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Bovine Parainfluenza Virus Vaccine, Living

General Notices

(Bovine Parainfluenza Virus Vaccine (Live), Ph. Eur. monograph 1176)

Ph Eur

1 DEFINITION

Bovine parainfluenza virus vaccine (live) is a preparation of a suitable strain of bovine parainfluenza 3 virus. This monograph applies to vaccines intended for the active immunisation of cattle against infection with bovine parainfluenza virus.

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), increase in virulence (section 2-3-2) and immunogenicity (2-3-3) 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 of the minimum age to be recommended for vaccination and preferably that do not have antibodies against bovine parainfluenza 3 virus or, where justified, use calves with a very low level of such antibodies as long as they have not been vaccinated against bovine parainfluenza virus and administration of the vaccine does not cause an anamnestic response. 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. Measure the body temperature of each calf on the day before vaccination, at the time of vaccination and for the 4 subsequent days.

The vaccine virus complies with the test if no abnormal effect on body temperature occurs and if no calf shows abnormal, local or systemic reactions or dies from causes attributable to the vaccine virus.

2-3-2 Increase in virulence

Carry out the test according to general chapter *5.2.6*, using calves that do not have antibodies against bovine parainfluenza 3 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.

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. On each of days 3 to 7 after administration of the virus, take nasal swabs from each calf and collect in not more than 5 mL of a suitable medium, which is then used to inoculate cell cultures to verify the presence of virus. Administer about 1 mL of the suspension from the swabs that contain the maximum amount of virus, as indicated by the titration of cell cultures, 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.

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; account is taken of the titre of excreted virus in the nasal swabs. 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.

2-3-3 Immunogenicity

A test is carried out for each route and method of administration to be recommended for vaccination using in each case calves of the minimum age to be recommended. 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 10 calves that do not have antibodies against bovine parainfluenza 3 virus; calves having low levels of such antibodies may be used if it has been demonstrated that valid results are obtained in these conditions. Collect sera from the calves before vaccination, 7 days and 14 days after the time of vaccination and just before challenge. Vaccinate not fewer than 5 calves, according to the schedule to be recommended. Maintain not fewer than 5 calves as controls. Challenge each calf after 20-22 days by a respiratory tract route with a sufficient quantity of a suspension of a low-passage virulent bovine parainfluenza 3 virus. Observe the calves at least daily for 14 days after challenge and monitor each of them for signs, in particular respiratory signs and virus shedding (by nasal swabs or tracheobronchial washing).

The test is not valid if tests for antibodies against bovine parainfluenza 3 virus on the sera indicate that there was intercurrent infection with the virus during the test or if, during the observation period after challenge, more than 2 of the 5 control calves show no excretion of the challenge virus, as shown by nasal swabs or samples harvested by tracheobronchial washing.

The vaccine virus complies with the test if, during the observation period after challenge, in vaccinated calves compared to controls there is a significant reduction in mean titre and in mean duration of virus excretion, and a notable reduction in general and local signs (if the challenge virus used produces such signs).

3 BATCH TESTS

3-1 Identification

The vaccine virus is identified using a suitable method, for example, an immunostaining test in susceptible cell cultures using a monospecific antiserum.

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 suitable cell cultures. 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 2-3-3) 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.