Australian Government
Australian Pesticides and Veterinary Medicines Authority

PERMIT TO ALLOW SUPPLY AND MINOR USE OF AN AGVET CHEMICAL PRODUCT

PERMIT NUMBER - PER13510

This permit is issued to the Permit Holder in response to an application granted by the APVMA under section 112 of the Agvet Codes of the jurisdictions set out below. This permit allows a Supplier (as indicated) to possess the product for the purposes of supply and to supply the product to a person who can use the product under permit. This permit also allows a person, as stipulated below, to use the product in the manner specified in this permit in the designated jurisdictions. This permit also allows the Permit Holder, the Supplier (if not one and the same) and any person stipulated below to claim that the product can be used in the manner specified in this permit.

THIS PERMIT IS IN FORCE FROM 3 AUGUST 2012 TO 3 AUGUST 2014 .

Permit Holder and Supplier:
PFIZER ANIMAL HEALTH
A DIVISION OF PFIZER AUSTRALIA P/L
38-42 Wharf Road
WEST RYDENSW2114

Persons who can use the product under this permit:
Registered veterinary surgeons who are accredited through the completion of the EquivacHeVVaccine e-learning module.

CONDITIONS OF USE

Product to be used:
EQUIVAC HeV HENDRA VIRUS VACCINE FOR HORSES
Containing:100µg /mL of Hendra virus G glycoprotein as the only active constituent.

Directions for Use:

Animal	Pest	Dose
Equine	Aid in the prevention of clinical disease caused by Hendra virus	1 ml 3 weeks apart in horses 4 months of age and above

Jurisdiction

All States

Withholding Period

Nil

Supply by Pfizer Animal Health

1. Pfizer Animal Healthmust supply the vaccine in a container that complies with the requirements of Reg 18(1)(a-e) of the Agricultural and Veterinary Chemicals Code Regulations.
2. Attached to the container must be a label which states that the product is authorised for use under APVMA permit number 13510. The label must contain the relevant label particulars as indicated in Attachment 1.
3. This vaccine must only be supplied to registered veterinary surgeons who have had appropriate training and accreditation on how to use this vaccine by Pfizer Animal Health.
4. Pfizer Animal Health must maintain records indicating:
    - Details of all vaccinated equines including breed, sex, age, batch of vaccine used and unique microchip identification details
    - Details of owner or manager and location of the equine at the time of vaccination
    - Vaccine inventory (including full auditable details of stock manufactured, supplied, used or returned)

    The above information must be provided to the CVO of the relevant State or Territory and the APVMA on request.
5. Pfizer Animal Health must provide CVOs access to the information in the HeVVaccine Online Registry at all times.
6. Pfizer Animal Health must record any reported adverse reaction, including lack of efficacy, resulting from the use of the vaccine, and must fully investigate and report all adverse reactions to the APVMA's Adverse Experience Reporting Program Coordinator as soon as possible.
7. Pfizer Animal Health must retain and store samples of each batch of the vaccine at the recommended temperature for at least two years past the nominal expiry date, to allow for testing as part of the required investigation of adverse reactions.

Use by registered veterinary surgeons

8. Persons who wish to prepare for use and/or use the vaccine for the purposes specified in this permit must read, or have read to them, the attached label (Attachment 1) and the permit, particularly the information included in details of the permit and Conditions of the permit.
9. The vaccine must only be used by registered veterinary surgeons who are accredited through the completion of the EquivacHeV e-learning module.
10. Each vaccinated equine must be permanently identified by a microchip carrying a unique identification sequence.
11. Record of each vaccination must be entered into the HeV Vaccine National Online Registry (managed by Pfizer Animal Health) within 48 hours of vaccination. The information must include:
    - Details of all vaccinated equines including breed, sex, age, batch of vaccine used and unique microchip identification details

- Details of owner or manager and location of the equine at the time of vaccination

12. Adverse reactions, including lack of efficacy, resulting from the use of the vaccine, must be reported to Pfizer Animal Health as soon as possible.

