No. K-11/36/2024-LH

Government of India

Ministry of Fisheries, Animal Husbandry and Dairying

Department of Animal Husbandry and Dairying

Krishi Bhawan, New Delhi
Dated 27th November 2024

Office Memorandum

Subject: Seeking Public Comments on the proposed draft for Guidelines for Bridging Studies

This Department (DAHD) invites comments/ suggestions on the attached draft of 'Guidelines for Bridging Studies for vaccines developed by the Department with inputs from Experts and Stakeholder.

The comments/suggestions may be sent at the following e-mail IDs - sharma.aruna@gov.in, vivek.3323@dahd.nic.in

The comments/inputs/feedback may be submitted within 10 days from the date of publishing the draft.

(Aruna Sharma)
Deputy Commissioner (AH)

Guidelines for Bridging Studies

The ICH E5 guideline defines a bridging study as a supplementary study conducted in the new region to provide pharmacodynamic or clinical data on efficacy, safety, dosage, and dose regimen to allow extrapolation of the foreign clinical data to the population of the new region. In human vaccine clinical research, bridging trials refer to a series of small-scale additional trials based on the confirmation of the original safety and efficacy of the vaccine in clinical trials to prove that the safety, immunogenicity and efficacy characteristics of the vaccine after changing from one component, population, vaccination schedule, etc. to other types are similar to those before the change, so that the original clinical trial data can be extrapolated.

In Veterinary vaccine, the bridging studies shall be considered in below mentioned scenarios of the vaccines for which field-trials were already done in India or outside India.

1. The vaccine is already licensed in regulated markets such as USA, Europe, Australia, Japan, etc subsequent to a field trial in a foreign country. The company is trying to get the license for the same vaccine in India without any change in manufacturing facility, manufacturing process of the vaccine, vaccine strain and indication of the vaccine.

   DAHD shall recommend conducting the bridging study, after providing due consideration to below points

   i. Relevance of the proposed vaccine for India shall be considered. Prevalence, severity, pathogenicity, etc of the disease/ organism for which the vaccine was recommended shall be considered based on the available research articles, publications in reputed journals or based on the internal data generated by the applicant. Suitability of the vaccine indications for species, age or physiological status of animals in the target population shall also be verified.

   ii. Relevance of the proposed vaccine strain and vaccine technology (live, inactivated, sub-unit, vectored vaccine, recombinant vaccine, etc) for India shall be evaluated. Serotype variations and prevalence of the disease / organisms shall be considered in such cases. Data on cross neutralization against local isolates shall be sought, only when: (1) The disease requires serotype/subtype-specific immunity for disease prevention, as per the available literature and (2) The vaccine does not include the particular serotype or subtype that is prevalent in India, based on available data. For

e.g. cross neutralization experiments, against pathogen prevalent in India by in-vitro or in-vivo method, as appropriate, may be sought.

iii. Risk assessment document on transmission of vaccine strains in Indian animal population, if any, shall be sought for the live vaccines.

2. The vaccine is already licensed in India subsequent to a field trial in India. However, the company proposes below mentioned changes in the vaccine process, composition, dose, schedule, etc. Otherwise, the level 1 Post approval changes (PAC) of a vaccine which require field trial as suggested by CDSCO can undergo bridging study.

   i. Manufacturing process is changed considerably to improve the yield, vaccine stability, improve process economy, adapting a latest technology, etc. However, the final product quality is same as the previously licensed vaccine as per the specification and COA.

   ii. Final product composition is changed. For example, preservative is added for multi-dose presentation, the antigen content/ titer is increased to meet or improve the potency/stability of the vaccine, the excipient composition is changed to improve the stability of the vaccine, etc

   iii. The vaccine was licensed earlier for the use in a particular species of animal and the company proposes to use the vaccine in another species.

   iv. A new vaccine regimen, new route of administration or extended utility of the vaccine to some new physiological condition of the animal is suggested.

A bridging study shall address the safety and efficacy (or correlate of protection such as sero-conversion) of the vaccine in a single study using smaller number of animals. The results of the test group of animals shall be compared with the results of earlier study in India or outside India. Statistical significance or non-significance, as the case may be, shall be calculated at 95% confidence interval level using ANOVA or any other suitable method

The trial may be conducted in a single site. The applicant may choose to conduct the study in more than one site if required (due to non-availability of sufficient animals in a single site).

Table 1. Summary on bridging study.

S. No.	Category of animal	Number of animals to be included in the trial	Number of trial sites to be included	Duration of trial
1	Small and large Ruminant trials	Minimum of 30 animals in vaccine treated group	Single trial site is sufficient if the site is having the required number of animals	Minimum of 1 months of follow-up period from the final dose of vaccine (Duration can be reduced in specific cases such as trial in broiler birds). The seroconversion shall also be assessed within this period of one month.
2	Canine and Feline trials	Minimum of 20 animals in vaccine treated group		
3	Poultry including chicken	Minimum of 150 birds in vaccine treated group		
4	Porcine trials	Minimum of 30 animals in vaccine treated group		

Safety parameters to be assessed

The clinical safety trials are primarily performed to verify the safety of the vaccine under field conditions after administration of one dose of vaccine as well as after repeated administration(s) depending on the recommendations for use.

Parameters used to determine systemic effects of vaccination may include allergic reactions, mortality, anorexia, pyrexia, changes in behavior (such as depression), weight gain, feed conversion, carcass quality, milk/wool/fur production, egg production and hatchability of breeding eggs as applicable. Additional or alternative parameters relevant for a specific pathogen may be used, where appropriate and justified.

In terms of local reactions, the size, duration and nature of any reactions appearing at the site of injection shall be monitored and recorded. The safety assessment shall be for the duration as mentioned in the above table 1. The safety results shall be compared with that of the earlier study

Assessment of efficacy under field conditions

Correlate of protection (for e.g. Antibody titer, T-cell response, reduced load of pathogen, etc), if available and duration of immunity, shall be sufficient for the evaluation of efficacy in Bridging studies. An indicator of protection should be shown to play a substantial role in the immune response and relevant for protection of the target species against the disease concerned. If the disease is having an established protective titer, the same can be used to evaluate the efficacy (for eg.>0.5 IU RFFIT titer for Rabies, >80 HI units for Canine Parvovirus and serotype specific SN_{50}

or Liquid phase blocking ELISA titer for FMD). If there is no established protective titer for the disease, the earlier trial results (from regulated market or India or from publications in reputed Journals) for Sero-conversion, Neutralization titer, T-cell response, reduced load of pathogen, etc shall be used as benchmark to assess the vaccine efficacy. In case of diseases where the in-vitro correlate is not available, part of the animals from the field trials shall be subjected to challenge trial using an appropriate containment facility, challenge strain and Species of animal, with minimum age for the vaccination. The data can be considered for efficacy. The immunogenicity/ efficacy assessment shall be for the duration as mentioned in the above table 1.

Applicant shall mention the inclusion and exclusion criteria, such as sero-negativity, age, sex, physiological condition of the animal, etc depending on the trial requirement. The criteria shall be scientifically justified.