# 3Rs implementation in veterinary vaccine batch release testing

Industry perspective

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# Who is HealthforAnimals?

HealthforAnimals represents 90% of the global animal health sector.

Members include:

- Manufacturers of veterinary pharmaceuticals
- Vaccines
- Other animal health products (incl. diagnostics)
- Associations that represent companies at national and regional level

# Who is HealthforAnimals?

Health for Animals
global animal health association

**28 Regional and National Associations**
working in **40 countries**

**Ten largest Animal Health companies – 100+ countries**

zoetis
Boehringer Ingelheim
Elanco
vetoquinol
ACHIEVE MORE TOGETHER
IDEXX
MERCK Animal Health
Virbac
Phibro
ANIMAL HEALTH CORPORATION
ceva
ZENOAQ

Vaccines, anti-parasiticides, diagnostics, digital services, antibiotics, etc.

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## Use of animals in science

# Use of animals in science

The pharmaceutical industry uses animals for scientific and regulatory reasons:

- to develop new medicines 
- to control product quality (vaccines) 

Strong push to move to non-animal methods:

- Use of animal tests are under increasing scrutiny for years 
- Ethical, scientific and animal welfare reasons 
- General public, authorities and industry 

# Use of animals in science

Some alternatives exist but :

1. not all tests can be replaced: safety & efficacy on target species in the course of development
2. not for all tests: technical & regulatory hurdles (incl. validation)

Do not over-promise or over-demand in such a cutting-edge field.

It will be a long journey.

# Use of animals in science

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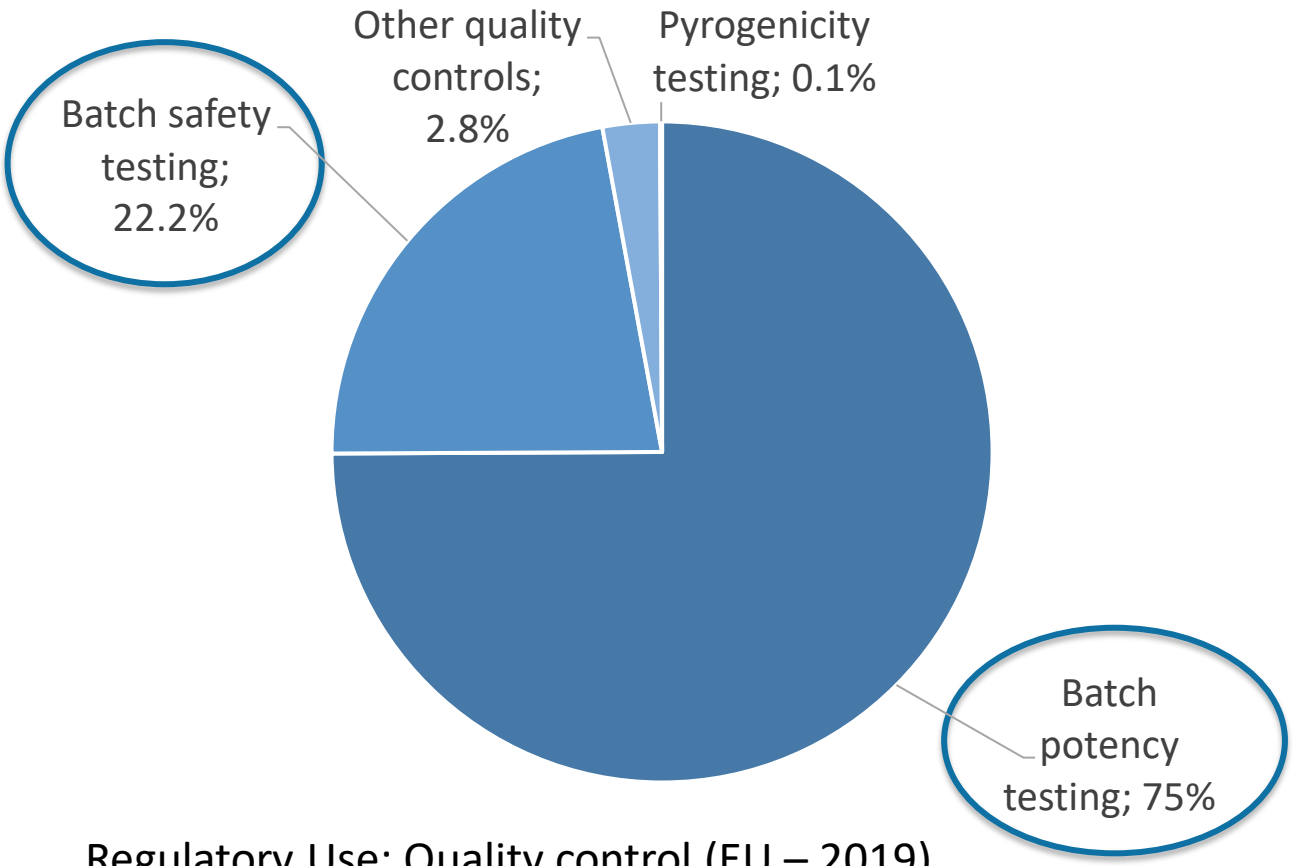
## Where should we act ? Example of EU




