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.**

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Canine Parainfluenza Virus Vaccine, Live

Canine Parainfluenza Virus Vaccine, Live, is a freeze-dried preparation containing one or more attenuated strains of canine parainfluenza virus grown in suitable cell cultures. This monograph applies to vaccines intended for the active immunisation of dogs against respiratory signs of infection with parainfluenza virus of canine origin.

Production

Preparation of Vaccine

The virus is propagated in suitable cell culture. The viral suspension is harvested, titrated and may be mixed with a suitable stabilizing agent. The vaccine is then freeze-dried and can be used either with any suitable diluent or after reconstitution with licensed liquid canine vaccine components.

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 production of veterinary vaccines (2.7.13). If continuous cell line is used for the vaccine manufacturing, the cell line should be from seed lot system. If primary chicken cells are used for manufacturing, the Embryo or chicken should be SPF flocks (2.7.7).

Master Seed Lot

Extraneous agents. Neutralize the vaccine virus with a suitable mono specific antiserum against canine parainfluenza virus and inoculate into cell cultures known for their susceptibility to viruses pathogenic for the dog. Carry out 2 passages with an interval of 6 to 8 days. The vaccine complies with the test if no cytopathic effect develops.

Identification

When inoculated into dogs, the vaccine stimulates the production of specific neutralizing antibodies against canine parainfluenza virus determined by suitable serological tests. Alternatively, suitable validated immunochemical/ molecular biology methods can be used with the approval of competent authority.

Choice of vaccine strain. A reference strain obtained from an authentic source shall be used for the vaccine production. The master seed which has been established as pure, safe and immunogenic for the species for which it is intended shall be used for vaccine production.

Test for reversion to virulence. Administer intranasally and by a recommended route to each of two dogs, 5 to 7 weeks old and which do not have antibodies against parainfluenza virus of 'quantity of virus that will allow recovery of sages described below. Use vaccine virus at the least attenuated passage level that will be present in a batch of the vaccine. Collect nasal swabs from each dog daily from 3 to 10 days after inoculation. Inoculate the suspension from the swabs into suitable cell cultures to verify the presence of virus. Use the suspension from the swabs that contain the maximum amount of virus and administer intranasally 1 ml of the

suspension into each of two other puppies of the same age and susceptibility. This operation is then repeated at least 5 times. If the virus is not recovered at a given passage level, a second series of passages is carried out. Inoculate virus from the highest recovered passage level to not fewer than five dogs, observe for 21 days and compare any reactions that occur with those seen in the test for safety described above. There is no indication of an increase in virulence as compared with the non-passaged virus.

Safety.

Carry out the test for each route and method of administration to be recommended for vaccination. Use vaccine virus at the least attenuated passage level that will be present in a batch of the vaccine. For each test, use not fewer than five dogs of the minimum age to be recommended for vaccination and that do not have antibodies against parainfluenza virus of canine origin. Administer to each dog 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 dogs at least daily for 21 days.

The vaccine virus complies with the test if no dog shows abnormal local or systemic reactions, signs of disease or dies from causes attributable to the vaccine virus

Immunogenicity.

Use method A or B

A. Inject each of eight susceptible dogs, between 8 and 14 weeks old that have been previously tested and shown to be preferably free from canine parainfluenza virus antibodies with a dose of the vaccine stated on the label. Use another two dogs of the same age group as unvaccinated controls. Observe the animals for a further 21 days. Challenge all the dogs with sufficient quantity of a suspension of canine parainfluenza virus by intranasal route. Observe the animals for further 14 days. Collect nasal swabs from day 5 to 10 days after challenge and test the samples for the presence of excreted virus. Use a scoring system for recording the incidence of coughing in each dog. The control dogs show typical signs of coughing or excretion of the virus. The vaccine complies with the test if the scores for coughing or virus excretion in the vaccinated dogs are significantly lower than the controls. If the potency test has been performed with satisfactory results on a representative batch of the vaccine from the seed lot, it may be omitted as a routine control test during production on other batches of the vaccine prepared from the same seed lot.

B. Inoculate six dogs of the minimum age and free of canine parainfluenza antibodies with a dose and route of administration of the vaccine as stated on the label. If the schedule recommends a booster dose, administer the booster dose by the same route as performed in the primary vaccination and draw blood samples 14 days alter from each animal for estimation of antibody titres. Collect the serum from the blood samples and inactivate them at 56° for 30 minutes. After inactivation add 0.9 ml of 20 per cent kaolin to 0.1ml of each serum sample. Place the sample on vortex mixer for 20 minutes at room temperature. After vortexing centrifuge the sample at 2000 rpm for 10 minutes and collect the supernatant. Dispense 25µl of saline to all the wells of a 96 well U bottom plate. Add 25µl of each serum sample to evaluate potency. Carry out two-fold serial dilutions and add 25µl of Canine Para influenza virus containing 4 HA units to all the wells except cell control. Incubate the mixture at 37° for 30 minutes. After incubation add 50µl of 1 per cent chicken RBC to all the wells including cell control. Incubate the plate at room temperature (20° to 25°) for 60 minutes. The last dilution of serum that fully inhibits the Haemagglutination which is indicated by button formation is considered as the HI titre. The seed lot complies for the potency of the geometric mean of the sera tested shows not less than 32 HI titres.

Batch Tests

Identification

The vaccine complies with the requirements of test mentioned under section of master seed lot. Alternatively, suitable validated immunochemical/ molecular biology methods can be used with the approval of competent authority.

Mycoplasmas (2.7.8). Complies with the test for mycoplasma.

Bacterial and Fungal Contamination (2.2.11) . Complies with the test for sterility.

Water (2.3.43). Not more than 3.0 per cent.

Virus titre. Not less than 10^3 $TCID_{50}$/$CCID_{50}$ per dose, determining the titre of the vaccine in a suitable cell culture with suitable medium or one dose of vaccine contains not less than quantity of virus equivalent to the minimum virus titre stated on the label.

Safety. Inject each of two susceptible dogs, between 8 and 14 weeks old, free from canine parainfluenza virus antibodies with a dose of the vaccine reconstituted with the sterile diluents equivalent to 10 times the dose and by the route stated on the label. Observe the animals for 14 days. None of the dogs shows any systemic or local reactions.

Note: General Requirements shall be referred regarding omission of the batch safety test.

Potency. The vaccine complies with the requirements of test mentioned under immunogenicity when administered 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 of the vaccine using a vaccinating dose containing not more than the minimum titre stated on the label. The virus titer is considered for a routine batch release provided the traceability of the vaccine strains used is from the same master seed.

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 or number of doses; (8) Minimum virus titre (9) Dose of vaccine