Calf coronavirus diarrhoea vaccine (inactivated)

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**CALF CORONAVIRUS DIARRHOEA VACCINE (INACTIVATED)**

Vaccinum inactivatum diarrhoeae vituli coronaviro illatae

**DEFINITION**

Calf coronavirus diarrhoea vaccine (inactivated) is a preparation of one or more suitable strains of bovine coronavirus, inactivated in such a manner that immunogenic properties are maintained. The vaccine is administered to the dam to aid in the control of coronavirus diarrhoea in offspring during the first few weeks of life.

**PRODUCTION**

Each virus strain is grown separately in suitable cell cultures (5.2.4). The viral suspensions of each strain are harvested separately and inactivated by a method that maintains immunogenicity. The viral suspensions may be purified and concentrated.

The test for inactivation 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 virus used in the test is equivalent to not less than 10 doses of vaccine. No live virus is detected.

The vaccine may contain an adjuvant.

**CHOICE OF VACCINE COMPOSITION**

The vaccine is shown to be satisfactory with respect to safety (5.2.6) and efficacy (5.2.7) in the pregnant cow. The following tests may be used during demonstration of safety and immunogenicity.

**Safety.** Carry out the test for each proposed route of administration. Administer by a proposed route and at the proposed stage or stages of pregnancy, a double dose of vaccine to each of not fewer than 10 pregnant cows that have not been vaccinated against bovine coronavirus. After the proposed interval, inject 1 dose into each cow. After each injection, measure the body temperature on the day of the injection and on the 4 following days. Observe the cows until calving. No abnormal local or systemic reaction occurs; any effects on gestation and the offspring are noted.

**Immunogenicity.** The test described under Potency is suitable to demonstrate immunogenicity of the strain.

**BATCH TESTING**

**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 suitable correlation with the test described under Potency has been established.

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. Vaccinate not fewer than 5 animals of a suitable species, free from specific antibodies against bovine coronavirus, using 1 injection of a suitable dose. Maintain not fewer than 2 animals as unvaccinated controls. Where the recommended schedule requires a booster injection to be given, a booster vaccination may also be given in this test 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 antibody level 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.

**IDENTIFICATION**

Injected into animals free from specific antibodies against bovine coronavirus, the vaccine stimulates the formation of such antibodies.

**TESTS**

**Safety.** Use cattle not less than 6 months old and preferably having no antibodies against bovine coronavirus or, where justified, use cattle with a low level of such antibodies as long as they have not been vaccinated against bovine coronavirus and administration of the vaccine does not cause an anamnestic response. Administer to each of 2 animals a double dose of vaccine by a recommended route. After 14 days, administer 1 dose to each animal. Observe the animals for 14 days. No abnormal local or systemic reaction occurs.

**Inactivation.** Carry out a test for residual infectious 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. No live virus is detected. If the vaccine contains an adjuvant which interferes with the test, separate it if possible from the liquid phase of the vaccine by a method that does not inactivate virus nor interfere in any other way with detection of live viruses.

**Extraneous viruses.** Carry out tests for antibodies on the cattle used for the safety test. Take a blood sample at the end of the second observation period. The vaccine does not stimulate the formation of antibodies against bovine herpes virus 1 (BHV1), bovine leukaemia virus (BLV) and bovine viral diarrhoea virus (BVDV).

**Sterility.** The vaccine complies with the test for sterility prescribed in the monograph on Vaccines for veterinary use (0062).

**POTENCY**

Use not fewer than 15 pregnant cows, where possible having no 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 animals. Vaccinate not fewer than 10 pregnant cows according to the recommended schedule. Keep not fewer than 5 pregnant cows as unvaccinated 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 recommended schedule. At 5-7 days after birth, challenge each calf by the oral administration of a suitable quantity of a virulent strain of bovine coronavirus. Observe the calves 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.

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

CALF ROTAVIRUS DIARRHOEA VACCINE (INACTIVATED)
Vaccinum inactivatum diarrhoeae vituli rotaviro illatae

DEFINITION
Calf rotavirus diarrhoea vaccine (inactivated) is a preparation of one or more suitable strains of bovine rotavirus, inactivated in such a manner that immunogenic properties are maintained. The vaccine is administered to the dam to aid in the control of rotavirus diarrhoea in offspring during the first few weeks of life.

PRODUCTION
Each virus strain is grown separately in suitable cell cultures (5.2.4). The viral suspensions of each strain are harvested separately and inactivated by a method that maintains immunogenicity. The viral suspensions may be purified and concentrated.

The test for inactivation 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 virus used in the test is equivalent to not less than 100 doses of vaccine. No live virus is detected.

The vaccine may contain an adjuvant.

CHOICE OF VACCINE COMPOSITION
The vaccine is shown to be satisfactory with respect to safety (5.2.6) and efficacy (5.2.7) in the pregnant cow. The following tests may be used during demonstration of safety and immunogenicity.

Safety. Carry out the test for each proposed route of administration. Administer by a proposed route and at the proposed stage or stages of pregnancy, a double dose of vaccine to each of not fewer than 10 pregnant cows that have not been vaccinated against bovine rotavirus. After the proposed interval, inject 1 dose into each cow. After each injection, measure the body temperature on the day of the injection and on the 4 following days. Observe the cows until calving. No abnormal local or systemic reaction occurs; any effects on gestation and the offspring are noted.

Immunogenicity. The test described under Potency is suitable to demonstrate immunogenicity of the strain.

BATCH TESTING
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 suitable correlation with the test described under Potency has been established.

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. Vaccinate not fewer than 5 animals of a suitable species, free from specific antibodies against bovine rotavirus, using 1 injection of a suitable dose. Maintain not fewer than 2 animals as unvaccinated controls. Where the recommended schedule requires a booster injection to be given, a booster vaccination may also be given in this test 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 antibody level 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.

IDENTIFICATION
Injected into animals free from specific antibodies against bovine rotavirus, the vaccine stimulates the formation of such antibodies.

TESTS
Safety. Use cattle not less than 6 months old and preferably having no antibodies against bovine rotavirus or, where justified, use cattle with a low level of such antibodies as long as they have not been vaccinated against bovine rotavirus and administration of the vaccine does not cause an anamnestic response. Administer to each of 2 animals a double dose of vaccine by a recommended route. After 14 days, administer 1 dose to each animal. Observe the animals for 14 days. No abnormal local or systemic reaction occurs.

Inactivation. Carry out a test for residual infectious 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. No live virus is detected. If the vaccine contains an adjuvant which interferes with the test, separate it if possible from the liquid phase of the vaccine by a method that does not inactivate virus nor interfere in any other way with detection of live viruses.

Extraneous viruses. Carry out tests for antibodies on the cattle used for the safety test. Take a blood sample at the end of the second observation period. The vaccine does not stimulate the formation of antibodies against bovine herpes virus 1 (BHV 1), bovine leukaemia virus (BLV) and bovine viral diarrheoa virus (BVDV).

Sterility. The vaccine complies with the test for sterility prescribed in the monograph on Vaccines for veterinary use (0062).

POTENCY
Use not fewer than 15 pregnant cows, where possible having no antibodies against bovine rotavirus. Where such cows are not available, use cows that: have not been vaccinated against bovine rotavirus; come from a farm where there is no recent history of infection with bovine rotavirus; and have a low level of antibodies against bovine rotavirus, the levels being comparable in all animals. Vaccinate not fewer than 10 pregnant cows according to the recommended schedule. Keep not fewer than 5 pregnant cows as unvaccinated 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, which may be born by Caesarean section, and maintained in an environment where they are not exposed to infection by bovine rotavirus. Feed colostrum