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Rabbit Haemorrhagic Disease Vaccine (Inactivated)

General Notices

(Ph. Eur. monograph 2325)

Ph Eur

1 DEFINITION

Rabbit haemorrhagic disease vaccine (inactivated) is a preparation of a suitable strain of rabbit haemorrhagic disease virus (RHDV), inactivated while maintaining adequate immunogenic properties. This monograph applies to vaccines intended for active immunisation of rabbits.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

The vaccine virus is grown in rabbits. The requirements for donor animals used for the production of vaccines are described in general chapter 5.2.5. *Management of extraneous agents in immunological veterinary medicinal products* (section 4-1-1-2-3 Animals). The rabbits are not vaccinated against RHDV, are free from antibodies against RHDV, and are not treated with antibiotics in the 15 days before their use. A suspension is prepared from a homogenate of suitable internal organs of those rabbits that are euthanised or that succumb to the infection within 120 h of inoculation. The virus in the suspension may be purified and concentrated, and is inactivated by a suitable method.

2-2 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 rabbits for which it is intended.

The following tests for safety (section 2-2-1) and immunogenicity (section 2-2-2) may be used during the demonstration of safety and efficacy.

2-2-1 Safety

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

For each test, use not fewer than 8 healthy rabbits from the same stock, not older than the minimum age to be recommended for vaccination and free from antibodies against RHDV. Administer to each rabbit 1 dose of the vaccine. If the schedule to be recommended requires a 2nd dose, administer 1 dose after an interval of at least 14 days. Observe the animals for at least 14 days after the last administration. Record the body temperature the day before vaccination, at vaccination, 4 h after vaccination and then daily for 4 days; note the maximum temperature increase for each animal.

The vaccine complies with the test if no rabbit shows abnormal local or systemic reactions or signs of disease, or dies from causes attributable to the vaccine, the average body temperature increase for all animals does not exceed 1.5 °C, and no animal shows a temperature rise greater than 2.0 °C.

2-2-2 Immunogenicity

A test is carried out for each route and method of administration to be recommended for vaccination.

The test is carried out using in each case rabbits not less than 10 weeks old. The vaccine administered to each rabbit is of minimum potency.

Use not fewer than 15 healthy, susceptible rabbits, free from antibodies against RHDV, from the same healthy stock, and reared in suitable isolation conditions to ensure absence of contact with RHDV. Administer 1 dose of vaccine to each of not fewer than 10 of the rabbits according to the instructions for use to be stated on the label. Maintain not fewer than 5 other rabbits as controls. Not less than 7 days after vaccination, challenge each rabbit by a suitable route with a quantity of a virulent strain of RHDV sufficient to cause signs of rabbit haemorrhagic disease (RHD) in a susceptible rabbit. Observe the rabbits for a further 14 days. Rabbits displaying severe clinical signs of RHD are euthanised to avoid unnecessary suffering.

The test is not valid if fewer than 80 per cent of control rabbits die with typical signs of RHD within 120 h of challenge.

The vaccine complies with the test if not fewer than 90 per cent of vaccinated rabbits show no signs of RHD.

2-3 MANUFACTURER'S TESTS

2-3-1 Residual live virus

A test for residual live virus is carried out on the bulk harvest of each batch to confirm inactivation of the RHDV. The test for inactivation is carried out on healthy susceptible rabbits, not less than 10 weeks old, that have not been vaccinated against RHDV, that do not have antibodies against RHDV and are from the same healthy stock that complies with the requirements for donor animals as described in general chapter *5.2.5*. 5 rabbits are inoculated by a suitable parenteral route (subcutaneous or intramuscular) with at least a 5 mL dose of the suspension. The rabbits are observed for not less than 7 days. At the end of the observation period, the animals are euthanised and liver extracts are tested by a suitable method for freedom from RHDV.

The inactivated virus harvest complies with the test if no rabbit dies and no RHDV antigen is detected in the livers.

2-3-2 Batch potency test

It is not necessary to carry out the potency test (section 3-3) for each batch of the 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 method is given as an example. Administer 1 dose of vaccine intramuscularly to each of 5 healthy rabbits, 10 weeks old, free from antibodies against RHDV and from the same healthy stock. Maintain 2 rabbits as unvaccinated controls. Collect serum samples from each rabbit just before administration of the vaccine and after the period defined when testing the reference vaccine; determine the antibody titre of each serum by a suitable immunological method, for example, ELISA. The antibody levels are not significantly lower than those obtained with a batch that has given satisfactory results in the test described under Potency.

The test is not valid if the sera collected from the unvaccinated controls and from the rabbits just before the administration of the vaccine show detectable specific antibodies.

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 Potency

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