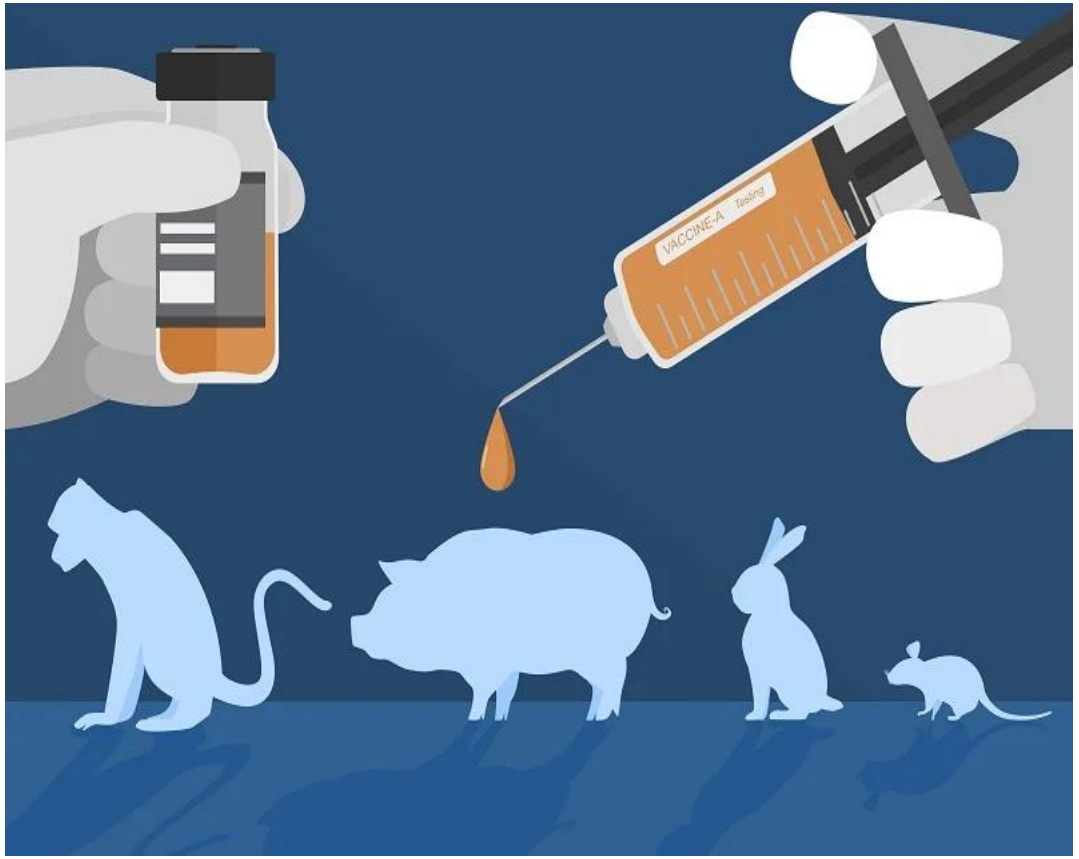
Waiver of TABST (Target Animal Batch Safety Test)

Date: 20th October 2022



IP 2018 & 2022 monograph of Veterinary Vaccine with requirement of TABST:

The test is invalid if specific *P. multocida* antibodies are detected before vaccination in one or more sera from chickens to be vaccinated or from controls; in 1 or more sera from control chickens 5 weeks after the day of administration of the vaccine.

Batch tests

Description. Homogenous suspension of inactivated bacteria.

Identification

The vaccine complies with the requirements of the test mentioned under the section of master seed lot.

Sterility (2.2.11). Complies with the test for sterility.

Safety. The vaccine complies with the requirements of the test mentioned under section of Manufacturer's tests.

Potency. The vaccine complies with the requirements of the test mentioned under section of master seed lot.

Labelling and Storage. Should comply with the requirements of 'Labelling and Storage' as laid down in the General Monograph on Veterinary Vaccines: General Requirements.

The label states: (1) the serotypes and the strains of bacteria used to prepare vaccine; (2) adjuvant used (3) dose and route of inoculation.

Expiry. Not more than 1 year from the date of manufacture.

