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

Description	**Details**
Document version	1.0
First Draft published on IPC website for public comments	24th July 2024
Last Date for Comments	6th September 2024
Monograph Revision proposed for Inclusion in	IP 2026
Tentative effective date of proposed amendment	January, 2026
Draft revision published on IPC website for public comments	6th January 2025
Further follow-up action as required.	

Infectious Avian Encephalomyelitis Vaccine, Live

Encephalomyelitis Vaccine Live: Epidemic Tremor Vaccine Live

Infectious Avian Encephalomyelitis Vaccine, Live is a freeze-dried preparation of an attenuated strain of Infectious avian encephalomyelitis virus.

This monograph applies to vaccines intended for administration to non-laying chickens to protect passively their future progeny and/or to prevent vertical transmission of virus via the egg.

Production

Preparation of the vaccine

The vaccine virus is grown in embryonated hens' SPF eggs or in cell cultures.

Substrate for virus propagation

Embryonated hens' SPF eggs. If the vaccine virus is grown in embryonated hens' SPF 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 the production of vaccines for veterinary use (*2.7.13*).

Seed lots

Extraneous Agent The master seed lot complies with the tests for extraneous agents (2.7.10).

Choice of vaccine virus The vaccine virus shall be shown to be satisfactory with respect to safety (2.7.17) and efficacy (2.7.12) for the chickens for which it is intended. The following tests for safety, test for reversion to virulence and immunogenicity may be used during the demonstration of safety and efficacy.

Identification. The master seed is identified using a suitable method as described below. Carry out either the test A or B.

a) Inoculate 0.1 ml of the undiluted reconstituted vaccine into the yolk sac of SPF embryonated eggs, between 5 to 6 days old. Keep them in an incubator and transfer to the setter for hatching. Observe the hatched chickens for 7 days. Not less than 50 per cent of the chickens show the typical symptoms characteristic of infectious avian encephalomyelitis-like weakness or paralysis of legs, sitting posture on hock joints and tremors.

b) When mixed with a monospecific avian encephalomyelitis virus antiserum, it is no longer able to infect embryonated hens' eggs from an SPF flock (2.7.7) or susceptible cell cultures (2.7.13) into which it is inoculated.

Alternatively suitable validated immunochemical/ molecular biology methods can be used with the approval of competent authority.

Safety. Carry out the test for each route and method of administration to be recommended for vaccination using chickens not older than the minimum age 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 10 chickens from an SPF flock (2.7.7). Administer to each chicken 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 chickens at least daily for 21-days. The test is not valid if non-specific mortality occurs. The vaccine virus complies with the test if no chicken shows abnormal signs of disease or dies from causes attributable to the vaccine virus.

Test for reversion to virulence. Carry out the test according to general chapter using 1-day-old chickens from an SPF flock (2.7.7). If the properties of the vaccine virus allow sequential passage through 5-groups with 10 birds per group via natural spreading, this method may be used, otherwise passage as described below is carried out. Administer to each chicken of the 1st group by a route and method to be recommended a quantity of the vaccine virus that will allow recovery of virus for the passages described below. 5-7 days later, prepare a suspension from the brain of each chicken and pool these samples. Administer a suitable volume of the pooled samples by the oral route to each chicken of the next group. Carry out this passage operation not fewer than 4 times; verify the presence of the virus at each passage. If the virus is not found at a passage level, repeat the passage by administration to a group of 10 chickens. If the 5th group of chickens shows no evidence of an increase in virulence indicative of reversion during the observation period, further testing is not required. Otherwise, carry out an additional safety test and compare the clinical signs and any relevant parameters in a group of at least 10 chickens receiving the material used for the 1st passage and another similar group receiving the virus at the final passage level.

The vaccine virus complies with the test if no indication of an increase in virulence of the virus recovered for the final passage compared with the material used for the 1st passage is observed. If virus is not recovered after an initial passage in 5 chickens and a subsequent repeat passage in 10 chickens, the vaccine virus also complies with the test.

Immunogenicity . If the vaccine is recommended for passive protection of future progeny carry out test A. If the vaccine is recommended for prevention of vertical transmission of virus via the egg, carry out test B. Test is carried out for each route and method of administration to be recommended, using in each case chickens from an SPF flock (2.7.7) not older than the minimum age to be recommended for vaccination. The quantity of the vaccine virus administered to each chicken is not greater 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 the vaccine.

