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 Bursal Disease Vaccine, Inactivated

Infectious Bursal Disease Vaccine, Inactivated consists of an emulsion or a suspension of a suitable strain/s of infectious bursal disease virus which has been inactivated in such a manner that immunogenic activity is retained.

Production

Preparation of the vaccine

The virus is propagated in fertilized eggs obtained from healthy flock (2.7.18) or in suitable cell culture derived from SPF eggs (2.7.13).The vaccine may contain one or more suitable adjuvant.

Substrate for virus propagation

Embryonated hens' eggs. If the vaccine virus is grown in embryonated hens' eggs, they are obtained from suitable healthy flocks (2.7.18) or flocks free from specified pathogens (2.7.7)

Cell cultures. If the vaccine is grown in cell cultures, it is grown on suitable cell culture derived from SPF eggs and they comply with the requirements for cell cultures for the production of vaccines for veterinary use (2.7.13) eggs.

Seed lots

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

Identification

Protects susceptible chickens against infectious bursal disease by producing specific antibodies on inoculation which can be demonstrated by suitable validated serological test. Potency test also serves the purpose of identity.

Choice of vaccine composition

The vaccine is shown to be satisfactory with respect to safety (2.7.17) and efficacy (2.7.12) for the birds for which it is intended.
The following tests for safety and immunogenicity may be used during the demonstration of safety and efficacy.

Safety. The test is carried out for each route 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. For each test, use not fewer than 10 chickens not older than the minimum age to be recommended for vaccination and from a flock free from specified pathogens (SPF) (2.7.7) or healthy susceptible chickens (2.7.18). Administer by a route and method to be recommended to each chicken double dose of the vaccine. Observe the chickens daily for at least 21 days after the administration of the vaccine. The test is not valid if non-specific mortality occurs. The vaccine complies with the test if no chicken shows abnormal signs of disease or dies from causes attributable to the vaccine.

Immunogenicity . A 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) or healthy susceptible chickens (2.7.18) and not older than the minimum age to be recommended for vaccination (close to the point of lay). The dose of vaccine administered to each chicken contains not more than the minimum potency to be stated on the label.
Where a challenge test is to be carried out, the following test may be used. Use 2 groups of not less than 20 hens treated as follows:
– group A: unvaccinated controls;
– group B: vaccinated with inactivated infectious bursal disease vaccine. Serum samples are collected from each unvaccinated control (group A) hen just before administration of the vaccine, 4-6 weeks later, and at the time of egg collection for hatching.

If a serological test is to be carried out for demonstration of immunogenicity by other routes, serum samples are also collected from each vaccinated (group B) hen at the time of egg collection for hatching. The antibody response is measured in a serum-neutralization test. Eggs are collected for hatching not less than 5 weeks after vaccination and the test described below is carried out with chickens at least 3 weeks old from that egg collection. 25 chickens from vaccinated (group B) hens and 10 control chickens of the same breed and age from unvaccinated (group A) hens are challenged with an eye-drop application of a quantity of a virulent strain of avian infectious bursal disease virus sufficient to produce severe signs of disease, including lesions of the bursa of Fabricius, in all unvaccinated chickens. 3-4 days after challenge, the bursa of Fabricius is removed from each chicken. The bursae are examined for evidence of infection by histological examination and by testing for the presence of avian infectious bursal disease antigen by a suitable method. The vaccine complies with the test if 3 or fewer of the chickens from group B hens show evidence of avian infectious bursal disease. The test is invalid unless all the chickens from group A hens show evidence of avian infectious bursal disease.

Where there is more than one recommended route of administration, the test described under Potency is carried out in parallel with the above immunogenicity test, using different groups of chickens for each recommended route. The serological response of the chickens inoculated by routes other than that used in the immunogenicity test should not be significantly less than the level recorded in the test for immunogenicity.

Manufacturer's test

Identification

Vaccine complies with the test as mentioned under Production. Alternatively, identification on the final bulk lot by molecular techniques is acceptable and can be used in the routine bulk lot release.