Fowl Pox Vaccine, Live

Pigeon Pox Vaccine, Live

Fowl Pox Vaccine, Live is a preparation of a suitable strain(s) of pigeon pox virus or fowl pox virus. This monograph applies to vaccines intended for administration to chickens for active immunization against avian pox virus.

Production

The vaccine virus is grown in embryonated hens' eggs from SPF flock (2.7.7) or in cell cultures derived from SPF eggs (2.7.7) or cell lines. The master seed lot complies with the tests for extraneous agents as described in the General monograph for Veterinary Vaccines (2.7.10).

Substrate for virus propagation

The vaccine virus is grown either in embryonated hens' eggs from flocks free from specified pathogens SPF (2.7.7) or in avian cell cultures obtained from flocks free from specified pathogens SPF (2.7.7) or cell lines.

the vaccine virus or inoculate the vaccine into eggs and notice the characteristic lesions.

Tests

Water (2.3.43). Not more than 3.0 per cent.

Mycoplasmas (2.7.9). Complies with the test for mycoplasmas.

Safety. Administer 10 doses of the vaccine to each of ten SPF chickens (2.7.7, Table 3) or healthy susceptible chickens 6 to 8 weeks old by the route stated on the label. Observe the birds for 21 days. No chicken dies from causes attributable to the vaccine or shows signs of toxicity other than mild, transient, local reactions. If during the observation period more than two chickens die from causes not attributable to the vaccine, repeat the test.

Virus titre. Not less than 10^2 EID_{50}/$TCID_{50}$ of the virus per dose, determining the titre by inoculation into the chorio-allantoic membrane of SPF embryonated eggs, between 9-11 days old, or one or more route for virus titration depending upon the strain.

Sterility (2.2.11). Complies with the test for sterility.

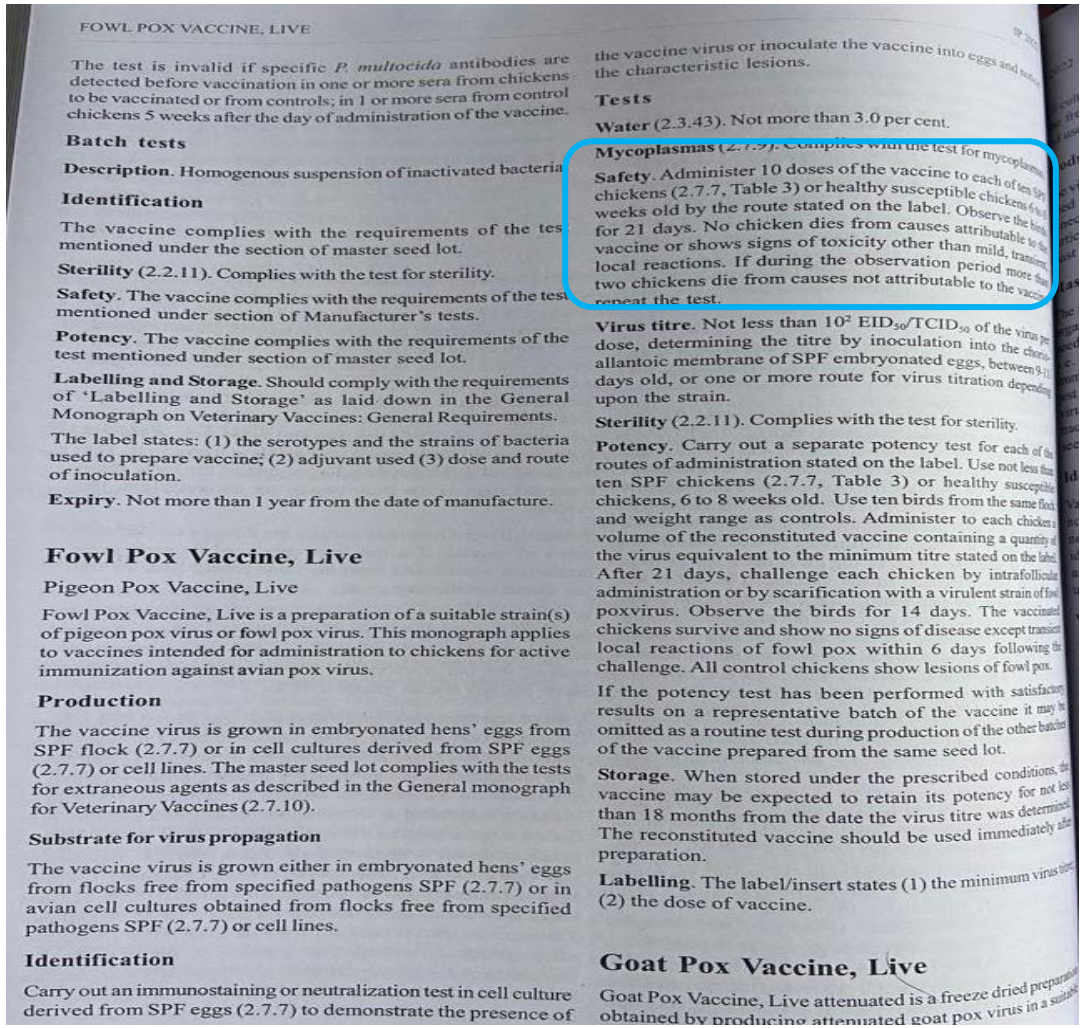
Potency. Carry out a separate potency test for each of the routes of administration stated on the label. Use not less than ten SPF chickens (2.7.7, Table 3) or healthy susceptible chickens, 6 to 8 weeks old. Use ten birds from the same flock and weight range as controls. Administer to each chicken a volume of the reconstituted vaccine containing a quantity of the virus equivalent to the minimum titre stated on the label. After 21 days, challenge each chicken by intrafollicular administration or by scarification with a virulent strain of fowl poxvirus. Observe the birds for 14 days. The vaccinated chickens survive and show no signs of disease except transient local reactions of fowl pox within 6 days following the challenge. All control chickens show lesions of fowl pox.

