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Infectious Bovine Rhinotracheitis Vaccine, Living

General Notices

(Infectious Bovine Rhinotracheitis Vaccine (Live), Ph. Eur. monograph 0696)

Ph Eur

1 DEFINITION

Infectious bovine rhinotracheitis vaccine (live) is a preparation of one or more suitable strains of infectious bovine rhinotracheitis virus (bovine herpesvirus 1). This monograph applies to vaccines intended for the active immunisation of cattle against bovine rhinotracheitis caused by bovine herpesvirus 1.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

The vaccine virus is grown in cell cultures.

2-2 SUBSTRATE FOR VIRUS PROPAGATION

2-2-1 Cell cultures

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

2-3 CHOICE OF VACCINE VIRUS

The vaccine virus is shown to be satisfactory with respect to safety (*5.2.6*) and efficacy (*5.2.7*) for the cattle for which it is intended.

The following tests for safety (section 2-3-1), abortigenicity and passage through the placenta (section 2-3-2), increase in virulence (section 2-3-3) and immunogenicity (section 2-3-4) 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. Use vaccine virus at the least attenuated passage level that will be present in a batch of the vaccine.

For each test, use not fewer than 5 calves, 3 months old or of the minimum age to be recommended for vaccination if this is less than 3 months, and that do not have antibodies against infectious bovine rhinotracheitis virus. Administer to each calf a quantity of the vaccine virus equivalent to not less than 10 times the maximum virus titre likely to be contained in 1 dose of the vaccine. Observe the calves at least daily for at least 14 days.

The vaccine virus complies with the test if no calf shows abnormal local or systemic reactions or dies from causes attributable to the vaccine virus.

2-3-2 Abortigenicity and passage through the placenta

Use not fewer than 24 pregnant cows that do not have antibodies against infectious bovine rhinotracheitis virus: 8 of the cows are in the 4th month of pregnancy, 8 in the 5th and 8 in the 6th or 7th month. Administer to each cow by a route to be recommended a quantity of the vaccine virus equivalent to not less than 10 times the maximum virus titre likely to be contained in 1 dose of the vaccine. Observe the cows at least daily until the end of pregnancy.

The vaccine virus complies with the test if:

— where abortion occurs, tests show that neither virus nor viral antigens are present in the foetus or placenta;

— on calves born at term before ingestion of colostrum, a test for antibodies against infectious bovine rhinotracheitis virus indicates no such antibodies are found.

2-3-3 Increase in virulence

Carry out the test according to general chapter *5.2.6* using calves 3 months old or of the minimum age to be recommended for vaccination if this is less than 3 months, and that do not have antibodies against infectious bovine rhinotracheitis virus. If the properties of the vaccine virus allow sequential passage through 5 groups via natural spreading, this method may be used, otherwise passage as described below is carried out.

Take suitable samples from the calves used for the test for safety at a time when the vaccinal virus can be easily detected, verify the presence and titre of the virus in the samples and mix them. Administer to each calf of the 1st group by the intranasal route a quantity of the vaccine virus that will allow recovery of virus for the passages described below. Administer the virus by the intranasal route to each calf of the next group. Carry out this passage operation not fewer than 4 times; verify the presence of the virus at each passage. If the virus is not found at a passage level, repeat the passage by administration to a group of 10 calves.

If the 5th group of calves shows no evidence of an increase in virulence indicative of reversion during the observation period, further testing is not required. Otherwise, carry out an additional safety test and compare the clinical signs and any relevant parameters in a group of at least 8 calves receiving the material used for the 1st passage and another similar group receiving the virus at the final passage level.

The vaccine virus complies with the test if no indication of increased virulence of the virus recovered for the final passage compared with the material used for the 1st passage is observed. If virus is not recovered after an initial passage in 2 calves and a subsequent repeated passage in 10 calves, the vaccine virus also complies with the test.

2-3-4 Immunogenicity

A test is carried out for each route and method of administration to be recommended for vaccination using in each case calves 2-3 months old. The quantity of vaccine to be administered to each calf is not greater than the minimum virus titre to be stated on the label and the virus is at the most attenuated passage level that will be present in a batch of vaccine. Use for the test not fewer than 7 calves that do not have antibodies against infectious bovine rhinotracheitis virus. Vaccinate not fewer than 5 calves, according to the schedule to be recommended. Maintain not fewer than 2 calves as controls. Challenge each calf after 20-22 days by the intranasal route with a sufficient quantity of a virulent infectious bovine rhinotracheitis virus. Observe the calves at least daily for 21 days after challenge, in particular for respiratory signs and virus shedding (by nasal swabs or tracheobronchial washing).

The test is not valid if the controls do not show typical signs of disease such as fever, ocular and nasal discharge and ulceration of the nasal mucosa.

The vaccine virus complies with the test if, during the observation period after challenge:

— the vaccinated calves show no more than mild signs;

— in not fewer than 4 of the 5 vaccinated calves, the maximum virus titre found in the nasal mucus is at least 100 times lower than the average of the maximum titres found in the control calves; and

— the average number of days on which virus is excreted is at least 3 days less in vaccinated calves than in the control calves.

3 BATCH TESTS

3-1 Identification

The vaccine is identified using a suitable method. For example, when mixed with a monospecific antiserum, it is no longer able to infect susceptible cell cultures into which it is inoculated.

3-2 Bacteria and fungi

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

3-3 Mycoplasmas (*2.6.7*)

The vaccine complies with the test for mycoplasmas.

3-4 Extraneous agents (*5.2.5*)

The vaccine is free from extraneous agents.

3-5 Virus titre

Titrate the vaccine virus in susceptible cell cultures at a temperature favourable to replication of the virus. The vaccine complies with the test if 1 dose contains not less than the minimum virus titre stated on the label.

3-6 Potency

The vaccine complies with the requirements of the test prescribed under Immunogenicity (section 2-3-4) when administered by a recommended route and method. It is not necessary to carry out the potency test for each batch of the vaccine if it has been carried out on a representative batch using a vaccinating dose containing not more than the minimum virus titre stated on the label.