Mannheimia vaccine (inactivated) for sheep

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MANNHEIMIA VACCINE (INACTIVATED) FOR SHEEP

Vaccinum mannheimiae inactivatum

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DEFINITION

Mannheimia vaccine (inactivated) for sheep is a preparation of one or more suitable strains of Mannheimia haemolytica (formerly Pasteurella haemolytica). This monograph applies to vaccines intended for administration to sheep for active immunisation and to protect passively their future progeny against disease caused by M. haemolytica.

PRODUCTION

Production of the vaccine is based on a seed lot system. The seed material is cultured in a suitable medium; each strain is cultivated separately and identity is verified using a suitable method. During production, various parameters such as growth rate are monitored by suitable methods; the values are within the limits approved for the particular product. Purity and identity of the harvest are verified using suitable methods. After cultivation, the bacterial suspensions are collected separately and inactivated by a suitable method. The vaccine may contain an adjuvant and may be freeze-dried.

CHOICE OF VACCINE COMPOSITION

The choice of composition and the strains to be included in the vaccine is based on epidemiological data on the prevalence of the different serovars of M. haemolytica and on the claims being made for the product, for example active and/or passive protection. The vaccine is shown to be satisfactory with respect to safety (5.2.6) and efficacy (5.2.7) in sheep. As part of the studies to demonstrate the suitability of the vaccine with respect to these characteristics the following tests may be carried out.

Safety

A. The test is carried out for each of the routes of administration to be stated on the label and in animals of each category (for example, young sheep, pregnant ewes) for which the vaccine is intended.

For each test, use not fewer than 10 animals that preferably do not have antibodies against the serovars of M. haemolytica or against the leucotoxin present in the vaccine. Where justified, animals with a known history of no previous Mannheimia vaccination and with low antibody titres (measured in a sensitive test system such as an ELISA) may be used.

Administer to each animal a double dose of vaccine containing not less than the maximum potency that may be expected in a batch of vaccine. Administer a single dose of vaccine to each animal after the recommended interval. Observe the animals for at least 14 days after the last administration. Record body temperature the day before vaccination, at vaccination, 2 h, 4 h and 6 h later and then daily for 4 days; note the maximum temperature increase for each animal. No abnormal local or systemic reaction occurs; the average body temperature increase for all animals does not exceed 1.5 °C and no animal shows a rise greater than 2 °C. If the vaccine is intended for use or may be used in pregnant ewes, vaccinate the ewes at the relevant stages of pregnancy and prolong the observation period until 1 day after lambing.

chosen for determining the amount of bacterial endotoxin present in the vaccine batch used in the safety test for determining the maximum acceptable level of endotoxin is used subsequently for testing of each batch.

IDENTIFICATION

When injected into healthy seronegative animals, the vaccine stimulates the production of specific antibodies against the serovars of M. haemolytica and/or against the leucotoxin present in the vaccine.

TESTS

Safety. Use 2 cattle of the minimum age recommended for vaccination that have not been vaccinated against mannheimiosis. Administer a double dose of vaccine to each animal by a recommended route. Observe the animals for 14 days. Record body temperature the day before vaccination, at vaccination, 2 h, 4 h and 6 h later and then daily for 2 days. The animals remain in good health and no abnormal local or systemic reaction occurs; a transient temperature increase not exceeding 2 °C may occur.

Sterility. It complies with the test for sterility prescribed in the monograph on Vaccines for veterinary use (0062).

POTENCY

Carry out a test for each serovar for which protection is claimed on the label.

Use not fewer than 16 animals of the minimum age recommended for vaccination, free from antibodies against M. haemolytica and against the leucotoxin of M. haemolytica. Vaccinate not fewer than 8 of the animals by a recommended route and according to the recommended schedule. Keep 8 animals as controls. 21 days after the last vaccination, challenge all the animals by the intratracheal route or by another appropriate route, with a suitable quantity of a low-passage, virulent strain of a serovar of M. haemolytica. Observe the animals for a further 7 days; to avoid unnecessary suffering, severely ill animals are killed and are then considered to have died from the disease.

During the observation period, the animals are examined for signs for disease for example, increased body temperature, dullness, abnormal breathing and the mortality is recorded. Kill surviving animals at the end of the observation period. Post-mortem examination is carried out on any animal that dies and those killed at the end of the observation period. The lungs are examined and the extent of lung lesions due to mannheimiosis is evaluated. Samples of lung tissue are collected for re-isolation of the challenge organisms. The clinical observations and lung lesions are scored and the results obtained for these parameters and the bacterial re-isolation results compared for the 2 groups.

The test is invalid if signs of M. haemolytica infection occur in less than 70 per cent of the control animals.

The vaccine complies with the requirements of the test if there is a significant difference between the scores obtained for the clinical and post-mortem observations in the vaccines compared to the controls. For vaccines with a claim for a beneficial effect on the extent of infection against the serovar, the results for the infection rates are also significantly better for the vaccines compared to the controls.

