DRAFT REVISED MONOGRAPH FOR COMMENTS

This draft revised monograph contain text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to further revisions prior to publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Comments received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in/ biologics-ipc@gov.in **before the last date for comments.**

Document History and Schedule for the Adoption Process

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Further follow-up action as required.	

Avian Infectious Laryngotracheitis Vaccine, Live

Laryngotracheitis Vaccine, Live

Avian Infectious Laryngotracheitis Vaccine, Live is a preparation of a suitable strain of avian infectious laryngotracheitis virus (gallid herpesvirus 1). This monograph applies to vaccines intended for administration to chickens for active immunisation against laryngotracheitis virus (gallid herpesvirus 1).

Production

Preparation of the Vaccine

The vaccine virus is grown in embryonated hens' eggs, from SPF flock (2.7.7) or in cell cultures derived from SPF eggs (2.7.7).

Substrate for virus propagation

Embryonated hens' eggs

If the vaccine virus is grown in embryonated hens' eggs, they are obtained from flocks free from specified pathogens (SPF) (2.7.7).

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 (2.7.13)

Seed Lot

Extraneous agents

The master seed lot complies with the tests for extraneous agents in seed lots (2.7.10). 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.

Choice of vaccine virus

The following tests for index of respiratory virulence, safety, test for reversion to virulence and immunogenicity may be used during the demonstration of safety and immunogenicity. The vaccine virus shall be shown to be satisfactory with respect to safety (2.7.17) and efficacy (2.7.12) for the chickens for which it is intended.

Index of respiratory virulence. Use for the test not less than sixty 10-day-old chickens from an SPF flock (2.7.7). Divide them randomly into 3 groups, maintained separately. Prepare 2 tenfold serial dilutions starting from a suspension of the vaccine virus having a titre of 10^5 EID_{50} or 10^5 $CCID_{50}$ per 0.2 ml or, if not possible, having the maximum attainable titre. Use vaccine virus at the least attenuated passage level that will be present in a batch of the vaccine. Allocate the undiluted virus suspension and the 2 virus dilutions each to a different group of chickens. Administer by the intratracheal route to each chicken 0.2 ml of the virus suspension attributed to its group. Observe the chickens for 10 days after administration and record the number of deaths. The index of respiratory virulence is the total number of deaths in the 3 groups divided by the total number of chickens. The vaccine virus complies with the test if its index of respiratory virulence is not more than 0.33.

Safety . For each test performed in chickens younger than 3 weeks of age, use not fewer than 10 chickens. For each test performed in chickens older than 3 weeks of age, use not fewer than 8 chickens. Administer to each chicken 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 chickens at least daily for at least 21 days.

The test is not valid if more than 10 per cent of the chickens younger than 3 weeks of age show abnormal signs of disease or die from causes not attributable to the vaccine. For chickens older than 3 weeks of age, the test is not valid if non-specific mortality occurs

Test for reversion to virulence

The test for reversion to virulence consists of the administration of the vaccine virus at the least attenuated passage level that will be present between the master seed lot and a batch of the vaccine to a group of 5 chickens not more than 2 weeks old, from an SPF flock (2.7.7), sequential passages, 5 times where possible, to further similar groups and testing of the final recovered virus for increase in virulence. If the properties of the vaccine virus allow sequential passage to 5 groups via natural spreading, this method may be used, otherwise passage as described below is carried out and the maximally passage virus that has been recovered is tested for increase in virulence. Care must be taken to avoid contamination by virus from previous passages. Administer by eye-drop a quantity of the vaccine virus that will allow recovery of virus for the passages described below. After the period shown to correspond to maximum replication of the virus, prepare a suspension from the mucosae of suitable parts of the respiratory tract of each chicken and pool these samples. Administer 0.05 ml of the pooled samples by eye-drop to each of 5 other chickens that are 2 weeks old and from an SPF flock (2.7.7). Carry out this passage operation not less than 5 times; verify the presence of the virus at each passage. If the virus is not found at a passage level, carry out a second series of passages. Determine the index of respiratory virulence using the unpassaged vaccine virus and the maximally passage virus that has been recovered; if the titre of the maximally passage virus is less than 10^5 EID_{50} or 10^5 $CCID_{50}$; prepare the tenfold, serial dilutions using the highest titre available.

