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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Canine Coronavirus Vaccine, Inactivated

Canine Coronavirus Vaccine, Inactivated, is a preparation containing canine coronavirus, inactivated in such a manner that its immunogenic activity is retained. It may be issued as a liquid or as a freeze-dried preparation to be reconstituted with a suitable liquid immediately before use. The liquid vaccine may contain a suitable adjuvant. This monograph applies to vaccines intended for the active immunization of dogs against canine coronavirus.

Production

Preparation of the Vaccine

The virus is grown in suitable cell culture systems. 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.

Substrate for virus propagation

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.

Test on Master Seed Lot

Identification. When inoculated into dogs, the vaccine stimulates the production of specific neutralizing antibodies against canine coronavirus as determined by suitable serological tests.

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

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. The vaccine is shown to be satisfactory with respect to safety (2.7.17) and efficacy (2.7.13) for the animals for which it is intended.

Safety. Carry out the test for each route and method of administration to be recommended for the vaccination. Inject double dose of the vaccine prepared from the master seed to ten healthy dogs in the age group and by the route stated on the label. Observe the animals for 14 days and no abnormal systemic or local reaction occurs. Such animals used in the test shall be preferably free of canine coronavirus antibodies.

Immunogenicity. Use method A or B

A. Inject each of 6 healthy susceptible dogs between 8 and 14 weeks old having antibody titre less than 6 SN_{50} per 50 µl of serum with a representative batch with the dose recommended on the label. Use 2 dogs of the same age as control. If a second dose is recommended, the second dose shall be administered at the time specified on the label. Not less than 14 days booster or not less than 21 days after single vaccination, challenge all the animals through appropriate route with a virulent virus strain of canine coronavirus. Observe the animals for 14 days. The vaccine complies with the test if the 5 vaccinated dogs remain healthy and show no sign of disease. The test is not valid unless the controls die or show clinical signs of canine coronavirus infection

B. Inject each of eight healthy dogs free of canine corona antibodies of the age recommended for the vaccination with a dose stated on the label and the routes recommended as stated on the label. Repeat the injection after l4 days with the same dose and route of administration in each dog. 14 days after the second injection collect blood samples and obtain the serum from each dog separately.

Inactivate each serum by heating at 56° for 30 minutes. Examine the serum samples for antibodies by the following method. Prepare 2-fold serial dilutions of serum in a medium suitable for canine cells. Add to each dilution an equal volume of a virus suspension containing 100 $TCID_{50}$ per ml and incubate the mixtures at 37° for 1 hour. Inoculate a suitable volume of canine cells into at least 4 replicates of serum virus mixtures and incubate at 37° for 4 days. Examine for evidence of specific cytopathic effects and calculate the antibody titre. The vaccine complies with the test if the mean antibody titre is not less than 45 SN_{50} per 50 µl of serum.

Manufacturer's 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.

Residual Live virus. The test for residual live virus is carried out in suitable cell culture spread over two passages lasting for 4 to 6 days for each passage. The quantity of inactivated virus harvest used is equivalent to or not less than 10 times doses of the vaccine. The inactivated virus harvest complies with the test if no live virus is detected

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.

Alternatively a validated methods can be used, the criteria for acceptance being set with reference to a batch of vaccine that has been given satisfactory results in the test described under potency.

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.

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 coronavirus antibodies with a quantity equivalent to 2 doses by the route stated on the label. Observe the animals for 14 days. The vaccine complies with the test if 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. *Carry out either the test A or B.*

A. Inject each of five healthy susceptible guinea-pigs, each weighing between 350 and 450 g, with half the minimum dose and by the route stated on the label. Repeat the injection after l4 days. 14 days after the second injection collect blood samples and obtain the serum from each guinea-pig separately. Inactivate each serum by heating at 56° for 30 minutes. Examine the serum samples for antibodies by the following method.

Prepare 2-fold serial dilutions of serum in a medium suitable for canine cells. Add to each dilution an equal volume of a virus suspension containing approximately 10^2 $TCID_{50}$ and incubate the mixtures at 37° for 1 hour. Inoculate a suitable volume of canine cells into at least 4 replicates of serum virus mixtures and incubate at 37° for 4 days. Examine for evidence of specific cytopathic

effects and calculate the antibody titre. The vaccine complies with the test if the mean antibody titre is not less than 45 SN_{50} per 50 µl of serum.

B. Inject each of two healthy susceptible dogs between 8 and 14 weeks old having antibody titre less than 6 SN_{50} per 50µl of serum with a representative batch with the dose recommended 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 two dose schedule collect blood 14 days after booster from each dog. Inactivate each serum sample by heating at 56° for 30 minutes. Examine the serum sample individually for the neutralizing antibodies. Prepare 2-fold serial dilutions of the serum in a suitable for canine cells. Add to each dilution an equal volume of a virus suspension containing approximately 10^2 $TCID_{50}$ and incubate the mixture at 37° for 1 hour. Inoculate a suitable volume of canine cells into at least 4 replicates of serum virus mixture and incubate at 37° for 4 days. Examine for evidence of specific cytopathic effects and calculate the mean antibody titre. Vaccine complies with the test, if the mean antibody titre in vaccinated dogs is not less than 45 SN_{50} per 50 µl of serum.

Labelling

The label must state that (1) the liquid preparation should not be allowed to freeze; (2) that the vaccine should be used immediately after reconstitution for freeze dried vaccine (3) the vaccine is for veterinary use only; (4) the recommended routes of administration; (5) the instructions for use, such as – "the preparation should be shaken well before use or reconstituted with the diluent supplied for reconstitution where applicable" (6) the animal species for which the vaccine is intended; (7) storage temperatures; (8) Batch Number, Manufacturing date and expiry date; (9) Precautions in pregnant [animals] (If applicable); (10) Total volume and number of doses; (11) Dose of vaccine.