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Calf Coronavirus Diarrhoea Vaccine (Inactivated)

General Notices

(Ph. Eur. monograph 1953)

Ph Eur

1 DEFINITION

Calf coronavirus diarrhoea vaccine (inactivated) is a preparation of one or more suitable strains of bovine coronavirus, inactivated while maintaining adequate immunogenic properties. This monograph applies to vaccines intended for the active immunisation of dams for passive protection of their progeny against coronavirus diarrhoea during the first few weeks of life.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

Each vaccine virus is grown separately in cell cultures. The viral suspensions of each vaccine virus are harvested separately and inactivated by a method that maintains immunogenicity. The viral suspensions 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 the production of vaccines for veterinary use (*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 pregnant cows for which it is intended.

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 in pregnant cows

Carry out the test for each route and method of administration to be recommended for vaccination, using in each case pregnant cows that have not been vaccinated against bovine coronavirus. Use a batch of vaccine containing not less than the maximum potency that may be expected in a batch of vaccine.

For each test, use not fewer than 8 cows per group at the stage or at different stages of pregnancy according to the schedule to be recommended. Administer to each cow 1 dose of the vaccine. If the schedule to be recommended requires a 2nd dose, administer another dose after an interval of at least 14 days. After each injection, measure the body temperature on the day of the injection and on the 4 following days. Observe the pregnant cows at least daily until calving.

The vaccine complies with the test if no pregnant cow shows abnormal local or systemic reactions or dies from causes attributable to the vaccine and if no adverse effects on gestation or the offspring are noted.

2-3-2 Immunogenicity

A test is carried out for each route and method of administration to be recommended. The vaccine administered to each cow is of minimum potency.

Use for the test not fewer than 15 pregnant cows, preferably that do not have antibodies against bovine coronavirus. Where such cows are not available, use cows that: have not been vaccinated against bovine coronavirus; come from a farm where there is no recent history of infection with bovine coronavirus; and have a low level of antibodies against bovine coronavirus, the levels being comparable in all cows. Vaccinate not fewer than 10 pregnant cows according to the schedule to be recommended. Maintain not fewer than 5 pregnant cows as controls. Starting at calving, take the colostrum and then milk from each cow and keep it in suitable conditions. Determine individually the protective activity of the colostrum and milk from each cow using calves born from healthy cows, and which may be born by Caesarean section, and maintained in an environment where they are not exposed to infection by bovine coronavirus. Feed colostrum and then milk to each calf every 6 h or according to the schedule to be recommended. At 5-7 days after birth, challenge each calf by the oral route with a sufficient quantity of a virulent strain of bovine coronavirus. Observe the calves at least daily for 7 days. Note the incidence, severity and duration of diarrhoea and the duration and quantity of virus excretion.

The vaccine complies with the test if there is a significant reduction in diarrhoea and virus excretion in calves given colostrum and milk from vaccinated cows compared to those given colostrum and milk from controls.

2-4 MANUFACTURER'S TESTS

2-4-1 Residual live virus

The test for residual live virus is carried out using 2 passages in cell cultures of the same type as those used for production or in cells shown to be at least as sensitive. The quantity of inactivated virus harvest used in the test is equivalent to not less than 10 doses of 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 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. The following test may be used.

To obtain a valid assay, it may be necessary to carry out a test using several groups of animals, each receiving a different dose. For each dose required, carry out the test as follows. Use for the test not fewer than 7 animals of a suitable species and that do not have specific antibodies against bovine coronavirus. Vaccinate not fewer than 5 animals using 1 injection of a suitable dose. Maintain not fewer than 2 animals as controls. Where the recommended schedule requires a booster injection, this may be administered provided it has been demonstrated that this will still provide a suitably sensitive test system. At a given interval not less than 14 days after the last injection, collect blood from each animal and prepare serum samples. Use a suitable validated test to measure the antibody response. The vaccine complies with the test if the antibody level in the vaccinates is not significantly less than that obtained with a batch that has given satisfactory results in the test described under Potency and there is no significant increase in antibody titre in the controls.

3 BATCH TESTS

3-1 Identification

The vaccine contains the antigen or antigens stated under Definition.

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 Residual live virus

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

Carry out a test for residual live virus using 10 doses of vaccine and 2 passages in cell cultures of the same type as those used for production of the vaccine or other cell cultures of suitable sensitivity. The vaccine complies with the test if no live virus is detected. If the vaccine contains an adjuvant that interferes with the test, separate it if possible from the liquid phase of the vaccine by a method that does not inactivate the virus or otherwise interfere with the detection of live viruses.

3-4 Potency

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

4 LABELLING

The label states the recommended schedule for administering colostrum and milk, post-partum.