S21: Remove ATT, TABST & LABST. How far away are we to global harmonization for those safety tests?
This Session

→ Laura Viviani (Humane Society International): Remove ATT, TABST & LABST. How far away are we to global harmonization for those safety tests?

→ Katrin Schutte (EPAA - European Partnership for Alternative Approaches to Animal Testing): REMOVE ATT, TABST & LABST. The journey of how they became obsolete.

→ Corinne Philippe (Boehringer Ingelheim): Waiving the Target Animal Batch Safety Tests of veterinary vaccines. An industry perspective.

→ Marcos Vinicius de Santana Leandro (Ministry of Agriculture Brazil): The interest to adopt a change on TABST & LABST in Brazil.

→ Brinda Poojary (Humane Society International, India): The process for the deletion of ATT, TABST and LABST in India.

→ Sunil Kumar Goel (Serum Institute of India): Removal of Abnormal Toxicity Test from human vaccines in India: a successful approach.
Objectives

Many institutions and organization have been working independently or jointly to remove those obsolete safety testing from the batch release testing for human (ATT) and veterinary vaccines (TABST, LABST). Many regulatory agencies and international organizations have successfully removed or recommended the deletion or the waiver of those tests. How far away are we from the global elimination of those tests?

Map the status of ATT, TABST & LABST deletion

Present the process and the stakeholders involved

Share some concrete and successful examples
Remove ATT, TABST & LABST. How far away are we to global harmonization for those safety tests?

Laura Viviani
Director, Biologicals Research & Toxicology
Humane Society International
About the Humane Society family of organizations

→ HSI & its affiliates together represent the largest force for animal protection globally, active on the ground in >50 countries across the Americas, Europe, Asia & Africa

→ Our team brings together experts in human & environmental toxicology, regulatory science, public policy, law, biomedicine, etc.

→ Working with lawmakers, regulators, industry, test developers & other stakeholders

→ Stakeholder status with the OECD, governmental & corporate advisory bodies on alternative methods & product safety, etc.
The AFSA Collaboration works to accelerate global adoption of a modern, species-relevant approach to safety assessment that will better protect people and our planet, and hasten the replacement of animal testing.

Listed organizations are members of at least 1 AFSA workstream; listing does not imply participation in or endorsement of other work areas.
10-15 million animals used for batch release testing*

Final animal-based batch release testing is still viewed as the ‘gold standard’ in many countries

Legacy vaccines: fundamental vaccines for worldwide health safety & highest consumption of animals; also where we can have the most significant economic, safety & availability impacts

3Rs + consistency approach being introduced & sometimes implemented in WHO, OIE, EU, US, Canadian & Indian regulations; others are considering it

3Rs + consistency approach can significantly reduce the cost of vaccines eliminating, reducing/replacing in vivo testing & can reduce lead-time of batch release**

* It is an estimation: few countries/regions collect precise numbers of animals used for research purposed
** ~$1K USD for a 28 days batch release test in India vs 5 USD for 1 day in vitro potency test. Source Vaccine Manufacturer, India
Current barriers

Implementation of innovative testing approaches

Lack of regulatory alignment
Varying national requirements challenge manufacturers, drive up costs & hinder transition to NAMs.

Industry/regulator relationships
The relationship between industry & regulators is complex, often hindered by uncertainty regarding data, priorities, perspectives & responsibilities; need greater openness regarding expectations, data requirements & information availability.

Regional infrastructures
Economic, technical & human resources challenges/possibilities differ among countries. No silver bullet; tailored approach is needed, based on a thorough understanding of local issues & complexities.

New methods for old products
Transitioning old products to non-animal-based methods can be a challenge due to poor product characterization &/or complexities in new methods development & validation.

Based on HSI’s experience and on the exercise reported in Bruyster et al. Biologicals 2017 and in Akkermans et al, 2020.
“

We are working to accelerate the removal of obsolete in vivo testing requirements from human & veterinary vaccine regulatory frameworks globally

“
Biologicals Workstream Projects

Scheduled Activities in 2021-22

ABNORMAL TOXICITY TEST DELETION
Human Immonobiologicals (incl. Vaccines)

Global
Prioritized Countries:
India (done for vaccines)
South Korea
Indonesia
China
Russia
Japan
South America

ANIMAL BATCH SAFETY TEST DELETION
Veterinary Vaccines

Global
Prioritized Countries:
North America
India
Brazil
South Korea
Indonesia
China
Russia

PYROGENICITY

Biologicals

Global
Brazil
India
International workshop on deletion of ATT & TABST

March 2019, Rome

- Brought together experts, regulators & industry from Argentina, Brazil, China, Europe, India, Russia, South Africa, Switzerland & USA
- Report accepted for publication in *Biologicals*
- Secured funding with the Bill & Melinda Gates Foundation to advance tests deletion in Russia, India, South Korea, Indonesia, China and Brazil till 2022.