Regulatory Use: Quality control (EU – 2019)

Source: ALURES published data

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## Animal Batch Safety Tests:

TABST (Target Animal Batch Safety Test)

LABST (Laboratory Animal Batch Safety Test)

# Target Animal Batch Safety Tests

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| − Animal Batch Safety Test | + Quality Control improvements |
| --- | --- |
| Use lots of animals | Stricter control of starting materials |
| Scientific relevance challenged | Enhancement of Good Manufacturing Practice |
| Failed to detect problematic batches | Improved post-marketing pharmacovigilance |
| Lack of specificity | Introduction of more stringent quality control measures |
| Lack of reproducibility | |

*Together, these advancements have led to calls for the **elimination of the TABST and LABST**.*

# Target Animal Batch Safety Tests

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| | |
|---|---|
| VICH GL50 | Harmonisation of criteria to waive target animal batch safety testing **for inactivated vaccines** for veterinary use<br>✓May 2013 |
| VICH GL55 | Harmonisation of criteria to waive target animal batch safety **testing for live vaccines** for veterinary use<br>✓May 2017 |
| VICH GL59 | Harmonisation of criteria to waive **laboratory animal batch safety testing** for vaccines for veterinary use<br>✓ Nov 2020 |

Large VICH Implementation today

Not straightforward however:

- Data on 10 tests minimum need to be generated on commercial batches
- A proactive regulatory action from the industry is still required
- Regulatory assessment takes some time

# Animal Batch Safety Tests

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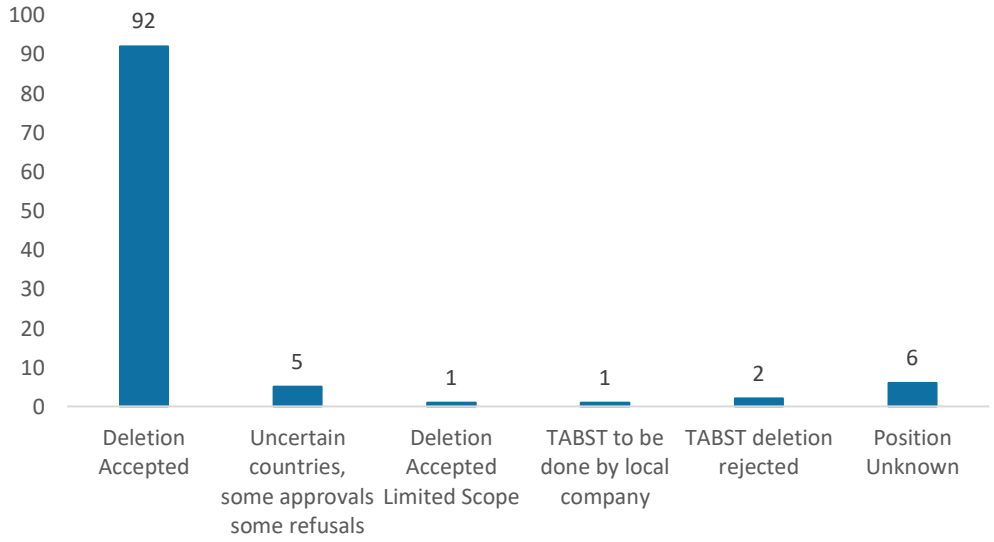
TABST definitively stopped in 2013: no data required & no specific issue since