LABELLING

The label states:

– the serovar(s) of M. haemolytica against which protection is claimed,
– the serovar(s) of M. haemolytica and/or the leucotoxin present in the vaccine.
The vaccine complies with the test if no animal shows abnormal local reactions or clinical signs of disease or dies from causes attributable to the vaccine. In addition, if the vaccine is intended for use in pregnant ewes, no significant effects on the pregnancy and offspring are demonstrated.

B. The animals used for the field trials are also used to evaluate safety. Carry out a test in each category of animals for which the vaccine is intended. Use not fewer than 3 groups of 20 animals with corresponding groups of not fewer than 10 controls in 3 different locations. Examine the injection sites for local reactions after vaccination. Record body temperatures the day before vaccination, at vaccination, and on the 2 days following vaccination. The vaccine complies with the test if no animal shows abnormal local or systemic reactions or clinical 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. Where the latter test is used, note the maximum temperature increase for each animal; the average body temperature increase for all animals does not exceed 1.5 °C and no animal shows a rise greater than 2 °C. In addition, if the vaccine is intended for use in pregnant ewes, no significant effects on the pregnancy and offspring are demonstrated.

Immunogenicity. As part of the studies to demonstrate the suitability of the vaccine with respect to immunogenicity, the tests described under Potency may be carried out for each proposed route of administration and using vaccine of minimum potency.

BATCH TESTING

Batch potency test. The relevant test or tests described under Potency are not carried out for routine testing of batches of vaccine. They are carried out, for a given vaccine, on one or more occasions, as decided by or with the agreement of the competent authority. Where the relevant test or tests are not carried out, a suitable validated batch potency test is carried out, the criteria for acceptance being set with reference to the results obtained with a batch of vaccine that has given satisfactory results in the test(s) described under Potency.

Bacterial endotoxins. A test for bacterial endotoxins (2.6.14) is carried out on the final lot or, where the nature of the adjuvant prevents performance of a satisfactory test, on the bulk antigen or the mixture of bulk antigens immediately before addition of the adjuvant. The maximum acceptable amount of bacterial endotoxins is that found for a batch of vaccine that has been shown satisfactory in safety test A given under Choice of vaccine composition or in the safety test described under Tests, carried out using 10 animals. Where the latter test is used, note the maximum temperature increase for each animal; the average body temperature increase for all animals does not exceed 1.5 °C. The method chosen for determining the amount of bacterial endotoxin present in the vaccine batch used in the safety test for determining the maximum acceptable level of endotoxin is used subsequently for testing of each batch.

IDENTIFICATION

When injected into healthy seronegative animals, the vaccine stimulates the production of specific antibodies against the serovars of M. haemolytica and/or against the leucotoxin present in the vaccine.

TESTS

Safety. Use 2 sheep of the minimum age recommended for vaccination or, if not available, of an age as close as possible to the minimum recommended age, and that have not been vaccinated against Mannheimia. Administer a double dose of vaccine to each animal by a recommended route. Observe the animals for 14 days. Record body temperature the day before vaccination, at vaccination, 2 h, 4 h and 6 h later and then daily for 2 days. The animals remain in good health and no abnormal local or systemic reaction occurs; a transient temperature increase not exceeding 2 °C may occur.

Sterility. It complies with the test for sterility prescribed in the monograph on Vaccines for veterinary use (0062).

POTENCY

Active immunisation. For vaccines with claims for active immunisation due to M. haemolytica, carry out a test for each serovar of M. haemolytica for which protection is claimed on the label.

Use not fewer than 20 lambs of the minimum age recommended for vaccination, free from antibodies against M. haemolytica and against the leucotoxin of M. haemolytica. Vaccinate not fewer than 10 of the animals by a recommended route and according to the recommended schedule. Keep 10 animals as controls. 21 days after the last vaccination, challenge all the lambs by the intratracheal route or by another appropriate route, with a suitable quantity of a low-passage, virulent strain of a serovar of M. haemolytica. Where necessary for a given serovar, prechallenge with parainfluenza type 3 (PI3) virus or another appropriate respiratory pathogen may be used. Observe the animals for a further 7 days; to avoid unnecessary suffering, severely ill animals are killed and are then considered to have died from the disease. During the observation period, the animals are examined for signs of disease (for example, increased body temperature, dulness, abnormal respiration) and the mortality is recorded. Kill surviving animals at the end of the observation period. Post-mortem examination is carried out on any animal that dies and those killed at the end of the observation period. The lungs are examined and the extent of lung lesions due to mannheimiosis is evaluated. Samples of lung tissue are collected for re-isolation of the challenge organisms. The clinical observations and lung lesions are scored and the results obtained for these parameters and the bacterial re-isolation results compared for the 2 groups.

The test is invalid if signs of M. haemolytica infection occur in less than 70 per cent of the control lambs.

The vaccine complies with the requirements of the test if there is a significant difference between the scores obtained for the clinical and post-mortem observations in the vaccines compared to the controls. For vaccines with a claim for a beneficial effect on the extent of infection against the serovar, the results for the infection rates are also significantly better for the vaccinates compared to the controls.