A) Passive immunity in chickens

Vaccinate not fewer than 10 breeder chickens from an SPF flock (2.7.7). Maintain separately not fewer than 10 breeder chickens of the same age and origin as controls. At the peak of lay, hatch not fewer than 25 chickens from eggs from vaccinated breeder chickens and 10 chickens from non-vaccinated breeder chickens. At 2 weeks of age, challenge each chicken by the intracerebral route with a sufficient quantity of virulent avian encephalomyelitis virus. Observe the chickens at least daily for 21 days after challenge. Record the deaths and the number of surviving chickens that show clinical signs of disease.

The test is not valid if:

– during the observation period after challenge fewer than 80 per cent of the control chickens die or show severe clinical signs of avian infectious encephalomyelitis,

– and/or during the period between the vaccination and challenge more than 20 per cent of control or vaccinated chickens show abnormal clinical signs or die from causes not attributable to the vaccine.

The vaccine virus complies with the test if during the observation period after challenge not fewer than 80 per cent of the progeny of vaccinated chickens survive and show no notable clinical signs of disease.

B) Passive immunity in embryos

Vaccinate not fewer than 20 breeder chickens from an SPF flock (2.7.7). Maintain separately not fewer than 10 breeder chickens of the same age and origin as controls. At the peak of lay, incubate not fewer than 36 eggs from the 2 groups, vaccinated and controls, and carry out an embryo sensitivity test. On the sixth day of incubation inoculate 100 EID_{50} of the Van Roekel strain of avian

encephalomyelitis virus into the yolk sacs of the eggs. 12 days after inoculation examine the embryos for specific lesions of avian encephalomyelitis (muscular atrophy). Deaths during the first 24 hour are considered to be non-specific. The test is not valid if fewer than 80 per cent of the control embryos show lesions of avian encephalomyelitis. The test is not valid if fewer than 80 per cent of the embryos can be given an assessment. The vaccine virus complies with the test if not fewer than 80 per cent of the embryos in the vaccinated group show no lesions of avian encephalomyelitis.

Batch tests
Identification
The vaccine complies with the test mentioned under Production.

Sterility (2.2.11). Vaccines intended for administration by injection comply with the test for sterility (2.2.11).Vaccines not intended for administration by injection either comply with the test for sterility (2.2.11) or with the following test: carry out the quantitative test for bacterial and fungal contamination; carry out identification tests for microorganisms detected in the vaccine; the vaccine does not contain pathogenic microorganisms and contain not more than 1 non pathogenic microorganisms per dose.
Any diluent supplied for reconstitution of the vaccine compiles with the test for sterility (2.2.11).

Mycoplasmas (2.7.9) Complies with the test for mycoplasmas.

Water (2.3.43) Not more than 3.0 per cent.

Extraneous agents (2.7.11) The vaccine is free from extraneous agents.

Safety . Administer ten SPF chickens (2.7.7, Table 3) or healthy susceptible chickens by ten doses of the vaccine by the recommended route. Observe the chickens for 21 days. No chicken develops signs of the disease or dies from causes attributable to the vaccine. Repeat the test if more than two chickens die from causes not attributable to the vaccine during the observation period.

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

Virus titre. Not less than $10^{2.5}$ $TCID_{50}/EID_{50}$ of the virus per dose, determining the titre of the virus in cell culture derived from SPF eggs (2.7.7) or by inoculation into the yolk sac of SPF embryonated hen eggs (2.7.7), between 5 to 6 days old.

Potency. Depending on the indications, the vaccine complies with the requirements of 1 or both of the tests prescribed under Immunogenicity, when administered by a recommended route and method. Virus titer can replace in-vivo potency testing during batch test if a correlation of virus titer and potency is established.
If potency test has been performed with satisfactory results on a representative batch of the vaccine, using one vaccinating it may be omitted as a vaccine test during production on the other batches of vaccine prepared from the same seed lot.

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 temperature; (6) Batch Number, Manufacturing date and expiry date; (7) Total volume and number of doses; (8) Minimum virus titre; (9) Dose of vaccine