The vaccine virus complies with the test if no indication of increase in virulence of the maximally passage 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.

Immunogenicity

A test is carried out for each route and method of administration to be recommended using in each case chickens not older than the youngest age to be recommended for vaccination. The quantity of the vaccine virus administered to each chicken is not more 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. Use for the test not less than 30 chickens of the same origin and from an SPF flock (2.7.7). Vaccinate by a recommended route not less than 20 chickens. Maintain not less than 10 chickens as controls. Challenge each chicken after 21 days by the intratracheal route with a sufficient quantity of virulent infectious laryngotracheitis virus. Observe the chickens daily for 7 days after challenge. Record the deaths and the number of surviving chickens that show clinical signs of disease. At the end of the observation period euthanise all the surviving chickens and carry out examination for macroscopic lesions: mucoid, haemorrhagic and pseudo membraneous inflammation of the trachea and orbital sinuses.

The test is not valid, if during the observation period after challenge less than 90 per cent of the control chickens die or show severe clinical signs of avian infectious laryngotracheitis or notable macroscopic lesions of the trachea and orbital sinuses or if during the period between the vaccination and challenge more than 10 per cent of the vaccinated or control chickens show notable clinical signs of disease or die from causes not attributable to the vaccine.

The vaccine virus compiles with the test if during the observation period after challenges not less than 90 per cent of the vaccinated chickens survives and shows no notable clinical signs of disease and/ or macroscopical lesions of the trachea and orbital sinuses.

Batch Tests

Identification. The vaccine, diluted if necessary and mixed with a monospecific infectious laryngotracheitis virus antiserum, no longer infects embryonated hens' eggs from an SPF flock (2.7.7) or susceptible cell cultures into which it is inoculated. Alternatively suitable validated immunochemical/ molecular biology methods can be used with the approval of competent authority.

Bacterial and fungal contamination (2.2.11). Complies with the test for sterility. Vaccines not intended for administration by injection either comply with the test for sterility prescribed in the monograph Vaccines for veterinary use or with the following test: carry out a quantitative test for bacterial and fungal contamination; carry out identification tests for microorganisms detected in the vaccine; the vaccine does not contain pathogenic micro-organisms and contains not more than 1 non- pathogenic micro-organism per dose. Any diluents supplied with the vaccine complies with test for sterility (2.2.11).

Mycoplasmas (2.7.9) Complies with the test for mycoplasmas.

Water (2.3.43). NMT 3% moisture content if it is a lyophilized formulation.

Extraneous agents (2.7.11). The vaccine complies with the tests for extraneous agents in batches for veterinary use.

Safety. Use not less than 10 chickens from an SPF flock (2.7.7) and of the youngest age recommended for vaccination. Administer by eye-drop to each chicken 10 doses of the vaccine. Observe the chickens daily for 21 days. The test is not valid if more than 20 per cent of the chickens show abnormal clinical signs or die from causes not attributable to the vaccine. The vaccine complies with the test if no chicken shows notable clinical signs of disease or dies from causes attributable to the vaccine.
Note: General Requirements shall be referred regarding omission of the batch safety test.

Virus titre. Titrate the vaccine virus by inoculation into embryonated hens' eggs from an SPF flock (2.7.7) or into suitable cell cultures (2.7.7). One dose vaccine contains not less than $10^{2.5}$ $TCID_{50}$ or EID_{50} per dose.

Potency . The vaccine complies with the requirements of the test prescribed under Immunogenicity 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.

Labelling

The label must state that (1) the vaccine is for veterinary use only; (2) the recommended routes of administration; (3) the instructions for use, such as – "reconstituted with the diluent supplied for reconstitution where applicable"(4) the animal species for which the vaccine is intended; (5) storage temperatures; (6) Batch Number, Manufacturing date and expiry date; (7) Total number of doses; (8) Minimum virus titer per dose of vaccine; (9) Dose of vaccine.