Passive protection. For vaccines with claims for passive protection against mannheimiosis carry out a test for each serovar of M. haemolytica for which protection is claimed on the label.

Use at least 6 ewes that preferably do not have antibodies against the serovars of M. haemolytica or against the leucotoxin present in the vaccine. Where justified, animals with a known history of no previous mannheimiosis vaccination, from a source with a low incidence of respiratory disease and with low antibody titres (measured in a sensitive test system such as an ELISA) may be used. Vaccinate the animals by 1 of the recommended routes, at the recommended stages of pregnancy and according to the recommended schedule. A challenge study is conducted with 20 newborn, colostrum-deprived lambs. 10 of these lambs are given colostrum from the vaccinated ewes and 10 control lambs are given colostrum or colostrum substitute without detectable antibodies to M. haemolytica. When the lambs are at the age claimed for the duration of the passive protection, challenge by the intratracheal route with
Marek's disease vaccine (live)  

Vaccinum morbi Marek vivum

1. DEFINITION

Marek's disease vaccine (live) is a preparation of a suitable strain or strains of Marek’s disease virus (gallid herpesvirus 2 or 3) and/or turkey herpesvirus (meleagrid herpesvirus 1). This monograph applies to vaccines intended for administration to chickens for active immunisation.

2. PRODUCTION

2-1. PREPARATION OF THE VACCINE

The vaccine virus is grown in cell cultures. If the vaccine contains more than 1 type of virus, the different types are grown separately. The vaccine may be freeze-dried or stored in liquid nitrogen.

2-2. SUBSTRATE FOR VIRUS PROPAGATION

2-2-1. Cell cultures

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

2-3. SEED LOTS

2-3-1. Extraneous agents

The master seed lot complies with the tests for extraneous agents in seed lots (2.6.24). In these tests on the master seed lot, the organisms used are not more than 5 passages from the master seed lot at the start of the tests.

2-4. 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 tests shown below for safety of the strain (section 2-4-1), increase in virulence (section 2-4-2) and immunogenicity (section 2-4-3) may be used during the demonstration of safety and immunogenicity. Additional testing may be needed to demonstrate safety in breeds of chickens known to be particularly susceptible to Marek's disease virus, unless the vaccine is to be contra-indicated.

2-4-1. Safety

Carry out the test for the route to be recommended for vaccination likely to be the least safe and in the category of chickens for which the vaccine is intended likely to be the most susceptible for Marek’s disease. 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 eighty 1-day-old chickens from a flock free from specified pathogens (SPF) (5.2.2.2). Divide them randomly into 2 groups of not fewer than 40 chickens and maintain the groups separately. Carry out examination for macroscopic lesions of each chicken that dies and of the surviving chickens at the end of the observation periods.

Administer to each chicken of one group (I) 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. Administer by a suitable route to each chicken of the other group (II) a quantity of virulent Marek's disease virus that will cause mortality and/or severe macroscopic lesions of Marek’s disease in not fewer than 70 per cent of the effective number of chickens within 70 days (initial number reduced by the number that die within the first 7 days of the test). Observe the chickens of group II at least daily for 70 days and those of group I at least daily for 120 days. The test is not valid if 1 or more of the following apply: more than 10 per cent of the chickens in any group die within the first 7 days of the test; fewer than 70 per cent of the effective number of chickens in group II show macroscopic lesions of Marek’s disease. The vaccine virus complies with the test if:

- no chicken of group I shows notable clinical signs or macroscopic lesions of Marek’s disease or dies from causes attributable to the vaccine virus,
- at 120 days the number of surviving chickens of group I is not fewer than 80 per cent of the effective number.

2-4-2. Increase in virulence

The test for increase in virulence is required for Marek’s disease virus vaccine strains but not for turkey herpesvirus vaccine strains, which are naturally apathogenic. Administer by the intramuscular route a quantity of the vaccine virus that will allow recovery of virus for the passages described below to each of five 1-day-old chickens from an SPF flock (5.2.2.2). Use vaccine virus at the least attenuated passage level that will be present between the master seed lot and a batch of the vaccine. Prepare 5 to 7 days later a suspension of white blood cells of each chicken and pool these samples. Administer a suitable volume of the pooled samples by the intraperitoneal route to each of 5 other chickens that are 1-day-old and from an SPF flock (5.2.2.2). Carry out this passage operation not fewer than 5 times; verify the presence of the virus at each passage. Care must be taken to avoid contamination by virus from previous passages. If the virus is not found at a passage level, carry out a second series of passages. Carry out the safety test (section 2-4-1) using the unpassaged vaccine virus and the maximally passaged virus that has been recovered. Administer the virus by the route to be recommended for vaccination likely to be the least safe for use in these birds. The vaccine virus complies with the test if no indication of increase in virulence of the maximally passaged virus compared with the unpassaged virus is observed. If virus is not recovered at any passage level in the first and second series of passages, the vaccine virus also complies with the test.

2-4-3. Immunogenicity

A test is carried out for each route and method of administration to be recommended using in each case chickens of the youngest age to be recommended for vaccination. The quantity of the vaccine