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Infectious Bovine Rhinotracheitis Vaccine (Inactivated)

General Notices

(Ph. Eur. monograph 2674)

Ph Eur

1 DEFINITION

Infectious bovine rhinotracheitis vaccine (inactivated) is a preparation of a suitable strain of infectious bovine rhinotracheitis virus, i.e. bovine herpesvirus 1 (BHV1), inactivated while maintaining adequate immunogenic properties. This monograph applies to vaccines intended for the active immunisation of cattle against bovine rhinotracheitis caused by bovine herpesvirus 1 (BHV1).

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

The vaccine virus is grown in cell cultures. The virus harvest is inactivated by a suitable method. 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 or maximum antigen content that may be expected in a batch of vaccine.

For each test, use not fewer than 8 calves of the minimum age to be recommended for vaccination and that do not have antibodies against infectious bovine rhinotracheitis virus. Administer to each calf 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 calves at least daily for at least 14 days after the last administration.

The vaccine complies with the test if no calf shows abnormal local or systemic reactions or signs of disease, or dies from causes attributable to the vaccine.

2-3-2 Immunogenicity

A test is carried out for each route and method of administration to be recommended for vaccination, using in each case calves that do not have antibodies against bovine rhinotracheitis virus. The vaccine administered to each calf is of minimum potency or minimum antigen content.

Use for the test not fewer than 10 calves of the minimum age to be recommended for vaccination. Vaccinate not fewer than 5 calves according to the schedule to be recommended. Maintain not fewer than 5 calves as controls. Challenge each animal at least 2 weeks after the last vaccination by a respiratory tract route with a sufficient quantity of virulent infectious bovine rhinotracheitis virus. Observe the calves at least daily for 14 days, in particular for respiratory signs and virus shedding (by nasal swabs or tracheobronchial washing).

The test is not valid if more than 1 of the 5 controls does not show virus excretion and typical signs of disease (e.g. fever, ocular and nasal discharge, coughing).

The vaccine complies with the test if, during the observation period after challenge:

— the vaccinated calves show no more than mild signs of disease;

— over the whole period of virus excretion by the controls, the average virus titre found in the nasal mucus of vaccinated calves is at least 100 times lower than the average virus titre found in the control calves.

2-4 MANUFACTURER'S TESTS

2-4-1 Residual live virus

The test for residual live virus is carried out using 2 passages in the same type of cell culture as that used for production, or in cell cultures shown to be at least as sensitive. The quantity of inactivated harvest used is sufficient to ensure a test of suitable sensitivity. The inactivated virus harvest complies with the test if no live virus is detected.

2-4-2 Antigen content

The content of an appropriate bovine herpesvirus glycoprotein is determined by a suitable immunochemical method (*2.7.1*).

2-4-3 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 assay may be used.

Serological assay Vaccinate not fewer than 5 animals that do not have antibodies against bovine herpesvirus 1 (BHV1) with a single injection of a suitable dose. Where the recommended schedule requires a 2nd injection, this may be given provided it has been demonstrated that this will still provide a suitably sensitive system. At a given interval within the range of 14-21 days after the last injection, collect blood from each animal and prepare serum samples. Use a suitable validated method such as seroneutralisation to measure the response to the antigen.

The vaccine complies with the test if the antibody levels are not significantly less than those obtained with a batch that has given satisfactory results in the test described under Potency.

In accordance with the provisions of the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes, manufacturers are encouraged to develop alternative *in vitro* methods to the animal test for batch release using appropriate tools such as the monitoring of production consistency (as stated in the General Notices, section 1.1) and the quantification of herpesvirus glycoprotein in the final product.

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 virus using 2 passages in the same type of cell culture as that used in the production, or in cell cultures shown to be at least as sensitive. The quantity of vaccine used is sufficient to ensure a test of suitable sensitivity. The vaccine complies with the test if no live virus is detected.

3-4 Potency

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