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Equine Herpesvirus Vaccine, Inactivated

General Notices

(Equine Herpesvirus Vaccine (Inactivated), Ph. Eur. monograph 1613)

Ph Eur

1 DEFINITION

Equine herpesvirus vaccine (inactivated) is a preparation of one or more suitable strains of equid herpesvirus 1 and/or equid herpesvirus 4, inactivated while maintaining adequate immunogenic properties or a suspension of an inactivated fraction of the virus. This monograph applies to vaccines intended for the active immunisation of horses against disease caused by equid herpesvirus 1 and/or equid herpesvirus 4.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

Each strain of vaccine virus is grown separately in cell cultures. The viral suspensions may be purified and concentrated and are inactivated; they may be treated to fragment the virus and the viral fragments may be purified and concentrated. The vaccine may be adjuvanted.

2-2 SUBSTRATE FOR VIRUS PROPAGATION

2-2-1 Cell cultures

The cell cultures comply with the requirements for cell cultures for production of veterinary vaccines (*5.2.4*).

2-3 CHOICE OF VACCINE COMPOSITION

The vaccine is shown to be satisfactory with respect to safety (*5.2.6*) and efficacy (*5.2.7*) for the horses for which it is intended. Where a particular breed of horse is known to be especially sensitive to the vaccine, horses from that breed are included in the test for safety.

The following tests for safety (section 2-3-1) and immunogenicity (section 2-3-2) may be used during the demonstration of safety and efficacy.

2-3-1 Safety

Carry out the test for each route and method of administration to be recommended for vaccination and in horses of each category for which the vaccine is intended. Use a batch of vaccine containing not less than the maximum potency that may be expected in a batch of vaccine.

Use for the test not fewer than 8 horses that have not been previously vaccinated with an equine herpesvirus vaccine, that have at most a low antibody titre not indicative of recent infection and that do not excrete equid herpesvirus. Administer to each horse 1 dose of the vaccine, then another dose after 14 days. Observe the horses at least daily until at least 14 days after the last administration.

The vaccine complies with the test if no horse shows abnormal local or systemic reactions or dies from causes attributable to the vaccine during the 28 days of the test.

2-3-2 Immunogenicity

The type of immunogenicity test depends on the claims for the product. For vaccines intended to protect against the disease of the respiratory tract, carry out test 2-3-2-1, using equid herpesvirus 1 and/or equid herpesvirus 4 depending on the claims for protection. For vaccines intended to protect against abortion carry out test 2-3-2-2.

A test is carried out for each route and method of administration to be recommended, using in each case horses that have not been vaccinated with an equine herpesvirus vaccine, that have at most a low antibody titre not indicative of recent infection, and that do not excrete equid herpesvirus. To demonstrate that no recent infection occurs, immediately before vaccination: draw a blood sample from each horse and test individually for antibodies against equid herpesviruses 1 and 4; collect 10 mL of heparinised blood and test the washed leucocytes for equid herpesviruses 1 and 4; collect a nasopharyngeal swab and test for equid herpesviruses 1 and 4. There is no indication of an active infection. Immediately before challenge collect a nasopharyngeal swab and test for equid herpesviruses 1 and 4. If there is an indication of virus excretion remove the horse from the test. Keep the horses in strict isolation. The vaccine administered to each horse is of minimum potency.

2-3-2-1 Vaccines intended for protection against disease of the respiratory tract. Use for the test not fewer than 10 horses, not less than 6 months old. Vaccinate not fewer than 6 horses according to the schedule to be recommended. Maintain not fewer than 4 horses as controls. At least 2 weeks after the last vaccination, challenge each horse by nasal instillation with a quantity of equid herpesvirus 1 or 4, sufficient to produce in a susceptible horse characteristic signs of the disease such as pyrexia and virus excretion (and possibly nasal discharge and coughing). Observe the horses at least daily for 14 days. Collect nasopharyngeal swabs daily from each individual horse to isolate the virus.

The vaccine complies with the test if the vaccinated horses show no more than slight signs; the signs in vaccinates are less severe than in controls. The average number of days on which virus is excreted and the respective virus titres are significantly lower in vaccinated horses than in controls.

2-3-2-2 Vaccines intended for protection against abortion. Use not fewer than 10 pregnant horses. In addition to the testing described above, 6, 4, 3, 2 and 1 month before the first vaccination draw a blood sample from each horse and test individually for antibodies against equid herpesviruses 1 and 4. There is no evidence of recent infection or virus excretion. Vaccinate not fewer than 6 horses according to the schedule to be recommended. Maintain not fewer than 4 horses as controls. Between day 260 and day 290 of pregnancy but not earlier than 3 weeks after the last vaccination, challenge each horse, by nasal instillation, with a quantity of equid herpesvirus 1 sufficient to produce abortion in susceptible horses. Observe the horses at least daily up to foaling or abortion. Collect samples of fetal lung and liver tissues from aborted fetuses and carry out tests for virus in cell cultures.

The test is not valid if more than one control horse gives birth to a healthy foal and if the challenge virus is not isolated from the aborted fetuses. The vaccine complies with the test if not more than one vaccinated horse aborts.

2-4 MANUFACTURER'S TESTS

2-4-1 Residual live virus

The test for residual live virus is carried out using 2 passages in the same type of cell culture as that used in the production or in cell cultures shown to be at least as sensitive. The quantity of inactivated virus harvest used in the test is equivalent to not less than 25 doses of the vaccine. The inactivated virus harvest complies with the test if no live virus is detected.

2-4-2 Batch potency test

It is not necessary to carry out the potency test (section 3-4) for each batch of vaccine if it has been carried out using a batch of vaccine with a minimum potency. Where the test is not carried out, an alternative validated method, preferably *in vitro*, is used, the criteria for acceptance being set with reference to a batch of vaccine that has given satisfactory results in the test described under Potency. In the absence of a suitable *in vitro* test, the following test may be used.

Vaccinate not fewer than 5 rabbits, guinea-pigs or mice with a single injection of a suitable dose. Where the recommended schedule requires a 2nd injection, this may be given provided it has been demonstrated that this will still provide a suitably sensitive test system. At a given interval within the range of 14-21 days after the last injection, collect blood from each animal and prepare serum samples. Use a suitable validated test such as an enzyme-linked immunosorbent assay to measure the response to each of the antigens stated on the label. The vaccine complies with the test if the antibody levels are not significantly less than those obtained with a batch that has given satisfactory results in the test described under Potency.

3 BATCH TESTS

3-1 Identification

The vaccine contains the antigen or antigens stated under Definition. The method used must distinguish between antibodies against equid herpesviruses 1 and 4.

3-2 Bacteria and fungi

The vaccine, including where applicable the diluent supplied for reconstitution, complies with the test for sterility prescribed in the monograph *Vaccines for veterinary use (0062)*.

3-3 Residual live virus

This test may be omitted for batch release, as stated in the monograph Vaccines for veterinary use (0062).

Carry out a test for residual live virus using not less than 25 doses of vaccine by inoculating cell cultures sensitive to equid herpesviruses 1 and 4; make a passage after 5-7 days and maintain the cultures for 14 days. The vaccine complies with the test if no live virus is detected. If the vaccine contains an adjuvant, separate the adjuvant from the liquid phase, by a method that does not inactivate the virus or otherwise interfere with the detection of live viruses, or carry out a test for inactivation on the mixture of bulk antigens before addition of the adjuvant.

3-4 Potency

The vaccine complies with the requirements of the test mentioned under Immunogenicity (section 2-3-2) when administered by a recommended route and method.