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Avian Infectious Bronchitis Vaccine, Living

General Notices

(Avian Infectious Bronchitis Vaccine (Live), Ph. Eur. monograph 0442)

Ph Eur

1 DEFINITION

Avian infectious bronchitis vaccine (live) is a preparation of one or more suitable strains of different types of avian infectious bronchitis virus. This monograph applies to vaccines intended for administration to chickens for active immunisation against respiratory disease caused by avian infectious bronchitis virus.

2 PRODUCTION

2-1 PREPARATION OF THE VACCINE

The vaccine virus is grown in embryonated hens' eggs or in cell cultures.

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 flocks free from specified pathogens (SPF) (*5.2.2*).

2-2-2 Cell cultures

If the vaccine virus is grown in cell cultures, they 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 shall be shown to be satisfactory with respect to safety (*5.2.6*) and efficacy (*5.2.7*) for the chickens for which it is intended.

The following tests for safety (section 2-3-1), increase in virulence (section 2-3-2) and immunogenicity (section 2-3-3) may be used during the demonstration of safety and efficacy.

2-3-1 Safety

2-3-1-1 Safety for the respiratory tract and kidneys. Carry out the test in chickens not older than the minimum age to be recommended for vaccination. Use vaccine virus at the least attenuated passage level that will be present between the master seed lot and a batch of the vaccine.

Use not fewer than 15 chickens of the same origin and from an SPF flock (*5.2.2*). Administer to each chicken by the oculonasal route 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. On each of days 5, 7 and 10 after administration of the virus, euthanise not fewer than 5 of the chickens and take samples of trachea and kidney. Fix kidney samples for histological examination. Remove the tracheas and prepare 3 transverse sections from the upper part, 4 from the middle part and 3 from the lower part of the trachea of each chicken; examine all tracheal explants as soon as possible and at the latest 2 h after sampling by low-magnification microscopy for ciliary activity. Score for ciliostasis on a scale from 0 (100 per cent ciliary activity) to 4 (no activity, complete ciliostasis); calculate the mean ciliostasis score (the maximum for each trachea being 40) for the 5 chickens euthanised on each of days 5, 7 and 10.

The test is not valid if more than 10 per cent of the chickens die from causes not attributable to the vaccine virus.

The vaccine virus complies with the test if:

— no chicken shows notable clinical signs of avian infectious bronchitis or dies from causes attributable to the vaccine virus;

— any inflammatory lesions seen during the kidney histological examination are, at most, moderate.

A risk/benefit analysis is carried out, taking into account the average ciliostasis scores obtained and the benefits expected from the use of the vaccine.

2-3-1-2 Safety for the reproductive tract. If the recommendations for use state or imply that the vaccine may be used in females less than 3 weeks old that are subsequently kept to sexual maturity, it shall be demonstrated that there is no damage to the development of the reproductive tract when the vaccine is given to chickens of the minimum age to be recommended for vaccination.

The following test may be carried out: use not fewer than 40 female chickens from an SPF flock (*5.2.2*) that are not older than the minimum age to be recommended for vaccination; use the vaccine virus at the least attenuated passage level that will be present between the master seed lot and a batch of the vaccine; administer to each chicken by a route to be recommended a quantity of virus equivalent to not less than the maximum titre likely to be present in 1 dose of vaccine; at least 10 weeks after administration of the vaccine virus, euthanise the chickens and carry out a macroscopic examination of the oviducts. The vaccine virus complies with the test if abnormalities are present in not more than 5 per cent of the oviducts.

2-3-2 Increase in virulence

Carry out the test according to general chapter *5.2.6* using 2-week-old SPF chickens (*5.2.2*). 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 chicken of the 1st group by eye-drop a quantity of the vaccine virus that will allow recovery of virus for the passages described below. 2-4 days after administration of the vaccine virus, prepare a suspension from the mucosa of the trachea of each chicken and pool these samples. Administer 0.05 mL of the pooled samples by eye-drop to each chicken 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 chickens. Carry out the test for safety for the respiratory tract and kidneys (section 2-3-1-1) and, where applicable, the test for safety for the reproductive tract (section 2-3-1-2) using the material used for the 1st passage and the virus at the final passage level. Administer the virus by the route to be recommended for vaccination that is likely to be the least safe.

