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.	

Canine Leptospirosis Vaccine, Inactivated

Canine Leptospirosis Vaccine, Inactivated is a suspension of inactivated whole organisms and/or antigenic extract(s) of one or more suitable strains of Leptospira interrogans: serovar canicola, serovar icterohaemorrhagiae or any other epidemiologically appropriate serovar, inactivated and prepared in such a way that adequate immunogenicity is maintained. This monograph applies to vaccines intended for the active immunization of dogs against leptospirosis.

Production

Choice of Vaccine strain. A reference strain of Leptospira serovars/strains obtained from an authentic source should be used. However, a local isolate from a particular area may also be used if the strain is shown to be satisfactory with respect to immunogenicity for the animals for which the vaccine is intended. 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.

Preparation of Vaccine. Leptospira serovars/strains used for production are grown in a suitable medium and the whole cultures are inactivated by addition of formaldehyde. Each strain is cultivated separately. During production, parameters such as purity is monitored by suitable methods. A suitable adjuvant may be added to the inactivated cultures. The following tests for safety and immunogenicity may be used during the demonstration of safety and efficacy.

Master Seed Lot

Identification. Carry out suitable validated molecular/serological based test for identification.

Inactivation. Carry out a test for inactivation by inoculation in specific medium. Inoculate 1 ml of the preparation into 100 ml of the medium, incubate at 28° to 30° for 14 days, subculture into a further quantity of the medium and incubate both media at 28° to 30° for 14 days: the bulk antigen complies with the test if no growth occurs in either medium. At the same time, carry out a control test by inoculating a further quantity of the medium with the vaccine together with a quantity of a culture containing approximately 100 leptospirae and incubating at 28° to 30°, growth of leptospirae occurs within 14 days. Above mentioned positive control in the test which should show the growth of leptospira.

Safety. Carry out the test for each route and method of administration to be recommended for vaccination and in dogs for which the vaccine is intended, using in each case dogs not older than the minimum age 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 2 dogs of the minimum age recommended for vaccination and which do not have antibodies to the leptospira serovar (s) present in the vaccine. Administer 2 doses of the vaccine having maximum potency to each dog by a recommended route. Observe the animals for 14 days. Record body temperatures the day before each vaccination, at vaccination, 4 hours later and daily for 4 days. The vaccine complies with the test if there is no untoward abnormal

local or systemic reactions except slight swelling at the site of inoculation which subsides in 4 to 5 days or show signs of disease or dies from causes attributable to the vaccine.

Immunogenicity. Carry out a separate immunogenicity test for each serotype if the vaccine is prepared with different serotypes. Inject each of 5 hamsters not more than 3 months old, the animals being drawn from the same stock, subcutaneously with 1/40 of the dose of the vaccine stated on the label for dogs. Use an equal number of animals of the species used for the test as controls. After 15 to 20 days inject intraperitoneally into each of the vaccinated and control animals an adequate dose of virulent culture of leptospirae of the serotype used to prepare the vaccine or a suspension of liver or kidney tissue obtained from animals infected with the serotype used to prepare the vaccine. Observe the animals for 14 days after the injection. Not less than four of the control animals die showing typical leptospira infection. Not less than four of the vaccinated animals remain in good health for not less than 14 days after the death of the four control animals.

Manufacturer's Tests

Identification. The vaccine complies with the requirements of test mentioned under section of master seed lot**.**

Potency. The vaccine complies with the test as mentioned under immunogenicity.

If leptospira from more than one serovar (for example L. interrogans serovar canicola and serovar icterohaemorrhagiae) has been used to prepare the vaccine, carry out a batch potency test for each serovar against which protective immunity is claimed on the label. Use for the test 10 healthy hamsters not more than 3 months old, that do not have antibodies against the principal serovars of L. interrogans (icterohaemorrhagiae, canicola, grippotyphosa, sejroe, hardjo, hebdomonadis, pomona, australis and autumnalis) and which have been obtained from a regularly tested and certified leptospira-free source. Administer 1/40 of the dose for dogs by the subcutaneous route to 5 hamsters. Maintain 5 hamsters as controls. Challenge each hamster after 15-20 days by the intraperitoneal route with a sufficient quantity of a virulent culture of leptospirae of the serovar against which protective immunity is claimed on the label. The vaccine complies with the test if not fewer than 4 of the 5 control hamsters die showing typical signs of leptospira infection within 14 days of receiving the challenge suspension and if not fewer than 4 of the 5 vaccinated hamsters remain in good health for 14 days after the death of 4 control hamsters.

Residual live bacteria. Carry out a test for residual live leptospirae by inoculation of a specific medium. Inoculate 1 ml of the bulk antigen into 100 ml of the medium. Incubate at 28°-30° for 14 days, subculture into a further quantity of the medium and incubate both media at 28°-30° for 14 days: the bulk antigen complies with the test if no growth occurs in either medium. At the same time, carry out a control test by inoculating a further quantity of the medium with the bulk antigen together with a quantity of a culture containing approximately 100 leptospirae and incubating at 28°- 30°. The test is not valid if growth of leptospirae does not occur within 14 days in the control test.

Batch Tests

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

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

Potency. The vaccine complies with the requirements of the potency test mentioned under manufacturers test when administered by a recommended route and method.

Safety. The vaccine complies with the tests for safety mentioned under master seed lot.
Note: General Requirements shall be referred regarding omission of the batch safety test.

Labelling.

The label must state that (1) the vaccine is for veterinary use only; (2) name of the strains incorporated in the vaccine; (3) the adjuvant used if any; (4) dose and 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 or the liquid preparation should not be allowed to freeze or that the vaccine should be used immediately after reconstitution for freeze dried vaccine 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;