed 6 months after the disease occurrence.

Equine influenza, caused by the orthomyxovirus equine influenza A type 2 (A/equine 2), is one of the most common infectious diseases of the respiratory tract of horses. It is endemic in the equine population of the United States and throughout much of the world, with the notable exceptions of New Zealand and Iceland. Equine influenza virus does not constantly circulate, even in large groups of horses, but is sporadically introduced by an infected horse. This epidemiologic finding and the rapid elimination of the virus by the equine immune response suggest that infection can be avoided by preventing entry of the virus into an equine population (ie. by the quarantine of newly arriving horses for at least 14 days), and by appropriate vaccination before exposure. All horses should be vaccinated against equine influenza unless they live in a closed and isolated facility.

To date, the most important factors associated with increased risk of infection have been identified as:

1) Age: Horses 1 to 5 years old are more susceptible. Older horses are generally less susceptible to infection, but immunity can be overwhelmed in horses frequently exposed at shows or similar athletic events.

2) Serum concentrations of influenza virus-specific antibody: The importance of local mucosal protection is difficult to quantitate by methods currently available.

3) Frequent contact with large numbers of horses.

Equine influenza is highly contagious and the virus spreads rapidly through groups of horses in aerosolized droplets dispersed by coughing. The severity of clinical signs depends on the degree of existing immunity, among other factors. Horses that are partially immune can become subclinically infected and shed virus. Immunity to the same (homologous) strain of virus following natural infection persists for approximately one year. Immunity following vaccination with inactivated influenza vaccines can be short-lived, allowing recently vaccinated horses to become infected and shed virus, thereby contributing to maintenance and spread of infection within the equine population. For these reasons, only vaccines of proven efficacy should be selected for use.

Although influenza is endemic in many countries and circulates continuously in the equine population, explosive outbreaks occur at intervals of several years when the immunity of the equine population wanes, and sufficient antigenic drift in the virus has occurred, allowing the virus to evade vaccinal immunity. Antigenic drift, by generating antigenically heterologous viruses, reduces the degree and duration of protection conferred by previous infection or vaccination. Although antigenic drift of equine influenza virus is slower than that of human influenza virus, it is still recommended that equine vaccines contain killed viral antigens from isolates obtained within the most recent 5 years, and ideally, representatives of both the American and Eurasian

lineages should be included. Alternatively, vaccines containing single strains of virus should have proven efficacy against both American and European lineage viruses.

Historically, equine influenza vaccines have been administered at intervals as short as every 3 months to horses considered at high risk of infection. All currently marketed equine influenza vaccines are likely to provide protection of at least six months duration. This is true for both of the modified live vaccines on the market today, and for inactivated vaccines. This performance depends on the quality of currently marketed vaccines, and maintaining this performance will depend on the inclusion of any new antigenically distinct equine influenza viruses that may appear in the horse population in the future.

Vaccines:

There are three types of equine influenza virus vaccine currently marketed:

Inactivated vaccines

Each of these has been shown to be efficacious in providing protection against clinical disease and viral shedding when used appropriately. These vaccines frequently include multiple strains of equine influenza virus A2 representing the major circulating strains. Some of these vaccines also contain the A1 strain (now thought to be extinct), because this was part of their original formulation; this strain will likely be phased out of all equine vaccines in time. The majority of these vaccines require two-dose priming regimens, although a three-dose priming regimen is recommended here as described below; a 3 dose regimen is required for at least one of the most effective inactivated vaccines. These vaccines are well suited to pre-foaling boosters designed to increase colostral antibody levels against influenza virus.

Modified-live cold-adapted equine influenza /A2 vaccine

This product is administered intranasally and has been available for several years. The vaccine has proven to be very safe and a single administration to naive horses is protective for 12 months, although only a 6-month claim is made on the product data sheet. Circulating antibody responses post-vaccination are minimal, suggesting that that other factors, such as local protection at the nasal mucosa may be enhanced by this vaccine. The product is licensed for vaccination of non-pregnant animals over 11 months-of-age using a single dose of vaccine, followed by boosters at 6-month intervals. Generally, horses shed vaccinal virus for less than 1 week after vaccination. However, the amount and duration of shed vaccinal virus is so minimal that other horses in contact with them will not be vaccinated. Incorporation of the MLV vaccine into a program which previously used inactivated vaccine can be easily accomplished by just substituting the MLV when routine boosters are scheduled.

