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Myxomatosis Vaccine (Live) for Rabbits

General Notices

(Ph. Eur. monograph 1943)

Ph Eur

1 DEFINITION

Myxomatosis vaccine (live) for rabbits is a preparation of a suitable strain of either myxoma virus that is attenuated for rabbits or Shope fibroma virus. This monograph applies to vaccines intended for the active immunisation of rabbits against myxomatosis.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

The vaccine virus is grown in cell cultures. The viral suspension is harvested and titrated and may be mixed with a suitable stabilising solution.

2-2 SUBSTRATE FOR VIRUS PROPAGATION

2-2-1 Cell cultures

The cell cultures comply with the requirements for cell cultures for the production of vaccines for veterinary use (*5.2.4*).

2-3 CHOICE OF VACCINE VIRUS

The vaccine virus 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 2-3-1), increase in virulence (section 2-3-2) and immunogenicity (2-3-3) 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, using in each case rabbits of the minimum age to be recommended for vaccination. Use vaccine virus at the least attenuated passage level that will be present in a batch of the vaccine.

For each test, use not fewer than 8 rabbits that do not have antibodies against myxoma virus. Administer to each rabbit a quantity of the vaccine virus equivalent to not less than 10 times the maximum virus titre likely to be contained in 1 dose of

the vaccine. Observe the rabbits at least daily for 28 days. 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 rabbit.

The vaccine virus complies with the test if no rabbit shows notable signs of disease or dies from causes attributable to the vaccine virus; the average temperature increase does not exceed 1.0 °C and no rabbit shows a rise greater than 2.0 °C. A local reaction lasting less than 28 days may occur.

2-3-2 Increase in virulence

(*This test is performed only for vaccines based on attenuated strains of myxoma virus*). Carry out the test according to general chapter *5.2.6*, using rabbits 5-7 weeks old that do not have antibodies against myxoma virus. If the properties of the vaccine virus allow sequential passage through 5 groups via natural spreading, this method may be used, otherwise passage as described below is carried out.

Administer to each rabbit by a route to be recommended a quantity of the vaccine virus that will allow recovery of virus for the passages described below. Administer the virus by the route to be recommended for vaccination most likely to lead to reversion of virulence. Euthanise the rabbits 5-10 days after inoculation and remove from each rabbit organs or tissues with sufficient virus to allow passage; homogenise the organs and tissues in a suitable buffer solution, centrifuge the suspension and use the supernatant for further passages. Inoculate the supernatant into suitable cell culture to verify the presence of virus. Administer by an appropriate route, at a suitable rate, a suitable volume of the supernatant to each rabbit of the next group. Carry out this passage operation not fewer than 4 times; verify the presence of the virus at each passage. If the virus is not found at a passage level, repeat the passage by administration to a group of 10 rabbits.

If the 5th group of rabbits shows no evidence of an increase in virulence indicative of reversion during the observation period, further testing is not required. Otherwise, carry out an additional safety test and compare the clinical signs and any relevant parameters in a group of at least 8 rabbits receiving the material used for the 1st passage and another similar group receiving the virus at the final passage level.

The vaccine virus complies with the test if no indication of increased virulence of the virus recovered for the final passage compared with the material used for the 1st passage is observed. If virus is not recovered after an initial passage in 2 rabbits and a subsequent repeat passage in 10 rabbits, the vaccine virus also complies with the test.

2-3-3 Immunogenicity

A test is carried out for each route and method of administration to be recommended for vaccination using in each case rabbits of the minimum age to be recommended. The quantity of vaccine virus to be administered to each rabbit is not greater than the minimum virus titre to be stated on the label and the virus is at the most attenuated passage level that will be present in a batch of vaccine.

Use for the test not fewer than 15 rabbits that do not have antibodies against myxoma virus and are reared in suitable isolation conditions to ensure absence of contact with myxoma virus. Administer 1 dose of vaccine to each of not fewer than 10 of the rabbits according to the schedule to be recommended. Maintain not fewer than 5 rabbits as controls. Challenge each rabbit not less than 21 days after the last vaccination by a suitable route with a quantity of a virulent strain of myxoma virus sufficient to cause typical signs of myxomatosis in a rabbit. Observe the rabbits at least daily for a further 21 days after challenge and monitor each of them.

The test is not valid if fewer than 90 per cent of the control rabbits display typical signs of myxomatosis. A vaccine containing myxoma virus complies with the test if, during the observation period after challenge, not fewer than 90 per cent of vaccinated rabbits show no signs of myxomatosis. A vaccine containing Shope fibroma virus complies with the test if, during the observation period after challenge, not fewer than 75 per cent of vaccinated rabbits show no signs of myxomatosis.

3 BATCH TESTS

3-1 Identification

The vaccine virus is identified using a suitable method, for example, an immunofluorescence test in susceptible cell cultures using a monospecific antiserum.

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 Mycoplasmas (*2.6.7*)

The vaccine complies with the test for mycoplasmas.

3-4Extraneous agents (*5.2.5*)

The vaccine is free from extraneous agents.

3-5 Virus titre

Titrate the vaccine virus in suitable cell cultures. The vaccine complies with the test if 1 dose contains not less than the minimum virus titre stated on the label.

3-6 Potency

The vaccine complies with the requirements of the test prescribed under Immunogenicity (section 2-3-3) when administered by a recommended route and method. It is not necessary to carry out the potency test for each batch of the vaccine if it has been carried out on a representative batch using a vaccinating dose containing not more than the minimum virus titre stated on the label.