The vaccine virus complies with the test if no indication of an increase in 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 5 chickens and a subsequent repeat passage in 10 chickens, the vaccine virus also complies with the test.

2-3-3 Immunogenicity

Immunogenicity is demonstrated for each strain of virus to be included in the vaccine. A test is carried out for each route and method of administration to be recommended using in each case chickens from an SPF flock (*5.2.2*) that are not older than the minimum age to be recommended for vaccination. The quantity of the vaccine virus administered to each chicken 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 the vaccine.

Either or both of the tests below may be used during the demonstration of immunogenicity.

2-3-3-1 Ciliary activity of tracheal explants. Use not fewer than 25 chickens of the same origin and from an SPF flock (5.2.2). Vaccinate by a route to be recommended not fewer than 20 chickens. Maintain not fewer than 5 chickens as controls. Challenge each chicken after 21 days by eye-drop with a sufficient quantity of virulent avian infectious bronchitis virus of the same type as the vaccine virus to be tested. Euthanise the chickens 4-7 days after challenge and prepare 3 transverse sections from the upper part, 4 from the middle part, and 3 from the lower part of the trachea of each chicken. Examine all tracheal explants as soon as possible and at the latest 2 h after sampling by low-magnification microscopy for ciliary activity. For a given tracheal section, ciliary activity is considered as normal when at least 50 per cent of the internal ring shows vigorous ciliary movement. A chicken is considered not affected if not fewer than 9 out of 10 rings show normal ciliary activity.

The test is not valid if:

— fewer than 80 per cent of the control chickens show cessation or extreme loss of vigour of ciliary activity;

— and/or during the period between the vaccination and challenge, more than 10 per cent of vaccinated or control chickens show abnormal clinical signs or die from causes not attributable to the vaccine.

The vaccine virus complies with the test if not fewer than 80 per cent of the vaccinated chickens show normal ciliary activity.

2-3-3-2 Virus recovery from tracheal swabs. Use not fewer than 30 chickens of the same origin and from an SPF flock (5.2.2). Vaccinate by a route to be recommended not fewer than 20 chickens. Maintain not fewer than 10 chickens as controls. Challenge each chicken after 21 days by eye-drop with a sufficient quantity of virulent avian infectious bronchitis virus of the same type as the vaccine virus to be tested. Euthanise the chickens 4-7 days after challenge and prepare a suspension from swabs of the tracheal mucosa of each chicken.

Use a suitable validated method to detect the challenge virus in the swabs.

The test is not valid if:

— the challenge virus is detected in less than 80 per cent of the control chickens;

— and/or during the period between vaccination and challenge, more than 10 per cent of the vaccinated or control chickens show abnormal clinical signs or die from causes not attributable to the vaccine.

The vaccine virus complies with the test if the challenge virus is detected in not more than 20 per cent of the vaccinated chickens.

3 BATCH TESTS

3-1 Identification

3-1-1 Vaccines containing 1 type of virus. The vaccine, diluted if necessary, is identified using a suitable method. For example, when mixed with avian infectious bronchitis virus antiserum specific for the virus type, it is no longer able to infect embryonated hens' eggs from an SPF flock (5.2.2) or susceptible cell cultures (5.2.4) into which it is inoculated.

3-1-2 Vaccines containing more than 1 type of virus. The vaccine, diluted if necessary, is identified using a suitable method. For example, when mixed with type-specific antisera against each strain present in the vaccine except that to be identified, it infects embryonated hens' eggs from an SPF flock (5.2.2) or susceptible cell cultures (5.2.4) into which it is inoculated, whereas after further admixture with type-specific antiserum against the strain to be identified it no longer produces such infection.

3-2 Bacteria and fungi

Vaccines intended for administration by injection comply with the test for sterility prescribed in the general monograph *Vaccines for veterinary use (0062)*.

Any diluent supplied for reconstitution of the vaccine 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 by inoculation into embryonated hens' eggs from an SPF flock (*5.2.2*) or into suitable cell cultures (*5.2.4*). If the vaccine contains more than 1 strain of virus, titrate each strain after having neutralised the others with type-specific avian infectious bronchitis antisera. The vaccine complies with the test if 1 dose contains for each vaccine virus not less than the minimum titre stated on the label.

3-6 Potency

The vaccine complies with the requirements of 1 of the tests prescribed under Immunogenicity (section 2-3-3) when administered according to the recommended schedule 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.
