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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Further follow-up action as required.	

Canine Adenovirus Vaccine (Live)

Canine Infectious Tracheobronchitis Vaccine, Live;
Canine Adenovirus-2 (CAV-2) Vaccine, Live

Canine Adenovirus Vaccine, Live is a freeze-dried preparation containing one or more attenuated strains of canine adenovirus-2 (CAV-2). This monograph applies to vaccines intended for the active immunization of dogs against canine contagious hepatitis and/or respiratory disease caused by canine adenovirus.

Production

Preparation of the vaccine. The virus is grown in suitable cell culture. The cell culture complies with the requirements for cell culture for production of veterinary vaccines. The harvested virus culture is titrated and may be mixed with a suitable stabilizing solution. The vaccine is freeze-dried and can be used with any suitable diluent or used after reconstitution with licensed liquid canine vaccine components.

Choice of vaccine virus. A reference strain obtained from an authentic source shall be used for the vaccine production. However, a suitable vaccine strain approved by competent authority may also be used if the strain is shown to be satisfactory with respect to safety and immunogenicity for the animals for which the vaccine is intended**.** 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. The vaccine is shown to be satisfactory with respect to safety (2.7.17) and efficacy (2.7.12) for the dogs for which it is intended.

Master Seed Lot

The following tests for identity, safety, test for reversion to virulence and immunogenicity may be used during the demonstration of safety and efficacy with master seed.

Identification

Identity shall be established by the development of specific neutralizing antibodies upon administration of the vaccine in dogs. Viral genome identification on the final lot by is acceptable as identity test and can be used in the routine batch release tests also.

The seed lot complies with the tests for identity and a batch of vaccine prepared from the master seed lot should comply with full range of control tests, i.e. safety and immunogenicity.

Safety. Carry out the test for each route and methods of administration to be recommended for vaccination. Use vaccine virus at least attenuated passage level that will be present between the master seed lot and a batch of the vaccine. Use not less than five dogs of the minimum age recommended for vaccination that do not have antibodies

against canine adenovirus. Administer each dog a quantity of vaccine virus equivalent to not less than 10 times of the maximum virus titre likely to be contained in one dose of the vaccine. Observe the dog daily for 14 days. The vaccine complies with the test if no dogs show abnormal local and/ or systemic reactions, sign of diseases or dies from causes attributed to the vaccine virus.

Test for reversion to virulence. The test consists of the administration of the vaccine virus at least attenuated passage level that will be present between the master seed lot and a batch of the vaccine to two dogs, 5 to 7 weeks old that do not have antibodies against canine adenovirus.

Administer to each dog by a route to be recommended a quantity of vaccine virus that will allow recovery of virus for the passage described below. Administer the virus by the route recommended for the vaccination most likely to lead to reversion of virulence. After 4 to 6 days of administration, euthanize the puppies and prepare a suspension from nasal and pharyngeal mucosa, tonsil, lungs and spleen and if they are likely to contain virus, liver and kidney of each dog and pool the sample. Administer 1 ml of the pooled sample by suitable route to each of the two dogs of same age. Carry out this passage operation not less than 5 times, verify the presence of virus in each passage. If the virus is not found at a passage level, carry out a second series of passage. Carry out the test for safety using unpassaged vaccine virus and maximally passage virus that has been recovered. The vaccine virus complies with the test if no indication of increased in virulence of the maximally passage virus compared with the unpassaged virus is observed. If virus is not recovered at any passaged level in the first and second series of passages, the vaccine virus also complies with the test.

Immunogenicity. A test is carried out of each route and method of administration to be recommended for vaccination using dogs of the minimum age to be recommended. The quantity of vaccine virus to be administered to each dog is not more than the minimum 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 vaccine.

Vaccine intended to protect against respiratory signs. Use for the test not fewer than twenty dogs that do not have antibodies against canine adenoviruses. Vaccinate not fewer than ten dogs, according to the schedule to be recommended. Maintain not fewer than ten dogs as controls. Challenge each dog after 20-22 days by the intranasal route with a quantity of a suspension of virulent Canine Adenovirus 2 sufficient to cause typical signs of respiratory disease in a dog that does not have antibodies against Canine Adenoviruses. Observe the dogs at least daily for 10 days after challenge. Record the incidence of signs of respiratory and general disease in each dog (for example, sneezing, coughing, nasal and lachrymal discharge, loss of appetite). Collect nasal swabs or washings from each dog daily from days 2 to 10 after challenge and test these samples to determine the presence and titre of excreted virus.

The vaccine complies with the test if there is a notable decrease in the incidence and severity of signs and in virus excretion in vaccinates compared to controls.

Batch test

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

Extraneous agents (2.7.19)**.** The vaccine is free from extraneous agents.

Virus titre. Not less than 10^3 $TCID_{50}$ of the virus 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 which protects the animal as established using the test mentioned under immunogenicity.

Mycoplasmas (2.7.8)**.** The vaccine complies with the test for freedom from mycoplasmas. Alternatively, molecular techniques for detection of mycoplasma nucleic acid are acceptable batch release test after proper validation.

Bacterial and fungal contamination (2.2.11)**.** The vaccine, including where applicable the diluent supplied for reconstitution, complies with the test for sterility.

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

Safety. Inject intramuscularly 10 times the minimum dose stated on the label into each of two dogs of the minimum age recommended for vaccination. Observe the animals for 21 days. None of the dogs shows abnormal local or systemic reactions or dies of any causes attributable to the vaccine.

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

Potency. The vaccine complies with the requirements of the immunogenicity test mentioned under section of master seed lot.

Labelling. The label must state that (1) the vaccine is for veterinary use only; (2) the recommended routes and dose of administration; (3) the instructions for use, such as – "the preparation should be shaken well before use or reconstituted with the diluent supplied for reconstitution where applicable"; (4) the virus titer per dose; (5) storage temperatures; (6) batch number, manufacturing date and expiry date; (7) the minimum dose; (8) total volume and number of doses.