If the potency test has been performed with satisfactory results on a representative batch of the vaccine it may be omitted as a routine test during production of the other batches of the vaccine prepared from the same seed lot.

Storage. When stored under the prescribed conditions, the vaccine may be expected to retain its potency for not less than 18 months from the date the virus titre was determined. The reconstituted vaccine should be used immediately after preparation.

Labelling. The label/insert states (1) the minimum virus titre; (2) the dose of vaccine.

Goat Pox Vaccine, Live



The test is invalid if specific *P. multocida* antibodies are detected before vaccination in one or more sera from chickens to be vaccinated or from controls; in 1 or more sera from control chickens 5 weeks after the day of administration of the vaccine.

Batch tests

Description. Homogenous suspension of inactivated bacteria

Identification

The vaccine complies with the requirements of the tes mentioned under the section of master seed lot.

Sterility (2.2.11). Complies with the test for sterility.

Safety. The vaccine complies with the requirements of the test mentioned under section of Manufacturer's tests.

Potency. The vaccine complies with the requirements of the test mentioned under section of master seed lot.

Labelling and Storage. Should comply with the requirements of 'Labelling and Storage' as laid down in the General Monograph on Veterinary Vaccines: General Requirements.

The label states: (1) the serotypes and the strains of bacteria used to prepare vaccine; (2) adjuvant used (3) dose and route of inoculation.

Expiry. Not more than 1 year from the date of manufacture.

Fowl Pox Vaccine, Live

Pigeon Pox Vaccine, Live

Fowl Pox Vaccine, Live is a preparation of a suitable strain(s) of pigeon pox virus or fowl pox virus. This monograph applies to vaccines intended for administration to chickens for active immunization against avian pox virus.

Production

The vaccine virus is grown in embryonated hens' eggs from SPF flock (2.7.7) or in cell cultures derived from SPF eggs (2.7.7) or cell lines. The master seed lot complies with the tests for extraneous agents as described in the General monograph for Veterinary Vaccines (2.7.10).

Substrate for virus propagation

The vaccine virus is grown either in embryonated hens' eggs from flocks free from specified pathogens SPF (2.7.7) or in avian cell cultures obtained from flocks free from specified pathogens SPF (2.7.7) or cell lines.

