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.	

Inclusion Body Hepatitis (IBH) Vaccine, inactivated

Hydropericardium Syndrome (HPS)

Inclusion Body Hepatitis (IBH) Vaccine, inactivated consists of an emulsion or a suspension of avian adenovirus(es) which have been inactivated in such a manner that the immunogenic activity is retained.

Production

Preparation of the vaccine

The vaccine virus is grown in healthy susceptible chicken or embryonated hens' eggs or in suitable cell culture or cell lines. The virus harvest is inactivated. The vaccine contain suitable adjuvant.

Substrate for virus propagation

Vaccine virus is grown in healthy susceptible chickens or SPF eggs (2.7.7) or in cell culture derived from SPF eggs (2.7.13)

Healthy susceptible chickens. If the vaccine virus is grown in healthy susceptible chickens, they are obtained from healthy flock (2.7.18).

Embryonated hens' eggs . If the vaccine virus is grown in embryonated hens' eggs, they are obtained from SPF chickens (2.7.7) or from a healthy flock (2.7.18).

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.

Seed lots

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

Identification. The vaccine virus is identified using suitable validated molecular biology / biochemistry /cell culture/ immunochemical techniques with the approval of competent authority.

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. Inject subcutaneously a quantity equivalent to double dose into each of 10 SPF chickens (2.7.7, Table 3) or healthy susceptible chickens of the recommended age at which vaccine is to be used. Observe the chickens for 21 days, no abnormal systemic or local reaction is seen.

Immunogenicity A test is carried out for each route and method of administration to be recommended using in each case animals of the minimum age to be recommended for vaccination.

Either test A or test B may be carried out.

A. Inject one dose by the route stated on label into each of 10 SPF chickens (2.7.7, Table 3) or healthy susceptible chickens at the age recommended by manufacturer. Use 10 similar chickens from same source as unvaccinated controls. After 21 days of immunization, challenge the birds with 10 per cent IBH positive infected liver suspension 0.5 ml per bird or cell culture derived challenge virus. Observe the birds for ten days. The vaccine passes the potency test when there is 90 per cent protection in vaccinated bird and 80 per cent deaths in unvaccinated controls.

B. At least five, 3-6 week old SPF chickens (2.7.7, Table 3) or healthy susceptible chickens are vaccinated with one field dose of vaccine by intramuscular route. Blood samples are collected between 3 and 5 weeks and the antibody response measured by ELISA. The mean antibody titre should be at least 10 $\log_2$ ELISA/ SNT units.

Manufacturer's tests

Identification. The vaccine virus is identified using appropriate molecular biology / biochemistry /cell culture/ immunochemical techniques

Residual live virus. To confirm inactivation an amplification test for residual live IBH/HPS virus is carried out on each batch of antigen immediately after inactivation or on final bulk (If the vaccine contains a mixture of inactivated antigens). The test is conducted on healthy susceptible chicken demonstrated to be free from antibodies to IBH/HPS virus or in fertilized eggs derived from SPF flock (2.7.7) if the vaccine virus is propagated in embryos/ cell line or cell culture (2.7.13), the same test may be used The quantity of inactivated virus used in the test equivalent to not less than 10 doses of the vaccine. Offer two serial passages of the inoculated substrate to arrive at conclusive interpretation. The inactivated virus harvest complies the test if no live virus is detected.

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

Batch test

Identification

Protects chickens against infection of IBH/HPS. Alternatively, the vaccine virus is identified using suitable biochemical, molecular, cell culture or serological assays.

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

Safety. Inject subcutaneously a quantity equivalent to 2 doses into each of 10 SPF chickens (2.7.7, Table 3) or healthy susceptible chickens of the recommended age at which vaccine is to be used. Observe the 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 . The vaccine complies with the requirements of the test mentioned under Immunogenicity when administered by a recommended route and method.

Suitable validated *in-vitro* tests such as such as SNT or ELISA can replace *in-vivo* potency test for batch release if a correlation is established between potency test and alternate test.

Labelling

The label must state that (1) the vaccine is for veterinary use only; (2) the recommended routes of administration; (3) the instruction for use, such as "the preparation should be shaken well before use; (4) The animal species for which thvaccine 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.