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.	

Infectious Canine Hepatitis Vaccine, Inactivated

Canine Adenovirus Vaccine-1, Inactivated

Infectious Canine Hepatitis Vaccine, Inactivated, is a preparation of one or more suitable strains of canine contagious hepatitis (CAV 1) virus, inactivated in such a manner that its immunogenic activity is retained. It may be freeze dried preparation or a liquid preparation containing a suitable adjuvant. This monograph applies to vaccines intended for the active immunisation of dogs against Infectious Canine Hepatitis infection.

Production

Preparation of the vaccine. The virus is grown in suitable cell culture system. The cell culture complies with the requirements for cell culture for production of veterinary vaccines (2.7.13). The vaccine may contain a suitable adjuvant.

Test on Master Seed Lot

Extraneous agents. The master seed lot complies with the test for extraneous agents (2.7.19).

Identification

When inoculated into dogs, the development of specific neutralizing antibodies against canine adenovirus-1 can be demonstrated by suitable serological tests.

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 shall be used for vaccine production.

Safety. Carry out the test for each route and methods of administration to be recommended for vaccination. Use a batch of vaccine containing not less than the maximum potency that may be expected in a batch of vaccine. Use not less than eight dogs of the minimum age to be recommended for vaccination and that do not have antibodies against canine adenovirus-1. Administer double dose of vaccine prepared from master seed to each dog. Observe the dogs daily at least until 14 days post immunization. The vaccine complies with the test, if no dogs show abnormal local or/ and systemic reactions, sign of diseases or dies from causes attributed to the vaccine virus.

Immunogenicity. Inject each of six healthy susceptible dogs, between 8 to 14 weeks old that have been previously tested and shown to be free from canine contagious hepatitis virus antibodies, with the minimum dose and the route stated on the label. If a second dose is recommended, the second dose shall be administered at the time specified on the label. For single dose schedule, collect blood after 21 days or for 2 dose schedules, collect blood 14 days after booster from each dog. Inactivate each serum sample by heating at 56° for 30 minutes and prepare serial dilutions in a suitable medium. Add to each dilution an equal volume of serum-virus suspension containing approximately 10^2 $TCID_{50}$. Incubate the mixture at 37° for 1 hour. Add suitable cell culture with minimum of four replicates for each dilution and incubate at 37° for 5 days and calculate the antibody titre. Vaccine complies with the test; if serum from each vaccinated dog contains not less than 80 SN_{50} per 0.05 ml of serum tested.

If any animal fails to respond to the vaccine or does not produce the stated antibody titre, repeat the test using fresh set of dogs as per the above procedure. In the repeat test, the vaccine complies to the potency if it meets the above criteria otherwise the vaccine does not comply to the potency requirement.

Manufacturer's tests

Identification

Vaccine complies with the requirements of the test mentioned under section of master seed lot. Identification by validated molecular / immunochemical methods/serological methods is acceptable.

Residual live virus. The test for residual live virus is carried out. The quantity of inactivated bulk antigen used is equivalent to or not less than 10 doses of the vaccine. The test sample is inoculated into susceptible cell lines, incubated at 37° and observed for 4 to 6 days and a second passage is carried out with the sample collected after the first passage. The inactivated bulk antigen complies for the freedom from residual live virus if no cytopathic effect is observed in both the passages.

Potency. The vaccine complies with the immunogenicity test as mentioned under master seed lot**.**

Water (2.3.43). Not more than 3.0 per cent (for freeze dried vaccine only).

Safety: Inject each of two healthy susceptible dogs in the recommended age group free from canine contagious hepatitis virus antibodies with a quantity equivalent to 2 doses by the route stated on the label. Observe the animals for 14 days. No abnormal systemic or local reaction occurs.

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

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

Potency. Inject each of two healthy susceptible dogs, between 8 to 14 weeks old that have been previously tested and shown to be free from canine contagious hepatitis virus antibodies, with the minimum dose and the route stated on the label. If a second dose is recommended, the second dose shall be administered at the time specified on the label. For single dose schedule, collect blood after 21 days or for 2 dose schedule, collect blood 14 days after booster from each dog. Inactivate each serum sample by heating at 56° for 30 minutes and prepare serial dilutions in a suitable medium. Add to each dilution an equal volume of serum-virus suspension containing approximately 10^2 $TCID_{50}$. Incubate the mixture at 37° for 1 hour. Add suitable cell culture with minimum of four replicates for each dilution and incubate at 37° for 5 days. Examine each culture for evidence of specific cytopathic effect and calculate the antibody titer. Vaccine complies with the test; if serum from each vaccinated dog contains not less than 80 SN_{50} per 0.05ml of serum tested.

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 – "the preparation should be shaken well before use or 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) Strain of virus used in preparing the vaccine