The Process for the Deletion of ATT, TABST and LABST in India

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History of ATT, TABST, & LABST

- Developed - 1900s
- Phenol derived preservatives in diphtheria sera
- Tetanus toxin in antiserum preparations.

- Regulatory mandated general safety test
- To avoid batch-to-batch differences in quality
- Use extended well beyond its original scope.

- No reliable conclusions
- Variable and non-reproducible
- Non-specific – body weight, species, strain

- Do Not conform to ICH validation criteria for a QC test
  - specificity
  - reproducibility
  - detection limit

- False positive results
- Lack evidence for usefulness to predict/control harmful batches/adverse events

AFSA

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## Rationale for deletion

- Seed lot system
- In-process testing requirements
- Controls of starting materials

<table>
<thead>
<tr>
<th>GMP, GLP</th>
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<tbody>
<tr>
<td>Pharmacovigilance</td>
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<td>3Rs as scientific and business relevant approach</td>
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### Deleted by European regulatory authorities

- 1997 – ATT and LABST
- 2013 - TABST

### Exception: LABST – vaccines of inherent safety risk

- Residual toxicity of bacterial toxin in bacterial and/or toxoid vaccines
- Residual live virus in vaccines containing an agent of public health concern

### Global Regulatory Harmonization

- Reduce burden on production’s logistics
- Reduce overall costs
- Facilitate products’ availability across various markets.
ATT Deletion from the Indian Pharmacopoeia Monographs

- Waiver in the IP since 2018
- 2018 – HSI India engagement
  - IPC
  - Key industry stakeholders
- Representation of HSI/India at Expert Committee Meeting for Human Vaccines since 2019
- IPC core committee for ATT deletion
- Industry representation from Serum Institute of India
- Representation from the National Control Laboratory and other regulators

July 2020 – IPC publication of Amendment List-0-6 to IP 2018
Stated the removal of ATT most human vaccine monographs
However, prevalence of ATT requirement for some vaccines in the monographs calls for extension of deletion for the same
F. No. T.11013/02/2018-AR&MD

Date: 15th July, 2020

To,
1. The Drug Controller General (India)
2. CDSCO Zonal Offices
3. All State Drug Controllers
4. Members of the Scientific Body of IPC
5. Members of Sub-Committees of the Scientific Body of IPC
6. Directors of Drugs Testing Laboratories
7. Government Analysts
8. IDMA/OPPI/BOMA/FSSAI/Small Scale Industry Associations

Subject: Amendment List-06 to IP 2018

The 8th Edition of Indian Pharmacopoeia (IP) 2018 has become effective from 1st January, 2018. Based on scientific inputs, some IP monographs needed up-gradation and accordingly Amendment List-06 to IP 2018 is issued containing such amendments.

This is for notice and compliance with the IP 2018.

(Dr. Jai Prakash) 22/07/2021
Secretary-cum-Scientific Director (1/c)

Encl. Amendment List-06 to IP 2018
Process of TABST and LABST deletion in India

Future of TABST and LABST in the Indian Pharmacopoeia Monographs

Key international and Indian experts and stakeholders in the field of veterinary vaccines met to discuss the future of the Targeted and the Laboratory Animal Batch Safety Test (TABST and LABST) in the Indian Pharmacopoeia monographs.

Representatives from the Indian Pharmacopoeia Commission (IPC), the Central Drugs Standard Control Organization (CDSCO), industry representatives from both, the Indian Federation of Animal Health Association (IFAAH) and the International Federation of Animal Health (IFAH), together with experts from Europe and animal health bodies from around the world, gathered in Mumbai on February 11, 2021, to discuss the future and role of TABST and LABST in the Indian Pharmacopoeia (IP). The event was organized by Humane Society International (HSI) India, in collaboration with the IPC.

The workshop aimed to address the issue of the phials and vacutainer tubes being used to collect blood samples that are subsequently used for the TABST and LABST tests. The tubes were found to be routinely used, even though they were not approved by the relevant authorities.

The workshop was attended by representatives from various organizations, including the IPC, IFAAH, and the Indian Pharmacopoeia Commission. The meeting was chaired by Dr. Luba Broshard, a consultant representing the European Commission for the Quality of Medicinal Products.

In 2020, HSI India organized a workshop on the future of TABST and LABST during Expert Meetings.

Future steps discussed and mutually agreed upon by industry and regulatory stakeholders:
- IPC
- National industry stakeholders
- Industry association – INFAH and AAHA
- International stakeholders - European Pharmacopoeia, VICH, and MSD

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4 Possible Scenarios Discussed for the Future of TABST and LABST in the IP Monographs

Deletion of general batch safety testing from Pharmacopeia(s) and Regulatory Requirements by Committee(s) or Authority(ies)

Stepwise approach:
1st step - temporary waiver
2nd step - deletion

Product specific variation with data package to support deletion of TABST from dossier

Product specific variation with data package to support waiver of TABST from dossier
Future of TABST and LABST in the Indian Pharmacopoeia Monographs – Next Steps

- Modification of the IP monographs

- Official IPC meeting to decide future of these tests, official approval and implementation

- Clear proposal specific to veterinary vaccine monographs where waiver/deletion can be applied

- Submission of Retrospective data of consecutive batches from domestic manufacturers to IPC and IVRI
HSI India Activities to Promote Non-Animal Methodologies

Collaboration
- Atal Incubation Centre – Centre for Cellular and Molecular Biology - 2019
- Establishment of the Centre for Predictive Human Model Systems - 2019

Funding
- Scientific and Regulatory Roundtables
- Proposals and representations for increasing funding into non-animal science

Capacity Building
- Grant for review papers on failing animal models for disease research
- Grant for development of Adverse Outcome Pathways and submission into OECD AOP Wiki
- Workshops on Adverse Outcome Pathways
- Free webinar series on Non-Animal Methodologies
- Whitepapers and scientific publications on non-animal methods

Regulatory Engagement
- Harmonization in regulatory requirements to increase uptake of non-animal methodologies and reduce/replace the use of animals across toxicity testing of substances

Scientific Roundtable to Promote Funding into Non-Animal Science in 2020

Meeting report published in ALTEX
Thank you!