



Edition: BP 2025 (Ph. Eur. 11.6 update)

## Pasteurella Vaccine (Inactivated) for Sheep



### [General Notices](#)

(Ph. Eur. monograph 2072)

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## 1 DEFINITION

Pasteurella vaccine (inactivated) for sheep is a preparation of one or more suitable strains of *Pasteurella trehalosi*, inactivated while maintaining adequate immunogenic properties. This monograph applies to vaccines intended for the active immunisation of sheep against disease caused by *P. trehalosi*.

## 2 PRODUCTION

### 2-1 PREPARATION OF THE VACCINE

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 be adjuvanted.

### 2-2 CHOICE OF VACCINE COMPOSITION

The choice of composition and the strains to be included in the vaccine are based on epidemiological data on the prevalence of the different serovars of *P. trehalosi*.

The vaccine is shown to be satisfactory with respect to safety ([5.2.6](#)) and efficacy ([5.2.7](#)) for the sheep for which it is intended.

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

#### 2-2-1 Safety

**2-2-1-1 Laboratory tests.** Carry out the tests for each route and method of administration to be recommended for vaccination and in sheep of each category for which the vaccine is intended (for example, young sheep, pregnant ewes). Use a batch of vaccine containing not less than the maximum potency that may be expected in a batch of vaccine.

For each test, use not fewer than 8 sheep that preferably do not have antibodies against the serovars of *P. trehalosi* or against the leucotoxin present in the vaccine. Where justified, sheep with a known history of no previous pasteurella vaccination and with low antibody titres (measured in a sensitive test system such as ELISA) may be used. Administer to each sheep 1 dose of the vaccine. If the schedule to be recommended requires a 2<sup>nd</sup> dose, administer another dose after an interval of at least 14 days. Observe the sheep at least daily 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 sheep.

The vaccine complies with the test if no sheep shows abnormal local reactions, notable signs of disease or dies from causes attributable to the vaccine, if the average body temperature increase for all sheep does not exceed 1.5 °C and no sheep shows a rise greater than 2.0 °C.

**2-2-1-2 Field studies.** The sheep used for the field trials are also used to evaluate safety. Carry out a test in each category of sheep for which the vaccine is intended. Use not fewer than 3 groups of 20 sheep 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 sheep shows abnormal local or systemic reactions, notable signs of disease or dies from causes attributable to the vaccine. The average body temperature increase for all sheep does not exceed 1.5 °C and no sheep shows a rise greater than 2.0 °C. In addition, if the vaccine is intended for use in pregnant ewes, no adverse effects on the pregnancy and offspring are demonstrated.

## **2-2-2 Immunogenicity**

Carry out a test for each serovar of *P. trehalosi* for which protection is to be claimed on the label.

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

Use not fewer than 20 lambs that do not have antibodies against *P. trehalosi* and against the leucotoxin of *P. trehalosi*. Vaccinate not fewer than 10 lambs according to the schedule to be recommended. Maintain not fewer than 10 lambs as controls. 20-22 days after the last vaccination, challenge each lamb by the subcutaneous or another suitable route, with a sufficient quantity of a low-passage, virulent strain of a serovar of *P. trehalosi*. Observe the lambs for a further 7 days; to avoid unnecessary suffering, severely ill lambs are euthanised and are then considered to have died from the disease. During the observation period, examine the lambs for any signs of disease (for example, severe dullness, excess salivation) and record the mortality. Euthanise surviving lambs at the end of the observation period. Carry out post-mortem examination on any lamb that dies and those euthanised at the end of the observation period. Examine the lungs, pleura, liver and spleen for haemorrhages and evaluate the extent of lung consolidation due to pasteurellosis. Collect samples of lung, liver and spleen tissue for re-isolation of the challenge organisms. Score the mortality, clinical observations and the post-mortem lesions and compare the results obtained for these parameters and the bacterial re-isolation results for the 2 groups.

The test is not valid if signs or lesions of *P. trehalosi* infection occur in less than 70 per cent of the control lambs. The vaccine complies with the test if there is a significant difference between the scores obtained for the clinical and post-mortem observations in the vaccinates 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.

## **2-3 MANUFACTURER'S TESTS**

### **2-3-1 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.

### **2-3-2 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 tests 2-2-1-1 given under Choice of vaccine composition. 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.

### **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 2-2-2) when administered by a recommended route and method.

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