Issued by

Dr Allen Bryce
Program Manager
Veterinary Medicines Program

LABEL (1 mL syringe)

EquivacHeVHendra Virus Vaccine for Horses
(B) 7347-
(E) mth/yr

FOR ANIMAL TREATMENT ONLY
EquivacHeVHendra Virus Vaccine for Horses
100 µgsG-protein/mL
READ ENCLOSED LEAFLET
CAUTION: Avoid accidental self-injection
Store at 2° to 8°C (Refrigerate).
APVMA Permit No. PER13510

(item numbers and version)

1 mL (Pfizer logo)

(B) 7347-
(E) mth/yr

LABEL (10 mL vial)

	KEEP OUT OF REACH OF CHILDREN **READ SAFETY DIRECTIONS** **FOR ANIMAL TREATMENT ONLY**
10 Doses 10 mL	**EquivacHeVHendra Virus Vaccine for Horses** **100 µgsG-protein/mL** **READ ENCLOSED LEAFLET** **CAUTION: Avoid accidental self-injection** Store at 2° to 8°C (Refrigerate. Do not freeze).
(Pfizer logo)	APVMA Permit No. 13510

(B)7347-
(E)mth/yr
(item numbers and version)

CARTON (20dose pack x 1 mL Syringe/ 10 mL vial)

Main Panel:	**KEEP OUT OF REACH OF CHILDREN** **READ SAFETY DIRECTIONS** **FOR ANIMAL TREATMENT ONLY**
1 x 1 mL Syringe/Vial (10 mL vial)	**EquivacHeVHendra Virus Vaccine for Horses** (horse picture) **100 µgsG-protein per mL** **0.1 mg/mL Thiomersal added** **For active immunisation of horses against Hendra Virus as an aid in the prevention of clinical disease caused by Hendra virus.**
(Pfizer logo)	**CAUTION: Avoid accidental self-injection**

Side Panel 1: **READ THE ENCLOSED LEAFLET BEFORE USING THIS PRODUCT**

DIRECTIONS FOR USE
Contents must be left in outer package until immediately before use.

For Intramuscular Use Only
Dose: 1 mL

MEAT WITHHOLDING PERIOD NIL

SAFETY DIRECTIONS

Caution: Care should be taken to avoid accidental self-injection and needle-stick injury when administering this product. In the event of accidental self-injection, seek medical advice immediately..
Personal Protective Equipment (PPE) should be worn whenever Hendra virus disease is suspected even in vaccinated horses as no vaccine can provide aguaranteed protection

(Bar Code)

Store between 2^{o}C and 8^{o}C (Refrigerate. Do not freeze). Protect from light.
(B) 7347-
EXPIRY
mth/yr (Item numbers and version)

Side Panel 2: **EquivacHeVHendra Virus Vaccine for Horses**
Pfizer Animal Health
A division of Pfizer Australia Pty Ltd
38-42 Wharf Road, West Ryde NSW 2114
AUSTRALIA

Australian Technical Services Toll Free 1800 814 883
www.pfizeranimalhealth.com.au
APVMA Permit Number:PER13510
1 x 1 mL Syringe/vial (10 Doses, 10 mL) (Recycle logo)

Side Panel 3: **EquivacHeVHendra Virus Vaccine for Horses**
1 x 1 mL Syringe/Vial

(10 Doses, 10 mL)
(Pfizer logo)

Side Panel 4: **EquivacHeVHendra Virus Vaccine for Horses**
Disposal: Dispose of empty syringes and needles by immediately placing into a designated and appropriately labelled ‘sharps’ container.

1 x 1 mL Syringe/Vial (10 Doses, 10 mL)

(Recyclelogo)

LEAFLET

KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS
FOR ANIMAL TREATMENT ONLY

EquivacHeVHendra Virus Vaccinefor Horses

For active immunisation of horses against Hendra Virus as an aid in the prevention of clinical disease caused by Hendra virus.

