NEW ZEALAND THOROUGHBRED RACING INC
Box 38386, Wellington MC ❖ Tel: +64 4 576 6240 ❖ Fax: +64 4 568 8866
Website: www.nzracing.co.nz ❖ E-mail: office@nzracing.co.nz

EI UPDATE
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EQUINE INFLUENZA VACCINATION – THE ONGOING DEBATE

The use and timing of vaccination in an Equine Influenza (EI) outbreak is always going to be a contentious issue. There are strong arguments both for and against vaccination and our decisions around vaccine use need to be constantly under review. With today's news that Australia is to import vaccine for use in "buffer zones" around EI hotspots we can expect another round of discussion and opinion on the merits of vaccination.

Vaccines are developed to trigger immunity against a specific infectious organism ie a virus or bacteria that causes disease. A vaccine aims to mimic the disease without producing any clinical signs.

There are three types of Equine Influenza vaccines available. These are:

Killed or inactivated vaccines – the virus is killed usually by chemicals and then mixed with a liquid carrier (adjuvant). The vaccine may use the whole virus, various virus proteins or viral DNA or RNA. These vaccines frequently include multiple strains of influenza virus A2 representing the major circulating strains. The main advantage of these vaccines is the absence of pathogenicity, virus replication and subsequent spread between hosts. They are administered by intramuscular injection and a course of two injections four to six weeks apart is recommended. Optimal immunity is not present until at least 7-14 days after the second dose. For ongoing protection from disease, manufacturers recommend a booster vaccination at 6 months.. Annual or more frequent boosters, depending on the likely exposure of the horse to circulating virus, are then required.

Live modified vaccines– these vaccines have been made safe through a process called attenuation (decreasing the virulence of the virus for the horse). Horses that have been infected by EI virus have been shown to be protected from reinfection for about 12 months so it would be expected that a live virus vaccine would give superior protection to the inactivated vaccines. However the vaccine did not provide this level of protection and while they did provide quicker and stronger immunity than inactivated vaccines anecdotal evidence suggests they have not had widespread uptake. They do present the risk of viral spread following their use. An intranasal cold adapted modified live equine influenza virus vaccine based on a Kentucky 1991 A/Equi 2 virus is available in North America. It 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. There is evidence of early onset of protection (as early as 7 days) following the use of this vaccine.

Recombinant vaccines – these vaccines are another form of "live vaccine" but because they require different technology and approvals process it is convenient to treat them as a separate type. In these vaccines selected genes from the equine

influenza virus are inserted into another “safe” non disease causing virus. A recombinant canary pox vector based equine influenza vaccine is available in Europe and the USA. The vaccine is given by intramuscular injection and a two dose priming regime 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 and this is probably one of the reasons that Australia is planning on importing to import this type of EI vaccine for use in creating their “buffer zones”.

The New Zealand Equine Health Association (NZEHA) has been preparing with MAF Biosecurity New Zealand (MAFBNZ) for the past ten years for an Equine Influenza incursion. As part of that preparedness we have registered two killed equine influenza vaccines. The registrations for these vaccines are held by MAFBNZ and at this time we have **no** stock of vaccine in NZ. The original plan was to have the vaccine registered so we could quickly source stocks from overseas in the face of an outbreak. It was planned to be able to vaccinate unaffected horses distant from an infected area to create a “buffer zone” while movement control was applied and eradication attempted in the affected group. We have since reviewed this approach and on balance we consider that while we have only inactivated vaccines to use in an incursion we would probably not initially use vaccination. Inactivated vaccines take too long to generate immunity in the horse and the real risk that vaccinated horses can still contract the disease, albeit with fewer or no symptoms, and excrete virus thus potentially adding to the spread of the disease is of real concern.

Most of the vaccines we encounter as humans are very effective and impart long standing immunity against the disease they are designed to protect against. When we look at the available vaccines against equine influenza and also human influenza this is not the case. To understand why, we have to look both at the virus and the vaccine.