Experience strongly supports the safety of the MLV intranasal vaccine when administered to foals less than 11 months of age. Similarly, the vaccine is protective when administered to foals six months of age or older. The onset of protection in previously unvaccinated horses has been documented as early as seven days after vaccination. The vaccine is not recommended for vaccination of mares in late pregnancy to boost colostral antibodies, as data available to date suggest that circulating antibody responses to vaccination are low.

Canary pox vector vaccine

This recently released product is to be administered by intra-muscular injection and has been shown to provide protection of at least six months duration. A two-dose priming regimen is recommended, with boosters at a six-month interval. The onset of immunity has been documented at 14 days after administration of the first dose of vaccine. The vaccine is safe to use in foals as young as four months of age, and there is some evidence of efficacy in the face of maternal immunity. Because this vaccine generates high levels of antibody response, it is likely to be suitable for pre-foaling boosters.

Vaccination Schedules:

Adult Horse, previously vaccinated: Mature performance, show, or pleasure horses constantly at risk of exposure should be revaccinated at 6-month intervals. Other adult horses could be vaccinated as infrequently as once a year.

Adult horses, unvaccinated or having an unknown vaccination history: Either one dose of the MLV intranasal vaccine or a primary series of 3 doses of the inactivated-virus vaccines is recommended. The ideal intervals between these vaccinations are three to four weeks between the first and the second vaccination, followed by an interval ideally as long as three to six months before the third vaccination. This regimen generally induces higher and more persistent antibody titers than those induced by use

of the previously recommended 2-dose initial series. Subsequent revaccination should be at intervals of 6 to 12 months, depending on the age of the horse as well as the degree and duration of risk of acquiring infection. If using a canary pox vector vaccine, use a 2-dose series with the second dose given 4 to 6 weeks after the first dose. Revaccinate semi-annually.

Pregnant broodmares, previously vaccinated: Vaccinate 4 to 6 weeks before foaling using the inactivated-virus vaccine or the canary pox vectored vaccine.

Pregnant broodmares, unvaccinated or having an unknown vaccination history: Use a 3-dose series of the inactivated-virus vaccines, with the second dose administered 4 to 6 weeks after the first dose and the third dose administered 4 to 6 weeks pre-partum. With a canary pox vector vaccine, a 2-dose series is recommended with the second dose administered 4 to 6 weeks after the first dose but no later than 4 weeks pre-partum.

Foals of vaccinated mares: Administer either a single dose of the MLV intranasal vaccine or a primary series of 3 doses of inactivated-virus vaccine beginning at 6 months of age. The recommended intervals between these vaccinations are 4 to 6 weeks between the first and the second vaccinations. The third dose should be administered between 10 and 12 months of age.

Foals of nonvaccinated mares: Administer either a single dose of the MLV intranasal vaccine or a primary series of 3 doses of inactivated virus vaccine at 6 months of age (see above), unless there is an unusual threat that recommends earlier vaccination. Because some maternal anti-influenza antibody is still likely to be present, a complete series of primary vaccinations should still be given after 6 months of age.

Outbreak Mitigation:

Vaccination to boost immunity in the face of an outbreak may be a valuable strategy if the outbreak is detected early enough. In previously vaccinated horses, any vaccine can be used for this purpose. In unvaccinated horses, or horses with an unknown vaccination history, the early onset of immunity after administration of the intranasal product (protection within 7 days), may recommend it for use. (View AAEP Infectious Disease Control Guidelines—Influenza.)

Equine monocytic ehrlichiosis is caused by *Neorickettsia risticii* (formerly *Ehrlichia risticii*). Originally described in 1979 as a sporadic disease affecting horses residing in the eastern United States near the Potomac River, the disease has since been identified in various other geographic locations in the United States and Canada. The disease is seasonal, occurring between late spring and early fall in temperate areas, with most cases in July, August, and September at the onset of hot weather.

