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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Duck Plague Vaccine, Live

Definition
Duck Plague Vaccine, Live is a preparation of attenuated strain of duck plague virus (alpha herpes virus anatid herpesvirus 1). This monograph applies to vaccines intended for administration to ducks for active immunisation against duck plague disease, also known as duck viral enteritis.

Production
Preparation of the vaccine. The vaccine virus is grown in SPF eggs (2.7.7) or in cell cultures. The vaccine may be freeze-dried.

Substrate for virus propagation
Embryonated hens' eggs
The vaccine virus is grown in embryonated hens' eggs or in cell cultures 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 production of vaccines for veterinary use (2.7.13). The vaccine virus is filled with suitable stabilizing agent and freeze dried.

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

Choice of vaccine virus
The vaccine virus shall be shown to be satisfactory with respect to safety (2.7.17) and efficacy (2.7.12) for the ducks for which the vaccine is intended. The following tests for safety increase in virulence and immunogenicity may be used during demonstration of safety and efficacy.

Safety

Carry out the test for each route and method of administration to be recommended for vaccination, using in each case ducks from a species considered to be the most susceptible among the species to be recommended for vaccination, not older than the minimum age to be recommended for vaccination and that do not have antibodies against duck plague virus. Use vaccine virus at the least attenuated passage level that will be present in a batch of the vaccine.
For each test performed in 10 susceptible ducks, administer to each duck a quantity of 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 ducks at least daily for 14 days. The test is not valid if more than 10 per cent of the duck show abnormal signs of disease or die from causes not attributable to the vaccine. The vaccine virus complies with the test if no duck shows abnormal signs of disease or dies from causes attributable to the vaccine virus.

Increase in virulence
Carry out the test according to general chapter (2.7.17) using domestic ducks that do not have antibodies against duck plague virus and of an age suitable for the multiplication of the virus. 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 of the five ducks in1st group by a route to be recommended and a quantity of the vaccine virus that will allow recovery of virus for the passages described below. 2 to 4 days later, take samples of liver

and spleen from each duck and pool all samples. Administer 0.1 ml of the pooled suspension by the oro-nasal or a parenteral route to each duck 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 4th passage level, repeat the passage by administration to a group of 10 ducks.

If the 5th group of ducks shows no evidence of an increase in virulence indicative of reversion during the observation period, further testing is not required. Otherwise, carry out an additional safety test and compare the clinical signs and any relevant parameters in a group of at least 10 ducks receiving the material used for the 1st passage and another similar group receiving the virus at the final passage level.

The vaccine virus complies with the test if no indication of an increase in virulence of the virus at the final passage level compared with the material used for the 1st passage is observed. If virus is not recovered after an initial passage in 5 ducks and a subsequent repeat passage in 10 ducks, the vaccine virus also complies with the test.

Immunogenicity
A test is carried out for each route and method of administration to be recommended for vaccination, using in each case domestic ducks not older than the minimum age to be recommended for vaccination. The quantity of the vaccine virus administered to each duck 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. For each test, use not fewer than 30 ducks of the same origin and that do not have antibodies against duck plague virus. Vaccinate by a route to be recommended not fewer than 20 ducks. Maintain not fewer than 10 ducks as controls. After 21 days, challenge each duck by a suitable route with a sufficient quantity of virulent duck plague virus. Observe the ducks at least daily for 14 days after challenge. Record the deaths and the number of surviving ducks that show clinical signs of disease. The test is not valid if during the observation period after challenge fewer than 80 per cent of the control ducks die or show typical signs of duck plague and/or if during the period between the vaccination and challenge more than 10 percent of control or vaccinated ducks show abnormal clinical signs of disease or die from causes not attributable to the vaccine. The vaccine virus complies with the test if during the observation period after challenge not fewer than 80 percent of the vaccinated ducks survive and show no notable clinical signs of duck plague.

Batch tests

Identification
The vaccine, diluted if necessary, is identified using a suitable method. For example, when mixed with a monospecific duck plague virus antiserum, it is no longer able to infect embryonated hens' eggs from an SPF flock (2.7.7) or susceptible cell cultures (2.7.13) into which it is inoculated. Duly validated molecular biology (NAT) technique can also be applied for identification of vaccine virus

Bacterial and fungal contamination (2.2.11). The vaccine complies with the test for sterility.
Vaccines intended for administration by injection comply with the test for sterility (2.2.11).Frozen or freeze-dried vaccines produced in embryonated eggs and not intended for administration by injection comply either with the test for sterility (2.2.11) or with the following test: carry out a quantitative test for bacterial and fungal contamination; carry out identification tests for micro-organisms 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 diluent supplied for reconstitution of the vaccine complies with the test for sterility (2.2.11).

Mycoplasmas (2.7.9)
The vaccine complies with the test for mycoplasmas.

Water (2.3.43**)** Not more than 3.0 per cent (for freeze dried vaccines only)

Extraneous agents (2.7.11**).**The vaccine is free from extraneous agents.

Safety

Use not fewer than 10 domestic ducks that do not have antibodies against duck plague virus and not older than the minimum age recommended for vaccination. Administer 10 doses of the vaccine in a volume suitable for the test by a recommended route and method to each duck. Observe the ducks at least dai1y for 21 days. The test is not valid if more than 20 percent of the ducks show abnormal c1inical signs of disease or die from causes not attributable to the vaccine. The vaccine complies with the test if no duck shows noticeable 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 (2.7.13). The vaccine complies with the test if 1 dose contains not less than 10^3 EID50 / TCID50 vaccine virus.

Potency
Inject subcutaneously each of ten healthy susceptible ducks that do not have antibodies against duck plague virus and not older than the minimum age recommended for vaccination with a volume of the reconstituted vaccine containing a quantity of the virus equivalent to the minimum dose stated on the label. Twenty one days later, challenge each of the vaccinated ducks and each of ten control ducks` of the same stock and weight range, subcutaneously with 10^2 ID_{50} of virulent duck plague virus. Observe the ducks for 21 days. None of the vaccinated ducks dies or shows any clinical symptoms of plague. The test is not valid unless the control ducks die from duck plague or show typical signs of serious infection during the observation period.

If potency test has been performed with satisfactory results on a representative batch of the vaccine, it may be omitted as a vaccine test during production on the other batches of vaccine prepared from the same seed lot.

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 volume and number of doses; (8) Minimum virus titre; (9) Dose of vaccine.