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Swine-Fever Vaccine (Live, Prepared in Cell Cultures), Classical

General Notices

(Ph. Eur. monograph 0065)

Ph Eur

1 DEFINITION

Classical swine-fever vaccine (live, prepared in cell cultures) is a preparation obtained from a strain of classical swine-fever virus that has lost its pathogenicity for the pig by *in vivo* and/or *in vitro* passage and has been adapted to growth in cell cultures.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

The vaccine virus is grown in cell cultures.

2-2 SUBSTRATE FOR VIRUS PROPAGATION

Cell cultures

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 swine for which it is intended.

The following tests described under Safety test in piglets (section 2-3-1), Safety test in pregnant sows and test for transplacental transmission (section 2-3-2), Non-transmissibility (section 2-3-3), Increase in virulence (section 2-3-4) and Immunogenicity (section 2-3-5) may be used during the demonstration of safety and immunogenicity.

2-3-1 Safety test in piglets

Carry out the test for each route to be recommended using in each case piglets not older than 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.

Use not fewer than 8 healthy piglets that do not have antibodies against pestiviruses. Administer to not fewer than 8 piglets 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 piglets at least daily for at least 14 days. The body temperature of each vaccinated piglet is measured on at least the 3 days preceding administration of the vaccine, at the time of administration, 4 h after and then daily for at least 14 days. The vaccine complies with the test if the average body temperature increase for all piglets does not exceed 1.5 °C, no piglet shows a temperature rise greater than 1.5 °C for a period exceeding 3 days, and no piglet shows notable signs of disease or dies from causes attributable to the vaccine.

2-3-2 Safety test in pregnant sows and test for transplacental transmission

Carry out the test by a route to be recommended using not fewer than 8 healthy sows or gilts of the same age and origin, between the 55th and 80th days of gestation, and that do not have antibodies against pestiviruses. Use vaccine virus at the least attenuated passage level that will be present in a batch of the vaccine.

Administer to not fewer than 8 sows or gilts a quantity of the vaccine virus equivalent to not less than the maximum virus titre likely to be contained in 1 dose of the vaccine. Record the body temperature on at least the 3 days preceding administration of the vaccine, at the time of administration, 4 h after and then daily for at least 15 days. Observe until farrowing.

Carry out tests for serum antibodies against classical swine-fever virus. No antibodies against classical swine-fever virus are found in sera taken from the newborn piglets before ingestion of colostrum. The test is not valid if the vaccinated sows do not seroconvert. The vaccine virus complies with the test if no abnormalities in the gestation or in the piglets are noted, no sow or gilt shows a temperature rise greater than 1.5 °C for a period exceeding 5 days, and no sow or gilt shows notable signs of disease or dies from causes attributable to the vaccine.

2-3-3 Non-transmissibility

Keep together for the test not fewer than 12 healthy piglets, 6-10 weeks old and of the same origin, and that do not have antibodies against pestiviruses. Use vaccine virus at the least attenuated passage level that will be present between the master seed lot and a batch of the vaccine. Administer by a route to be recommended to not fewer than 6 piglets a quantity of the vaccine virus equivalent to not less than the maximum virus titre likely to be contained in 1 dose of the vaccine. Maintain not fewer than 6 piglets as contact controls. The mixing of vaccinated piglets and contact piglets is done 24 h after vaccination.

After 45 days, euthanise all piglets. Carry out appropriate tests on the piglets to detect antibodies to classical swine-fever. Carry out appropriate tests on the control piglets to detect classical swine-fever virus in the tonsils. The vaccine complies with the test if antibodies are found in all vaccinated piglets and if no antibodies and no virus are found in the control piglets.

2-3-4 Increase in virulence

Carry out the test according to general chapter *5.2.6*, using piglets 6-10 weeks old that do not have antibodies against pestiviruses. 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 piglet of the 1st group by a route to be recommended a quantity of the vaccine virus equivalent to not less than the maximum virus titre likely to be contained in 1 dose of the vaccine. Collect an appropriate quantity of blood from each piglet daily between day 2 and day 7 after administration of the vaccine virus, and pool the samples taken on the same day. Administer 2 mL of the pooled blood with the highest virus titre by a route to be recommended to each piglet of the next group. Carry out this passage operation not fewer than 4 times, verifying the presence of the virus at each passage. If no virus is found, repeat the test once. If virus is found, carry out a 2nd series of passages by administering 2 mL of positive blood by a route to be recommended to each piglet of a group of 10 animals.

If the 5th group of animals 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 animals 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 increasing 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 animals and a subsequent repeat passage in 10 animals, the vaccine virus also complies with the test.

2-3-5 Immunogenicity

2-3-5-1 Protective dose The efficacy of the vaccine is expressed by the number of 50 per cent protective doses (PD_{50}) for pigs contained in the vaccinal dose as indicated on the label. The vaccine contains at least 100 PD_{50} per dose.

Use 1 or more groups of piglets aged 6-10 weeks and that do not have antibodies against pestiviruses. Each group of piglets is vaccinated with 1 dilution of the vaccine dose. Use an additional group of piglets of the same age and origin as controls. 14 days after the single injection of vaccine, challenge the piglets by a suitable route with a suitable strain of virulent virus and a dose that kills not fewer than 50 per cent of the non-vaccinated piglets in less than 21 days. Observe the piglets for 21 days and record the body temperature 3 days before challenge and daily after challenge for 21 days. The PD_{50} is calculated by the usual statistical methods (for example, *5.3*), taking into account the surviving piglets that have no clinical signs of swine fever, including cutaneous lesions or an increase in body temperature.

The test is not valid if fewer than 50 per cent of the control piglets display typical signs of serious infection with swine-fever virus, including cutaneous lesions, or die, and if fewer than 100 per cent of the control piglets show clinical signs of disease within the 21 days following challenge. The vaccine complies with the test if the minimum dose stated on the label corresponds to not less than 100 PD_{50}.

2-3-5-2 Protection against transplacental infection Use at least 8 sows that do not have antibodies against pestiviruses, randomly allocated to either the vaccine group (n = 6) or the control group (n = 2).

Between the 40^{th} and 50^{th} day of gestation, all sows allocated to the vaccine group are vaccinated once with 1 dose of vaccine containing not more than the minimum titre stated on the label. On day 60 of gestation, all sows are challenged by a route to be recommended with a suitable strain of virulent virus. Just before farrowing and about 5-6 weeks after challenge, the sows are euthanised and their foetuses are examined for classical swine-fever virus. Serum samples from sows and foetuses are tested for the presence of antibodies against classical swine-fever virus. Isolation of classical swine-fever virus is carried out from blood of the sows (collected 7 and 9 days after challenge and at euthanasia), and from homogenised organ material (spleen, kidneys, lymph nodes) of the foetuses.

The test is not valid if one or more of the vaccinated sows do not seroconvert after the vaccination and the control sows do not seroconvert after the challenge, or if no virus is found in more than 50 per cent of the foetuses from the control sows (excluding mummified foetuses).

The vaccine complies with the test if no virus is found in the blood of vaccinated sows and in foetuses from the vaccinated sows, and no antibodies against classical swine-fever virus are found in the serum of the foetuses from the vaccinated sows.

3 BATCH TESTS

3-1 Identification

The vaccinal strain is identified using a suitable method, for example, with specific classical swine-fever monoclonal antibodies.

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.

3-4 Extraneous agents (*5.2.5*)

The vaccine is free from extraneous agents.

3-5 Virus titre

Titrate the vaccine virus in suitable cell cultures (*5.2.4*). 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 2-3-5) 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.

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