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Bovine Viral Diarrhoea Vaccine (Inactivated)

General Notices

(Ph. Eur. monograph 1952)

Ph Eur

1 DEFINITION

Bovine viral diarrhoea vaccine (inactivated) is a preparation of one or more suitable strains of bovine diarrhoea virus inactivated while maintaining adequate immunogenic properties. This monograph applies to vaccines intended for the active immunisation of heifers and cows for protection of their progeny against transplacental infection.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

The vaccine virus is grown 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 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 cattle 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

Carry out the test for each route and method of administration to be recommended for vaccination and in each category of cattle 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.

2-3-1-1 General safety. For each test, use not fewer than 8 cattle of the minimum age to be recommended for vaccination and that do not have bovine diarrhoea virus or antibodies against the virus. Administer to each animal 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. Observe the cattle at least daily for at least 14 days.

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

2-3-1-2 Safety in pregnant cattle. If the vaccine is intended for use in pregnant cattle, use not fewer than 8 cattle at the beginning of each semester for which use is not contraindicated. Administer to each animal 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. Observe the cattle at least daily until calving.

The vaccine complies with the test if no animal 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.

2-3-1-3 Examination of reproductive performance. If the vaccine is intended for administration shortly before or at insemination, absence of undesirable effects on conception rate must be demonstrated.

2-3-2 Immunogenicity

The following test is suitable to demonstrate the immunogenicity of the vaccine with respect to bovine diarrhoea virus of genotype 1; if protection against bovine diarrhoea virus of genotype 2 is claimed, an additional test, similar to that described below, but using bovine diarrhoea virus of genotype 2 for challenge, is carried out.

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

Use for the test not fewer than 20 heifers free from bovine diarrhoea virus and that do not have antibodies against bovine diarrhoea virus. Vaccinate not fewer than 13 heifers according to the schedule to be recommended. Maintain not fewer than 7 heifers as controls. Keep all the animals as one group. Inseminate the heifers. Take a blood sample from non-vaccinated heifers shortly before challenge. The test is discontinued if fewer than 10 vaccinated heifers or 5 non-vaccinated heifers are pregnant at the time of challenge. Challenge each heifer between the 60th and 90th days of gestation. For both test models described (observation until calving and harvest of foetuses at 28 days), challenge may be made by the intranasal route with a sufficient quantity of a non-cytopathic strain of bovine diarrhoea virus or alternatively, where the heifers are observed until calving, challenge may be made by contact with a persistently viraemic animal. Observe the heifers clinically at least daily from challenge either until the end of gestation or until harvest of foetuses after 28 days. If abortion occurs, examine the aborted foetus for bovine diarrhoea virus by suitable methods. If cattle are observed until calving, immediately after birth and prior to ingestion of colostrum, examine all calves for viraemia and antibodies against bovine diarrhoea virus. If foetuses are harvested 28 days after challenge, examine the foetuses for bovine diarrhoea virus by suitable methods. Transplacental infection is considered to have occurred if virus is detected in foetal organs or in the blood of newborn calves or if antibodies are detected in precolostral sera of calves.

The test is not valid if any of the control heifers have neutralising antibody before challenge or if transplacental infection fails to occur in more than 10 per cent of the calves from the control heifers. The vaccine complies with the test if at least 90 per cent of the calves from the vaccinated heifers are protected from transplacental infection.

2-4 MANUFACTURER'S TESTS

2-4-1 Residual live virus

The test for residual live virus is carried out using a quantity of inactivated virus harvest equivalent to not less than 25 doses of vaccine in cells of the same type as those used for production of the vaccine or cells shown to be at least as sensitive; the cells are passaged after 7 days and observed for a total of not less than 14 days. 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.

Use for the test 7 suitable laboratory animals or calves that do not have antibodies against bovine diarrhoea virus. Administer by the subcutaneous route to 5 animals a suitable dose of the vaccine. Maintain 2 animals as controls. A 2nd dose of vaccine may be administered after a suitable interval if this has been shown to provide a suitably discriminating test system. Collect blood samples before the 1st vaccination and at a given interval between 14 and 21 days after the last vaccination. Determine the antibody titres against bovine diarrhoea virus by seroneutralisation on suitable cell cultures.

The test is not valid if the control animals show antibodies against bovine diarrhoea virus. The vaccine complies with the test if the level of antibodies in the vaccinates is not lower than that found for a batch of vaccine 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.

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 bovine diarrhoea virus by inoculating not less than 10 doses onto cells known to be sensitive to bovine diarrhoea virus; passage the cells after 7 days and observe the 2nd culture for not less than 7 days. The vaccine complies with the test if no live virus is detected. If the vaccine contains an adjuvant, separate the adjuvant if possible from the liquid phase 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.