The Equine Influenza virus is constantly changing how it is seen by horse’s immune system. These subtle changes are called antigenic drift (the virus presents a different face to the horse’s immune system). Every so often there is significant change in the virus and a new subtype is identified. New subtypes are named after the place where they were first identified so we see names like Prague, Suffolk, Ohio, Miami, Kentucky, Wisconsin etc. attached to the influenza virus. These constant subtle changes in the virus are the reason why horses can catch influenza more than once, even in consecutive years. Although vaccination can prevent disease, the available EI vaccines neither fully prevent infection nor transmission of the virus. However, vaccinated horses, in response to EI infection, shed less virus for shorter periods and show fewer or no detectable clinical signs than fully susceptible horses.

The immunity generated in horses after vaccination is relatively short lived so unless a horse is constantly challenged its immunity wanes and it can be reinfected quite quickly. There is no carrier state (ie the virus does not remain in the normal recovered horse as is the case with Equine Herpes Virus) in horses that have been infected with Equine Influenza. In countries where the virus is endemic it is because the infection keeps circulating through the horse population. For vaccination to have much impact on the rate at which EI circulates and reinfects horses, in a country in which the disease is endemic, it is necessary to have a strict vaccination program involving about 70% of the horse population. If we were to apply this to New Zealand with approximately 120,000 horses, we would need to vaccinate 84000 and at a cost of approximately $375 +Gst for an initial three dose course of killed vaccine per horse the first year cost would be about $30 million.

With these subtle changes to the virus, vaccine manufacturers are always chasing a moving target. They are constantly upgrading their vaccines with the latest subtypes. This process takes a couple of years at least. So when there is a new outbreak it is important to firstly type the virus and then select the most appropriate vaccine. Most influenza vaccines have at least two subtypes and generally include American and European strains. We have no word yet from Australia as to the subtype they have but if it is the Wisconsin 2003 subtype as widely suggested, vaccines containing Kentucky 1997 subtype would be as close as we could get and we understand it would be relatively effective.

This combination of poor immunity, antigenic drift and the use of out of date or wrong subtype vaccines gives rise to a real problem we have already alluded to when confronted with this disease. Vaccinated horses will be reinfected and as they have some protection they will show few if any symptoms (ie be subclinical) but still shed virus and be a source of new infections. This makes detection more difficult and more expensive as we have to rely on a wider range of laboratory tests. In the face of an outbreak there is the confusion created with positive blood results as to whether they are due to vaccine or natural infection. In those countries where vaccination is practised there are regular episodes of disease and every five or so years there is a major outbreak.

It must be pointed out that vaccination on its own has not ever resulted in EI eradication. It may have a place alongside stringent biosecurity measures and movement controls. Vaccination may be used to protect animals in certain sub sectors /regions of the horse industry and /or to reduce the economic impact of this disease. In conclusion I would like to include a table taken from a recent Australian Consultative Committee on Emergency Animal Diseases' paper on the pros and cons of vaccination. I have taken the liberty of making it relevant to New Zealand with our current EI freedom.

Advantages and disadvantages of vaccination for EI

Advantages

- Vaccination can prevent clinical disease.
- Vaccination reduces the susceptibility of at-risk horses, reduces the severity of clinical signs and the level of viral shedding if they become infected.
- Vaccination can reduce farm-to-farm spread of infection.

Disadvantages

- Vaccination may mask clinical signs so vaccinated horses will need to be identified and monitored for evidence of infection.
- Serological monitoring will be difficult, even though tests are available to differentiate vaccinated horses. Some tests used in this respect may not be internationally validated.
- The movement of sub-clinically infected vaccinated horses may spread infection to previously unaffected areas.
- Vaccination may prolong the need for movement restrictions because it may slow the transmission and spread of infection within areas.
- Vaccinating selected regions will lead to the country being separated into free and vaccinated areas. This will result in differential movement requirements and the need for infrastructure (permits, border controls, etc) to maintain integrity of free areas.
- Vaccination will have an impact in terms of registration and passport issues and the practical control measures required before many horse events can proceed.
- Vaccination is not an immediate option, it will take time to import vaccine (permit process), deploy vaccine and train vaccinators, vaccinate the population and for

immunity to develop.

- In the case of the recombinant vaccine there may difficulties with its registration and there would likely be restrictions placed on how and who may use the vaccine.
- Vaccination may affect performance in the short term.
- Vaccine use is likely to extend the duration of an outbreak and delay ability to declare freedom.

Dr John O'Flaherty
Technical Adviser
New Zealand Equine Health Association Inc.