Identification

Carry out an immunostaining or neutralization test in cell culture derived from SPF eggs (2.7.7) to demonstrate the presence of

the vaccine virus or inoculate the vaccine into eggs and notice the characteristic lesions.

Tests

Water (2.3.43). Not more than 3.0 per cent.

Mycoplasmas (2.7.9). Complies with the test for mycoplasmas.

Safety. Administer 10 doses of the vaccine to each of ten SPF chickens (2.7.7, Table 3) or healthy susceptible chickens 6 to 8 weeks old by the route stated on the label. Observe the birds for 21 days. No chicken dies from causes attributable to the vaccine or shows signs of toxicity other than mild, transient, local reactions. If during the observation period more than two chickens die from causes not attributable to the vaccine, repeat the test.

Virus titre. Not less than 10^2 EID_{50}/$TCID_{50}$ of the virus per dose, determining the titre by inoculation into the chorio-allantoic membrane of SPF embryonated eggs, between 9-11 days old, or one or more route for virus titration depending upon the strain.

Sterility (2.2.11). Complies with the test for sterility.

Potency. Carry out a separate potency test for each of the routes of administration stated on the label. Use not less than ten SPF chickens (2.7.7, Table 3) or healthy susceptible chickens, 6 to 8 weeks old. Use ten birds from the same flock and weight range as controls. Administer to each chicken a volume of the reconstituted vaccine containing a quantity of the virus equivalent to the minimum titre stated on the label. After 21 days, challenge each chicken by intrafollicular administration or by scarification with a virulent strain of fowl poxvirus. Observe the birds for 14 days. The vaccinated chickens survive and show no signs of disease except transient local reactions of fowl pox within 6 days following the challenge. All control chickens show lesions of fowl pox.

If the potency test has been performed with satisfactory results on a representative batch of the vaccine it may be omitted as a routine test during production of the other batches of the vaccine prepared from the same seed lot.

Storage. When stored under the prescribed conditions, the vaccine may be expected to retain its potency for not less than 18 months from the date the virus titre was determined. The reconstituted vaccine should be used immediately after preparation.

Labelling. The label/insert states (1) the minimum virus titre; (2) the dose of vaccine.

Goat Pox Vaccine, Live

Goat Pox Vaccine, Live attenuated is a freeze dried preparation obtained by producing attenuated goat pox virus in a suitable

Updates…

VICH GL50: WAIVE TARGET ANIMAL BATCH SAFETY TESTING FOR INACTIVATED VACCINES

(Published on May 2017 for implementation by May 2018)

Data Requirements for Waiving of Target Animal Batch Safety Tests:

The TABST may be waived by the regulatory authority when a sufficient number of production batches have been produced under the control of a seed lot system and found to comply with the test, thus demonstrating consistency of the manufacturing process.

In general, it is sufficient to evaluate existing information which is available from routine batch quality control and pharmacovigilance data, without the need for any additional supplementary studies. The data which should be presented by the manufacturer to support an application to waive TABST are presented below. However, this should not be taken as an exhaustive list, and in all cases applications for waiving the TABST should be accompanied by a summary of all the data and a conclusion on the assurance of the product's safety being maintained.

In exceptional cases, significant changes to the manufacturing process may require resumption of target animal batch safety testing to re-establish consistency of the safety profile of the product. The occurrence of unexpected adverse events or other pharmacovigilance problems which could be avoided using a TABST may also lead to the resumption of the test. For products with an inherent safety risk, it may be necessary to continue to conduct the TABST on each batch.

Procedure for waiving the target animal batch safety test:

A report should provide an overall assessment of the consistency of the product's safety and would include taking into account the number of batches manufactured, the number of years the product has been on the market, the number of doses sold and the frequency and seriousness of any adverse reactions in the target species and any investigations into the likely causes of these events.

Updates…

VICH GL55: WAIVE TARGET ANIMAL BATCH SAFETY TESTING FOR IN LIVE VACCINES

(Published in May 2017 for implementation by May 2018)

Data Requirements for Waiving of Target Animal Batch Safety Tests :

The TABST may be waived by the regulatory authority when a sufficient number of production batches have been produced under the control of a seed lot system and found to comply with the test, thus demonstrating consistency of the manufacturing process.

