Bovine viral diarrhoea vaccine (inactivated)

Vaccinum diarrhoeae viralis bovineae inactivatum

DEFINITION

Bovine viral diarrhoea vaccine (inactivated) is a preparation of one or more suitable strains of bovine diarrhoea virus inactivated by a suitable method. This monograph applies to vaccines intended for vaccination of heifers and cows to protect the foetus against transplacental infection.

PRODUCTION

The vaccine virus strain or strains are grown in suitable cell cultures (5.2.4). The test for inactivation is carried out using a quantity of virus 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. No infectious virus is detected.

CHOICE OF VACCINE COMPOSITION

The vaccine shall be shown to be satisfactory with respect to safety (5.2.6) and immunogenicity (5.2.7) in cattle.

The following tests may be used during the demonstration of safety and immunogenicity.

Safety. Carry out a safety test for each recommended route and for each category of cattle for which the vaccine is intended. Use cattle of the minimum age recommended for vaccination and that are free from bovine diarrhoea virus and from antibodies against the virus. Inject a double dose of vaccine into each of not fewer than 10 animals. Observe the animals for 14 days. No abnormal local or systemic reaction occurs. If the vaccine is intended for administration to pregnant cattle, carry out the test in these animals at the beginning of each trimester for which use is not contra-indicated and extend the observation period to calving. No undesirable effect on gestation or the offspring occurs. If the vaccine is intended for administration shortly before or at insemination, absence of undesirable effects on conception rate must be demonstrated.

Immunogenicity. The test for potency 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 under Potency, but using bovine diarrhoea virus of genotype 2 for challenge, is carried out.

BATCH POTENCY TEST

The test described under Potency is not carried out for routine testing of batches of vaccine. It is carried out for a given vaccine on one or more occasions as decided by or with the agreement of the competent authority. Where the test is not carried out, a suitable validated test is carried out, 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 after a satisfactory correlation with the test described under Potency has been established.

Inject subcutaneously a suitable dose of the vaccine into each of 5 suitable seronegative laboratory animals or calves. Keep 2 animals as controls. A second 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 first 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 invalid if the control animals show antibodies against bovine diarrhoea virus. The vaccine complies with the test if the level of antibodies is not lower than that found for a batch of vaccine that has given satisfactory results in the test described under Potency.

IDENTIFICATION

When administered to animals free from specific neutralising antibodies against bovine diarrhoea virus, the vaccine stimulates the production of such antibodies.

TESTS

Safety. Inject a double dose of the vaccine by a recommended route into each of 2 cattle not older than the minimum age recommended for vaccination and that are free from bovine diarrhoea virus and antibodies against the virus. Observe the animals for 14 days. No abnormal local or systemic reaction occurs.

Inactivation. Carry out a test for residual infectious 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 second culture for not less than 7 days. 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 interfere with the detection of possible live virus.

Bacteria and fungi. The vaccine complies with the requirement for sterility prescribed in the monograph on Vaccines for veterinary use (0062).

POTENCY

Use heifers free from bovine diarrhoea virus that do not have neutralising antibodies against bovine diarrhoea virus. Vaccinate not fewer than 13 animals using the recommended schedule. Keep not fewer than 7 heifers as non-vaccinated 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. Between the 60th and 90th days of gestation, challenge the animals. For both test models described (observation until calving and harvest of foetuses at 28 days), challenge may be made by the intranasal inoculation of a suitable quantity of a non-cytopathic strain of bovine diarrhoea virus or alternatively, where the animals are observed until calving, challenge may be made by contact with a persistently viraemic animal. Observe the animals clinically 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 animals 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 invalid if any of the non-vaccinated heifers have neutralising antibody before challenge or if transplacental infection fails to occur in more than 10 per cent of non-vaccinated heifers. The vaccine complies with the test if 90 per cent or more of the vaccinated animals are protected from transplacental infection.