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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Avian Infectious Bronchitis Vaccine, Inactivated

Avian Infectious Bronchitis Vaccine, Inactivated consists of an emulsion or a suspension of one or more serotypes of avian infectious bronchitis virus which have been inactivated in such a manner that the immunogenic activity is retained. This monograph applies to vaccines intended to protect birds against drop in egg production or egg quality; vaccines also intended for protection against respiratory signs and nephropathic-symptoms, a demonstration of efficacy additional to that described under potency is required.

Production

Preparation of the vaccine

The virus is propagated in embryonated hen's eggs obtained from suitable healthy flocks or SPF eggs (2.7.7) or in suitable cell culture derived from SPF eggs (2.7.7). 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 or from flocks free from specified pathogens (2.7.18)

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

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

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 and for each avian species for which the vaccine is intended. 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 birds not older than the minimum age to be recommended for vaccination. In the case of chickens, use chickens from a flock free from specified pathogens (SPF) (2.7.7) or healthy susceptible chickens 2.7.18) and if the vaccine is used for species other than chickens, they have not been vaccinated and do not have antibodies against avian infectious bronchitis virus. Administer by a route to be recommended and method to each bird 2 dose of the vaccine. Observe the birds for 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 bird 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 for each serotype in the vaccine. The vaccine administered to each chicken is of minimum potency.

Use for the test 4 groups, each of not fewer than 30 chickens treated as follows:

– group A: unvaccinated controls;

– group B: vaccinated with inactivated avian infectious bronchitis vaccine;

– group C: vaccinated with live avian infectious bronchitis vaccine and inactivated avian infectious bronchitis vaccine according to the schedule to be recommended;

– group D: vaccinated with live avian infectious bronchitis vaccine.

Monitor egg production and quality in all chickens from point of lay until at least 4 weeks after challenge. At the peak of lay, challenge all groups with a quantity of virulent avian infectious bronchitis virus sufficient to cause a drop in egg production or quality over 3 consecutive weeks during the 4 weeks following challenge. The test is invalid unless there is a drop in egg production in group A compared to the normal level noted before challenge of at least 35 per cent where challenge has been made with a Massachusetts-type strain; where it is necessary to carry out a challenge with a strain of another serotype for which there is documented evidence that the strain will not cause a 35 per cent drop in egg production, the challenge must produce a drop in egg production commensurate with the documented evidence and in any case not less than 15 per cent. The vaccine complies with the test if egg production or quality is significantly better in group C than in group D and significantly better in group B than in group A.

Manufacturer's tests

Identification

In susceptible birds, the vaccine stimulates the production of specific antibodies against each of the virus strain incorporated in the vaccine, detectable by suitable validated serological method.

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

Residual live virus

An amplification test for residual live avian infectious bronchitis virus is carried out on each batch of antigen immediately after inactivation and on the final bulk vaccine or, if the vaccine contains an adjuvant, on the bulk antigen or mixture of bulk antigens immediately before the addition of adjuvant; the test is carried out in embryonated hen eggs from SPF flocks (2.7.7) 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 doses of 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 10 dose into the allantoic cavity of ten 9- to 11-day-old embryonated hens' eggs from an SPF flock (2.7.7) and incubate. Observe for 5-6 days and pool separately the allantoic liquid from eggs containing live embryos and that from eggs containing dead embryos, excluding those that die within the first 24 h after injection. Examine for abnormalities in all embryos which die after 24 h of injection or which survive 5-6 days. No deaths or abnormality attributable to the vaccine virus occurs.

Inject into the allantoic cavity of each of ten 9 to 11 day old embryonated hens' eggs from an SPF flock (2.7.7) 0.2 ml of the pooled allantoic liquid from the live embryos and into each of 10 similar eggs 0.2 ml of the pooled liquid from the dead embryos and incubate for 5-6 days. Examine for abnormalities in all embryos which die after 24 hour of injection or which survive 5-6 days. No deaths or abnormality attributable to the vaccine virus occurs. If more than 20 per cent of the embryos die at either stage repeat the test from that stage. The vaccine complies with the test if there is no death or abnormality attributable to the vaccine virus

B. For vaccine prepared with cell-culture-adapted strains of virus, inoculate ~~2/5th~~ 10 doses of the vaccine into suitable cell cultures. If the vaccine contains an oil adjuvant, eliminate it by suitable means. Incubate at 36 ± 1° for 7 days. Make a passage on another set of cell cultures and incubate at 36 ± 1° for 7 days. The vaccine complies with the test if none of the cultures show signs of infection.

Safety. Inject intramuscularly a quantity equivalent to 2 doses into each of ten SPF chickens (2.7.7) or healthy susceptible chickens of minimum age recommended for vaccination. Observe all chickens for 21 days. No abnormal systemic or local reaction is seen

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

Potency test

Inject one dose by the route stated on the label into each of 10 SPF chickens (2.7.7) or healthy susceptible chickens, 3 to 4 weeks old. Use 5 similar chickens as controls & house them together with the vaccinated chickens. After 28 days, collect serum samples from each of the vaccinated and control chickens and perform haemagglutination inhibition test on each serum using 4 haemagglutinating (HA) units of antigen and chicken erythrocytes, testing all serum samples at the same time. The vaccine passes the test, if the mean antibody titre of the vaccinated group is not less than 1:64 and no specific antibody is detected on the control chickens. Alternatively, serum neutralization test may be carried out in SPF eggs (2.7.7). Serum neutralization titre should not be less than 10^2 neutralization units.

Batch tests

Identification. Vaccine complies with the test mentioned under manufacturers test.

Bacterial and Fungal contamination (2.2.11). The vaccine complies with the test for sterility

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

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) The label states whether the strain in the vaccine is embryo-adapted or cell-culture-adapted.