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Swine Influenza Vaccine, Inactivated

General Notices

(Porcine Influenza Vaccine (Inactivated), Ph. Eur. monograph 0963)

Ph Eur

1 DEFINITION

Porcine influenza vaccine (inactivated) is a preparation of one or more suitable strains of swine or human influenza virus inactivated while maintaining adequate immunogenic properties. Suitable strains contain both haemagglutinin and neuraminidase. This monograph applies to vaccines intended for the active immunisation of pigs against porcine influenza.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

The vaccine virus is grown in embryonated hens' eggs or in cell cultures. Each virus strain is cultivated separately. After cultivation, the viral suspensions are collected separately and inactivated by a suitable method. If necessary, they may be purified. The vaccine may be adjuvanted.

2-2 SUBSTRATE FOR VIRUS PROPAGATION

2-2-1 Embryonated hens' eggs

If the vaccine virus is grown in embryonated hens' eggs, they are obtained from a healthy flock (*5.2.13*).

2-2-2 Cell cultures

If the vaccine virus is grown in cell cultures, they comply with the requirements for cell cultures for production of veterinary vaccines (*5.2.4*).

2-3 CHOICE OF VACCINE COMPOSITION

The choice of strains is based on the antigenic types and sub-types observed in Europe. The vaccine is shown to be satisfactory with respect to safety (*5.2.6*) and efficacy (*5.2.7*) for the pigs 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

2-3-1-1 Laboratory tests. Carry out the tests for each route and method of administration to be recommended for vaccination and where applicable, in pigs of each category for which the vaccine is intended (sows, fattening pigs), using in each case pigs not older than the minimum age to be recommended for vaccination. Use a batch of vaccine containing not less than the maximum potency that may be expected in a batch of vaccine.

2-3-1-1-1 General safety. For each test, use not fewer than 8 pigs that do not have antibodies against swine influenza virus. Administer to each pig 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 pigs at least daily until 14 days after the last administration.

The vaccine complies with the test if no pig shows abnormal local or systemic reactions or dies from causes attributable to the vaccine during the test.

2-3-1-1-2 Safety in the pigs used in test 2-3-2 for immunogenicity. The pigs used in the test for immunogenicity are also used to evaluate safety. Measure the body temperature of each vaccinated pig at the time of vaccination and 24 h and 48 h later. Examine the injection site at slaughter for local reactions.

The vaccine complies with the test if no pig shows:

— abnormal body temperature;

— other systemic reactions (for example, anorexia);

— abnormal local reactions attributable to the vaccine.

2-3-1-2 Field studies. The pigs used for field trials are also used to evaluate safety. Carry out a test in each category of pigs for which the vaccine is intended (sows, fattening pigs). Use not fewer than 3 groups each of not fewer than 20 pigs in at least 2 locations with corresponding groups of not fewer than 10 controls. Measure the body temperature of each vaccinated pig at the time of vaccination and 24 h and 48 h later. Examine the injection site at slaughter for local reactions.

The vaccine complies with the test if no pig shows:

— abnormal body temperature;

— abnormal local reactions attributable to the vaccine.

2-3-2 Immunogenicity

The following test carried out using an epidemiologically relevant challenge strain or strains is suitable to demonstrate the immunogenicity of the vaccine. It is carried out for each subtype used in the preparation of the vaccine.

A test is carried out for each route and method of administration to be recommended, using in each case pigs of the minimum age to be recommended for vaccination. The vaccine administered to each pig is of minimum potency.

Use for the test not fewer than 20 pigs that do not have antibodies against swine influenza virus. Vaccinate not fewer than 10 pigs according to the schedule to be recommended. Maintain not fewer than 10 pigs as controls. Take a blood sample from all control pigs immediately before challenge. 3 weeks after the last administration of vaccine, challenge all the pigs by the intratracheal route with a sufficient quantity of a virulent influenza field virus. Euthanise half of the vaccinated and control pigs 24 h after challenge and the other half 72 h after challenge. For each pig, measure the quantity of influenza virus in 2 lung tissue homogenates, one from the left apical, cardiac and diaphragmatic lobes, and the other from the corresponding right lung lobes. Take equivalent samples from each pig.

The test is not valid if antibodies against influenza virus are found in any control pig immediately before challenge. The vaccine complies with the test if, at both times of measurement, the mean virus titre in the pooled lung tissue samples of vaccinated pigs is significantly lower than that for control pigs, when analysed by a suitable statistical method such as the Wilcoxon Mann-Whitney test.

2-4 MANUFACTURER'S TESTS

2-4-1 Residual live virus

An amplification test for residual live virus is carried out on each batch of antigen immediately after inactivation by passage in the same type of substrate as that used for production (cell cultures or eggs) or a substrate shown to be at least as sensitive. The quantity of inactivated virus harvest used in the test is equivalent to not less than 10 doses of the vaccine.

2-4-1-1 Vaccines prepared in cell cultures. If the vaccine has been prepared in cell cultures, carry out a suitable test for residual live virus using 2 passages in the same type of cell culture as used in the production of vaccine. The inactivated

virus harvest complies with the test if no live virus is detected.

2-4-1-2 Vaccines prepared in eggs. If the vaccine has been prepared in eggs, inoculate 0.2 mL of inactivated virus harvest into the allantoic cavity of each of 10 fertilised hen eggs, 9-11 days old. Incubate at a suitable temperature for 3 days. The death of any embryo within 24 h of inoculation is considered as non-specific mortality and the egg is discarded. The test is not valid if fewer than 80 per cent of the eggs survive. Collect the allantoic fluid of each egg, pool equal quantities and carry out a 2nd passage on fertilised eggs in the same manner. Incubate for 4 days; the inactivated virus harvest complies with the test if the allantoic fluid of these eggs shows no haemagglutinating activity.

2-4-2 Batch potency test

It is not necessary to carry out the potency test (section 3-3) 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 test may be used.

Use 5 guinea-pigs, 5-7 weeks old and that do not have antibodies against swine influenza virus. Vaccinate each guinea-pig by the subcutaneous route with a quarter of the recommended dose. Collect blood samples before the vaccination and 21 days after vaccination. Determine for each sample the level of specific antibodies against each virus subtype in the vaccine by haemagglutination-inhibition or another suitable test. The vaccine complies with the test if the level of antibodies is not lower than that found for a batch of vaccine that gave satisfactory results in the potency test in pigs (see Potency).

2-4-3 Bacterial endotoxins

For vaccines produced in eggs, the content of bacterial endotoxins is determined on the virus harvest to monitor production.

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 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.