This vaccine is under development at Pfizer Veterinary Medicine Research and Development. EquivacHeVHendravirus vaccinefor horsescontainssoluble forms of G glycoprotein [sG] of Hendra Virusadjuvanted with immunostimulating complex. Each mL of vaccine provides 100 μg G glycoprotein of Hendra Virus[sG– protein]. Thiomersal 0.1 mg/mL has been added as a preservative.

Initial trials have showncomplete protection when vaccinated horses were subject to lethal challenge with a virulent strain of Hendra virus. All vaccinated animals were protected from disease and neither Hendra virus nor evidence of virus replication was detected in any tissue of the immunised horses.
EquivacHeVHendra virus vaccine for horses is used as an aid to prevent clinical disease in horses caused by Hendra virus, and also to reduce viral shedding. Following vaccination, horses produce antibodies that neutralise the Hendra virus by binding to the G protein of the virus, rendering it unavailable for attachment to the cells of the animal and thereby preventing infection.

EquivacHeVHendra virus vaccine for horses does not contain genetically modified organisms and there is no live or inactivated Hendra virus in this product.

DIRECTIONS FOR USE
Contraindications and Precautions

The effect of this product on pregnant mares or on horses intended for breeding is not known, therefore use in these animals must be weighed against the risk of serious illness or death from disease caused by infection with Hendra virus.

The extent and duration of effect of booster doses of vaccine have not been studied.

There is no data to support the use of this vaccine in sick horses

The effectiveness of EquivacHeV vaccine in the face of Hendra virus disease outbreak has not been studied

Personal Protective Equipment (PPE) should be worn whenever HeV is suspected even in vaccinated horses as no vaccine can provide a guaranteed protection

Dosage and Administration
The dose on all occasions is **1 mL injected intramuscularly in horses 4 months of age and older**. The most convenient site for injection is the centre of the side of the neck. Before the vaccine is injected, the proposed site of inoculation on the horse's skin may be cleaned by swabbing with cotton-wool soaked in a suitable antiseptic solution, such as methylated spirits.

For primary immunisation two doses of vaccine should be administered 3 weeks apart. Effective levels of serological antibodies for the control of Hendra virus infection develops approximately 21days after administration of the second dose of vaccine in most horses. Primary immunisation should be completed in advance of when the desired vaccination effect is needed. For continued effect, further booster doses will likely be required.

Side Effects
Transient swelling may develop at the site of vaccination in some horses but should resolve within one week without treatment.
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Efficacy:
Clinical trials of Equivac® HeV vaccine containing either 100 µg or 50 µgsG in a prime-boost regime resulted in seroconversion in allvaccinated horses. Following challenge of a small number of vaccinated horses with a lethal dose of HeV, immunised horses remained clinically well throughout the period of observation (7-9 days post challenge). By contrast, non-vaccinated control horses showed clinical signs consistent with HeV infection from 4 days following challenge.

There was no evidence of viral shedding by immunised horses after Hendra virus challenge, as reflected by PCR negative test results on all daily clinical samples. In non-immunised (control) horses or (surrogate control) guinea pigs, after challenge viral genome was detected in respiratory secretions during the incubation period as well as in oral and rectal swabs, urine and blood at disease onset (horses) or in major organs and blood on day 5 after exposure to the virus (guinea pigs). Following euthanasia of immunized horses (7 to 9 days post challenge, and 1-3 days after clinical signs first became apparent in control horses), there was no evidence of HeV viral replication in any tissue of immunised horses collected at post mortem examination, after what would be expected to be the period of acute infection. In contrast, HeV genome and antigen were distributed widely among the tissues of control animals in a pattern consistent with acute HeV infection, and vasculopathy typical of HeV infection was also identified. Clinical, histological and immunohistological findings corroborate a diagnosis of acute HeV infection in these animals.

In summary all vaccinated animals were protected from disease against a virulent challenge with Hendra virusuntil 1-3 days after the onset of acute disease in unvaccinated horses. Neither Hendra virus nor evidence of virus replication was detected in any tissue of the immunised horses.