Clinical signs are variable but may include: fever, mild to severe diarrhea, laminitis, mild colic, and decreased abdominal sounds. Uncommonly, pregnant mares infected with *N. risticii* (usually in the middle trimester between 90 and 120 days) can abort due to fetal infection at 7 months of gestation.

If Potomac Horse Fever has been confirmed on a farm or in a particular geographic area, it is likely that additional cases will occur in future years. Foals appear to have a low risk of contracting the disease. Vaccination against this disease has been questioned because field evidence of benefit is lacking. Proposed explanations for this include lack of seroconversion and multiple field strains whereas only one strain is present in available vaccines.

Vaccine

The currently available commercial vaccines are killed, adjuvanted products. Two of these are also available combined with a rabies vaccine. None of the current vaccines carry a label claim for the prevention of abortion.

Vaccination Schedules

Due to the seasonal incidence of disease, vaccination should be timed to precede the anticipated peak challenge during the summer months or fall.

Adult horses, previously vaccinated: Manufacturers recommend revaccination at 6- to 12-month intervals. However, veterinarians may consider an interval of 3 to 4 months for horses in endemic areas because protection following vaccination can be incomplete and short-lived.

Adult horses, previously unvaccinated or with unknown vaccinal history: Administer a primary series of 2 doses, at a 3- to 4-week interval. Peak protection occurs 3 to 4 weeks after the second dose.

Pregnant mares previously vaccinated against PHF: Vaccinate semi-annually to annually. Schedule 1 dose to be administered 4 to 6 weeks before foaling. To date no studies have been published that examine the efficacy of PHF vaccines to prevent *N. risticii* induced abortion.

Pregnant mares unvaccinated or with unknown vaccinal history: Administer a primary series of 2 doses, at a 3- to 4-week interval. Schedule so that 2nd dose is administered 4 to 6 weeks before foaling.

Foals: Due to the low risk of clinical disease in young foals and the possible maternal antibody interference, primary immunization for most foals can begin after 5 months of age. The manufacturer's recommendation is for a 2-dose series administered at a 3- to 4-week interval. However, as with other killed products, a third dose at 12 months of age is recommended. If the primary series is initiated when foals are less than 5 months of age, additional doses should be administered at monthly intervals up to 6 months of age to ensure that an immunologic response is achieved.

Horses having been naturally infected and recovered: Administer a primary series (as described above) or booster vaccine (if previously vaccinated) 12 months following recovery from natural infection.

*Streptococcus equi*subspecies *equi* (*S. equi var. equi)* is the bacterium which causes the highly contagious disease strangles (also known as "distemper"). Strangles commonly affects young horses (weanlings and yearlings), but horses of any age can be infected. Vaccination against *S. equi* is recommended on premises where strangles is a persistent endemic problem or for horses that are expected to be at high risk of exposure. Following natural infection, a carrier state of variable duration may develop and intermittent shedding may occur. The influence of vaccination on intermittent shedding of *S. equi* has not been adequately studied.

The organism is transmitted by direct contact with infected horses or sub-clinical shedders, or indirectly by contact with: water troughs, hoses, feed bunks, pastures, stalls, trailers, tack, grooming equipment, nose wipe cloths or sponges, attendants' hands and clothing, or insects contaminated with nasal discharge or pus draining from lymph nodes of infected horses. *Streptococcus equi* has demonstrated environmental survivability particularly in water sources and when protected from exposure to direct sunlight and disinfectants, and can be a source of infection for new additions to the herd.

Infection by *S. equi* induces a profound inflammatory response. Clinical signs may include fever (102-106^{o} F); dysphagia or anorexia; stridor; lymphadenopathy (+/- abscessation); and copious mucopurulent nasal discharge.

S. equi and *S. zooepidemicus* are antigenically similar organisms. However, exposure to, or vaccination against, one does not confer reliable immunity to the other.

Following natural or vaccinal exposure to streptococcal antigens, certain individuals may unpredictably develop purpura hemorrhagica, an acute, non-contagious syndrome caused by immune-mediated, generalized vasculitis. Clinical signs develop within 2 to 4 weeks following natural or vaccinal exposure to streptococcal antigens. Clinical signs may include urticaria with pitting edema of the limbs, ventral abdomen and head; subcutaneous and petechial hemorrhage; and sloughing of involved tissues. Severe edema of the head may compromise breathing. Immediate medical attention should be sought for individual horses suspected of having purpura hemorrhagica.