Residual live virus

An amplification test for residual live avian infectious bursal disease virus is carried out on each batch of antigen immediately after inactivation to confirm inactivation; the test is carried out in embryonated hens' eggs or in suitable cell cultures (2.7.13) whichever is the most sensitive for the vaccine strain; the quantity of inactivated virus harvest used in the test is equivalent to not less than 10 dose of the vaccine. The inactivated virus harvest complies with the test if no live virus is detected.

A. **For vaccine prepared with embryo-adapted strains of virus**, inject not less then 10 doses into the allantoic cavity or onto the chorio-allantoic membrane of ten 9- to 11-day-old embryonated hen eggs from an SPF flock (2.7.7). Incubate the eggs at 37° ± 1° and observe at least daily for 6 days. Pool separately the allantoic liquid or membranes from eggs containing live embryos, and that from eggs containing dead embryos, excluding those that die from non-specific causes within 24 h of the injection.

Inject into the allantoic cavity or onto the chorio-allantoic membrane of each of ten 9 to 11 day old SPF eggs 0.2 ml of the pooled allantoic liquid or crushed chorio-allantoic membranes from the live embryos and, into each of 10 similar eggs, 0.2 ml of the pooled liquid or membranes from the dead embryos and incubate for 6 days. Examine each embryo for lesions of avian infectious bursal disease. If more than 20 per cent of the embryos die at either stage repeat that stage. The vaccine complies with the test if there is no evidence of lesions of avian infectious bursal disease and if, in any repeat test, not more than 20 per cent of the embryos die from non-specific causes. Antibiotics may be used in the test to control extraneous bacterial infection.

B. **For vaccine prepared with cell-culture-adapted strains of virus**, If the vaccine contains an inactivating agent, neutralize it with a suitable neutralizing agent before testing. Inoculate 10 doses of the vaccine into atleast 150 cm^2 primary or secondary chicken embryo fibroblasts (CEF). Incubate at 36 ± 1° for 7 days. After one cycle of freezing and thawing, the supernatant from this culture is

passaged to a fresh CEF culture. Incubate at 36 ± 1° for 7 days. After final inoculation the culture are inspected for CPE. The vaccine complies with the test if the cultures show no signs of virus.

Safety. The test is carried out for each route of administration to be recommended for vaccination. For each test, use not fewer than 10 chickens not older than the minimum age to be recommended for vaccination and from a flock free from specified pathogens (SPF) (2.7.7) or healthy susceptible chickens (2.7.18). Administer double dose of vaccine to each chicken by the recommended route and method. Observe the chickens daily for at least 21 days after the administration of the vaccine. The test is not valid if non-specific mortality occurs. The vaccine complies with the test if no chicken shows abnormal signs of disease or dies from causes attributable to the vaccine.

Potency. Inject each of ten SPF chickens (2.7.7) or healthy susceptible chickens (2.7.18), 3 to 4 weeks old, with the minimum dose and by the route stated on the label. Use ten chickens of the same flock and age as controls. After 21 days, collect serum samples from each bird including the ten-control chickens and perform quantitative agar gel precipitation test or serum neutralizing test on each serum sample. The mean antibody titre of sera in vaccinated group shall be 1:8 by agar gel diffusion test and 10000 units per ml by serum neutralization test and there are no IBD specific antibodies in the sera of control chickens.

Batch test

Identification. Vaccine complies with the test mentioned under Production.

Sterility (2.2.11). The vaccine complies with the test for sterility.

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

Potency. The vaccine complies with the requirements of the test prescribed under manufacturer's test when administered by a recommended route and method.
Alternative suitably validated in-vitro method can be used as potency test for batch release if a correlation is established between potency test and alternative test and with the approval of competent authority.

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";(4) the animal species for which the vaccine is intended; (5) storage temperatures; (6) Batch Number, Manufacturing date and expiry date; (7) Total volume and number of doses; (8) Strain of virus used in preparing the vaccine; (9) Route of administration; (10)The label states whether the strain in the vaccine is embryo-adapted or cell-culture-adapted.