AFSA Roadmap for the Elimination of ATT, TABST & LABST

- Establish a climate that is conducive, and fertile, to the use of innovative non-animal methods and delete obsolete testing.
- Build multi-stakeholders collaborations: involving all stakeholders in an exercise of mutual transparent cooperation and trust-building.
- Facilitate science-driven dialogue, mindful of various cultural and policy difference.
- Share virtuous examples to promote what is possible.
- Leverage benefits in terms of costs, time and safety to stimulate regulatory and industry to take onboard innovation.

Download the AFSA Roadmap for the Elimination of ATT, TABST & LABST: English, Chinese, Korean, Portuguese, Russian
www.afsacollaboration.org/biologicals/vaccines-regulatory-alignment
CONFIRMED DELETION
(Test removed from regulatory requirements)
→ Europe
→ Canada
→ United States
→ India (almost all vaccines)
→ Brazil (one exception)
→ Argentina (one exception)

STILL REQUIRED
(Recently reported interest in advancing discussions)
→ Mexico
→ Turkey
→ Vietnam

DISCUSSION on DELETION or WAIVER ONGOING
(different level of engagement and planning, test still required)
→ South Korea
→ Indonesia
→ China
→ Japan (waivers)
→ South Africa
→ Russia
→ Thailand

WHO RTS 1016, 2018 recommended the deletion of the test

* Eurasian Pharmacopoea will replace the Russian Pharmacopoeia and will be the regulation for Russia, Armenia, Belarus, Kazakhstan, Kirgizistan. The regulatory requirements will be the same as per the current Russian Pharmacopoeia.

** Africa has not yet an harmonized regulatory system. Laboratories follows mainly the WHO International Pharmacopoeia.
ATT Deletion Status

WHAT IS HAPPENING AND WHERE


→ **Argentina**, 7th Edition, 2013 - not required in the vaccines' marketing authorization and in the batch release testing. (aP vaccine still has ATT but the monograph is under review).

→ **South Africa**, the NCL stopped to perform ATT in December 2019.

→ **Japan**, May 2020, the notification No.221 introduced ATT exemption rule for the Influenza HA vaccine, Haemophilus b conjugate vaccines, pneumococcal polysaccharide vaccine and Japanese encephalitis vaccine lot release (Hepatitis B vaccine exemption was already in place).

→ **India**, deleted from IP2018 for almost all human vaccines in July 2020.

→ **South Korea** plans to delete ATT within 2021 (not performed by the NCL since 2020).

→ **China**: still required in the Chinese Pharmacopoeia 2020.

→ **Russia**: long-term plan to reduce the testing, products for which the production stability has been confirmed, the ATT can be performed only for 1 series every 5.
**TABST&LABST Global Status**

**CONFIRMED DELETION**

(Tests removed from regulatory requirements)

→ Europe

**CONFIRMED WAIVER**

(Waivers are approved based on data submission to regulatory authorities)

→ United States
→ Japan
→ Canada

**AD-HOC WAIVER AUTHORIZED**

Leading multinational veterinary vaccines manufacturers have been able to waive TABST for some products based on variations requests submitted to local regulatory authorities even where the waiver is not officially recognized within the regulatory framework. Company specific and product specific experience.

**DISCUSSION on DELETION or WAIVER ONGOING**

(different level of engagement and planning, test still required)

→ India
→ Brazil

**STILL REQUIRED**

(Tests required, limited options for policy changes or difficulties in stakeholders engagement)

→ South Korea
→ China
→ Russia
TABST&LABST Global Status

- Harmonisation of criteria to waive TABST / LABST for veterinary vaccines
- GLs developed by VICH experts
- Outreach to VICH Forum members to extend waivers implementation
- Country/region differences in quality standards and pharmacovigilance systems
- Country specific strategy (Brazil, India)

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<tr>
<th>Animal species</th>
<th>Inactivated vaccines</th>
<th>Live vaccines</th>
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<td></td>
<td>1st release in 2013</td>
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<tr>
<td>Laboratory animals</td>
<td>GL59 (2020)</td>
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<td>(mice, guinea pigs)</td>
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Next Steps

Accelerating Global Deletion of the Abnormal Toxicity Test.
Planning common next steps.

A workshop organized by AFSA/HSI and EFPIA in collaboration with IABS
October 14th, 2021 // 12:30 – 16:30 CET
To register go to
www.afsacollaboration.org
www.efpia.eu
Thank you!

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