In general, it is sufficient to evaluate existing information which is available from routine batch quality control and pharmacovigilance data, without the need for any additional supplementary studies. The data which should be presented by the manufacturer to support an application to waive TABST are presented below. However, this should not be taken as an exhaustive list, and in all cases applications for waiving the TABST should be accompanied by a summary of all the data and a conclusion on the assurance of the product's safety being maintained.

In exceptional cases, significant changes to the manufacturing process may require resumption of target animal batch safety testing to re-establish consistency of the safety profile of the product. The occurrence of unexpected adverse events or other pharmacovigilance problems which could be avoided using a TABST may also lead to the resumption of the test. For products with an inherent safety risk, it may be necessary to continue to conduct the TABST on each batch.

Procedure for waiving the target animal batch safety test :

A report should provide an overall assessment of the consistency of the product's safety and would include taking into account the number of batches manufactured, the number of years the product has been on the market, the number of doses sold and the frequency and seriousness of any adverse reactions in the target species and any investigations into the likely causes of these events.

Updates…

PURPOSE:
This memorandum provides guidance to licensed firms on requesting an exemption under title 9, Code of Federal Regulations (9 CFR), part 113.4, to target animal safety testing as required in section V.B. of the Outline of Production and 9 CFR 113.64, 113.100, and 113.300. The Center for Veterinary Biologics (CVB) will consider granting an exemption to target animal safety testing for specific products with a documented history of acceptable safety results and controlled manufacturing processes that have ensured batch-to-batch consistency and sterility.

Japan has implemented VICH GL50 and 55, and authorities are receptive to granting waivers following VICH guidelines. (Ref: National Veterinary Assay Laboratory No. 3000 Feb 2014)

Updates….

- The World Organization for Animal Health (OIE) accepted a comment (from EPAA, submitted via the European DG SANTE in December 2017} on the possibility to mention VICH Guidelines 50 and 55 on the removal of the test in two chapters of its Terrestrial Manual. Amendments were adopted by the OIE World Assembly of Delegates at the end of May 2018: "Safety tests are not required by many regulatory authorities for the release of each batch or serial where the seed-lot system is used. Other regulatory authorities may allow waiving target animal batch safety tests in line with VICH GL50 and 55."

- Also, we understand that the Indian Pharmacopoeia Commission (IPC} traditionally required the Abnormal Toxicity Test (ATT} for product testing, but after the introduction of GMP and Good Laboratory Practice, and in view of the efforts for global harmonization of testing requirements, IPC has abolished ATT for Human vaccines in July 2020. (http://www.ipc.gov.in/images/Amendment_List- 06_to_IP-2018.pdf)

Way forward ……. Waiver of TABST

Harmonization of IPC with VICH guidelines and EU Pharmacopeia:

Two VICH guidelines, the revised GL50 Harmonization of criteria to waive TABST for inactivated vaccines for veterinary use, and the GL55 Harmonization of criteria to waive target animal batch safety test for live vaccines for veterinary use has recommended the following documents to be submitted to regulatory authorities for approval for the waiver of TABST, which provides an overall assessment of the consistency of the product's safety.

List of documents to be submitted for waiver of TABST :-

- **Current EU Ph. monographs where TABST is deleted and earlier monographs where TABST was practiced.**
- **Safety data for 5 batches per product, number of doses sold in the last year five years with a year-wise break-up**
- **Number of countries the product is registered (regulatory overview) a report on serious adverse events, if any.**
- **Safety tests performed on master seed and safety data.**
- **Data on adverse events observed globally.**

Journey so far……Waiver of TABST

As part of the Global Harmonization initiative, AAHA member companies represent to IPC on 15th Mar 2022 and requested for consideration of TABST waiver for veterinary vaccines based on the documents submitted inline with VICH guidelines.

Joint representation by INFAH and AAHA on 31st Aug 22 for waiver of TABST and submission of data on safety test compliance, ADR, batch consistency reports of veterinary vaccines for 5-10 batches by domestic manufacturers & importers at IPC.

AAHA
Asian Animal Health Association
A Member of HealthforAnimals

Thank You