Vaccines:

Vaccination in the face of an outbreak should be carefully considered, as there is significantly increased risk of adverse reactions in exposed horses. Purpura hemmorrhagica can be associated

with vaccine administration. In a recent retrospective study of 53 horses with purpura hemorrhagica, 5 cases were vaccinated with a S. equi M protein vaccine. Outbreak mitigation and the prevention of spread of *S. equi* infection are centered on management of horses, personnel, and facilities.

(View AAEP Infectious Disease Control Guidelines—*S. equi*.; view ACVIM Strep equi consensus statement)

Killed vaccines

Killed vaccines are an adjunct to the prevention of strangles. Vaccination with these products should not be expected to prevent disease. However, appropriate pre-exposure vaccination with these products appears to attenuate the severity of clinical signs in affected horses, should disease occur, and has been shown to reduce the incidence of disease by as much as 50% during outbreaks.

All injectable, inactivated *S. equi.* vaccines, particularly the whole-cell bacterin, are associated with an increased rate of injection site reactions as compared to other equine vaccines. Due to the limited variability between commercially available vaccinal bacteria and field isolates, autogenous bacterins are not advocated.

Modified live vaccine

An intranasal product has been shown to stimulate a high level of immunity against experimental challenge. The inductive sites are the pharyngeal and lingual tonsils. Vaccinal organisms must reach these sites in sufficient numbers to trigger protective responses; therefore, accurate vaccine delivery is critical to vaccine efficacy. In a small percentage of cases, residual vaccinal organism virulence may result in formation of slowly developing mandibular or retropharyngeal abscesses.

Maternal antibody interference with respect to the development of mucosal immunity needs to be studied further.

In order to avoid inadvertent contamination of other vaccines, syringes and needles, it is advisable and considered a good practice to administer all parenteral vaccines or other injectables before the handling and administration of the intranasal vaccine against *S. equi*.

Vaccination Schedules:

Adult horses previously vaccinated: Vaccinate every 6 to 12 months based on risk assessment and manufacturers' recommendations.

Adult horses unvaccinated or having unknown vaccinal history

Killed vaccine:

Manufacturers' recommendations are for primary vaccination with a series of 2 or 3 doses administered at intervals of 2 to 4 weeks, depending on the product used, followed by annual revaccination. Revaccinate at 6- month intervals, regardless of the injectable product used.

Modified live vaccine:

Administer intranasally a 2-dose primary series with a 3-week interval between doses. Semiannual (6-month intervals) or annual revaccination is recommended.

Broodmares previously vaccinated

Killed vaccine:

Vaccinate 4 to 6 weeks pre-partum with approved products that contain inactivated M-protein. Maternal antibody interference is not known to occur when injectable, M-protein vaccines are administered.

Broodmares previously unvaccinated or having unknown vaccinal history
Administer primary series of killed vaccine containing M-protein (see above, *Adult horses unvaccinated)* with final dose to be administered 4 to 6 weeks pre-partum.

Foals

Killed vaccine:

For foals at high risk for exposure to strangles, administer a 3-dose primary series of an M-protein product beginning at 4 to 6 months of age. An interval of 4 to 6 weeks between doses is recommended.

Modified live vaccine:

Administer intranasally at 6 to 9 months of age a 2-dose primary series with a 3-week interval between doses. This vaccine has been safely administered to foals as young as 6 weeks of age when there is a high risk of infection, such as occurs during an outbreak, but the efficacy of its use in very young foals has not been adequately studied. If administered to young foals in this manner, a third dose of the modified live vaccine should be administered 2 to 4 weeks before the foal is weaned to optimize protection during that time of high risk of infection.

Horses having been naturally infected and recovered: Following recovery from strangles, most horses develop a durable immunity, persisting in over 75% of animals for 5 years or longer. This indicates that stimulation of a high level of immunity is biologically feasible given appropriate presentation of protective immunogens. Currently, a diagnostic test is available and may be used to assess the level of immunity conferred by natural exposure or vaccination. Since natural exposure or vaccination can provide variable levels of immunity, use of this test may provide a guideline in determining the need for current or future vaccination.