To demonstrate the immunogenicity of the vaccine under field conditions two trials were conducted. Horses were given two single doses ofthe vaccine by intramuscular injection on Days 0 and 21. 100% of vaccinated animals in both trials seroconverted, confirming thattwo doses of EquivacHeV given 3 weeks apart are sufficient to generate an antibody response in horses from 4 months of age. Serumneutralising antibody levels on day 42 (3 weeks after the 2nd dose of vaccine) in all vaccinated horses from both trials were equivalent to those seen in the challenge studies described above,in which vaccinated horses were protected from challenge with Hendra virus.

Safety:
The safety profile of EquivacHeV was assessed in completely randomized, negatively controlled safety trials in foals aged between 4 and 6months and in adult horses (aged between 3 and 23 years). For overdose safety, foals were given one double dose of EquivacHeV by intramuscular injection onDay 42, having previously received two single dose

injections on Days 0 and 21. All foals remained healthy throughout the course of thestudy, with no evidence of decreased appetite, altered demeanor or abnormal gait. One animal in the vaccinate group recorded a high rectaltemperature following the double dose; however this was short-lived, having resolved by the following morning. In addition one of thecontrol animals demonstrated marked pyrexia at the same time point, which indicates that this event may not be vaccine related. There wereno visible, palpable or discharging injection sites in any of the study animals at any point throughout the study, and the vaccine did notappear to cause any pain at the injection site at any stage, even when administered as a double dose. There were no systemic vaccinereactions or other abnormal reactions to the vaccine and no adverse events were reported throughout the course of the study.

Of the adult horses, 3.4% of animals in the vaccinate group had an injection site reaction following the first dose of vaccine. 34.5% ofanimals were recorded as having visible and/or palpable injection site reactions the day after the second dose of vaccine was administered,as did one animal in the control group (administered saline as a placebo). By Day 28 (7 days post-vaccination) these had all resolved, apartfrom one small intradermal lesion (measuring 0.004cm3) that may not have been vaccine related. No painful injection site reactions wererecorded at any stage and all horses remained healthy. There were no systemic vaccine reactions or other abnormal reactions to the vaccineand no adverse events were reported throughout the course of the study.In summary, the vaccine has been demonstrated to be safe in horses from 4 months old.

MEAT WITHHOLDING PERIOD NIL

SAFETY DIRECTIONS
Caution: In the event of an outbreak of Hendra virus appropriate personal safety precautions should be implemented and strictly enforced even around vaccinated horses.

Personal Protective Equipment (PPE) should be worn whenever Hendra virus disease is suspected even in vaccinated horses as no vaccine can provide a guaranteed protection

Care should be taken to avoid accidental self-injection and needle-stick injury when administering this product. In the event of accidental self-injection, seek medical advice immediately.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126.

This material may cause a mild allergic reaction in sensitive individuals on skin contact. Avoid skin contact. If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water. If splashed in eyes, wash out immediately with water.

STORAGE
Store between 2°C and 8°C (Refrigerate. Do not freeze). Protect from light.

DISPOSAL
Dispose of containers and syringes by wrapping in paper and putting in garbage. Discarded needles should immediately be placed in a designated and appropriately labelled ‘sharps’ container.

NOTE
This vaccine has been tested for potency, sterility and safety before issue but it must be stressed that the correct vaccination procedure in the field is equally important if secondary injection-related infection is to be prevented. Very occasionally, pathogenic organisms from

the animal's skin or lying dormant in the animal's tissues are activated at the time of vaccination and are able to initiate a local infection at the site of injection. This may lead to the horse's death, but fortunately is of rare occurrence. To the maximum extent permitted by law, Pfizer does not accept any claim, loss, liability, cost or expense in respect of:

(a) Disability or death of horses following vaccination as a result of failure to use the correct vaccination procedure described on the label.

(b) The failure of any horse to conceive or maintain a pregnancy following use of the product.

Pfizer Animal Health ABN 50 008 422 348
A division of Pfizer Australia Pty Ltd
38-42 Wharf Road, West Ryde NSW 2114, Australia
Australian Technical Services Toll Free 1800 814 883
www.pfizeranimalhealth.com.au
APVMA Permit Number:PER13510

(item number and version) (Recycling logo)
(Month, Year)