2015 → 2019

- 42% of animal use for TABST

Source: ALURES published data

## Status of the TABST in major countries




Brazil recently adopted VICH TABST/LABST guidelines

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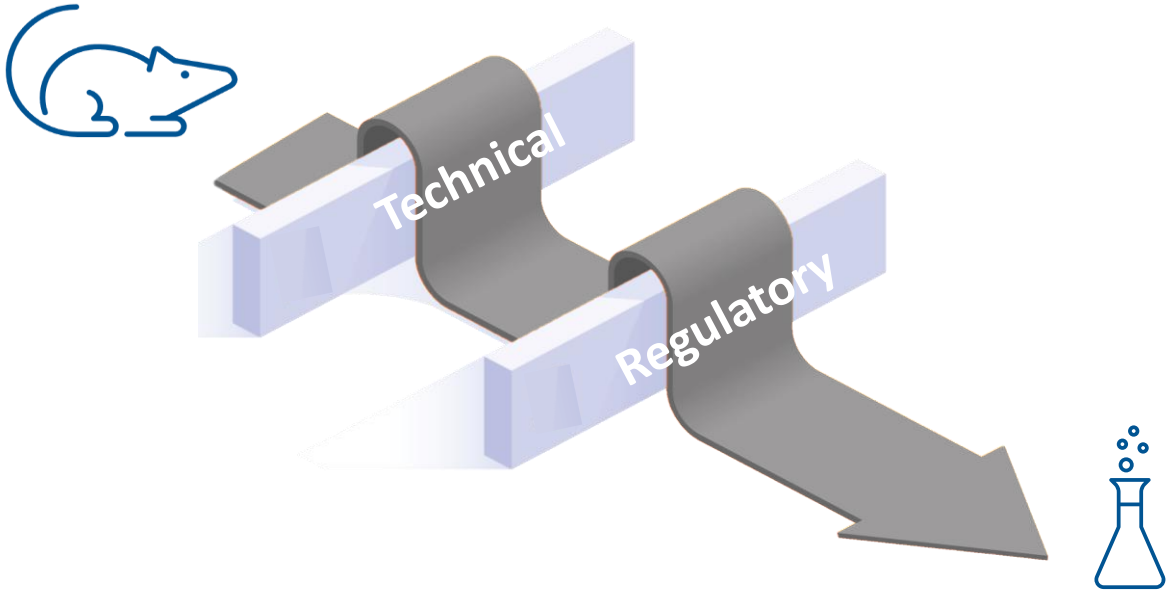
# Potency Tests: assets, challenges & perspectives

# Potency tests

Potency test aims at confirming the consistent quality, safety and efficacy of each batch.

Some alternatives exist but not for all tests:

1. Overcome technical hurdles
2. Improve regulatory hurdles (incl. validation)



# Potency tests

**Technical progress:**

Several key in-vitro potency tests now available & registered in some regions or countries.

Replace historical severe animals' tests:  Rabies, Leptospira, Clostridium, FMD, etc…

**Regulatory progress:**

VICH, USDA, EMA, Ph.Eur. Monographs & OCDE promote and open doors to the implementation of in-vitro potency tests. Supported by many initiatives (ECVAM, Vac2Vac, IABS…).

Other sector: ban on animal testing for cosmetic products since 2013 in EU.

# Assets of in-vitro potency tests

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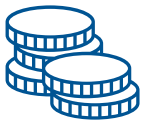
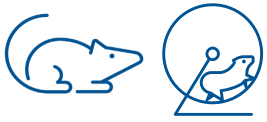
Beyond ethical aspects:

- more precise, cheaper and quicker for batch release
- eliminate the animal variability

↳ apply also to official authorities' batch release.

| Release of 1 inactivated Rabies batch (inactivation, identity & potency done on mice) | Release of 1 inactivated Leptospira batch (potency on hamsters) |
|---|---|
|  |  |
|  **2800 €** | **< 250 €**  |
|  **2100 €** | |
| **28 days**  | **24h**  |

# Challenges

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Replacement is a challenge:

- Linked to the immunogenicity knowledge of the disease/vaccine
- Years of experience with tests on animals globally accepted
- Direct correlation between historical and new tests often not possible



That requires:

- Some change of mind-set
- New scientific consensus
- State-of-the-art technical capacities
- Quite a significant amount of data



Pre-requisite to switch : a minimal implementation of reliable quality systems

& pharmacovigilance systems

# Potency tests: moving forward !

**Overcoming technical hurdles to** increase in-vitro release tests development.

- Active participation of industry in consortium
- Prioritise the efforts on tests that use huge numbers of animals or have severe endpoints
- Publish !

**Increasing regulatory acceptance:**

- **Ph. Eur. 0062** (Vaccines for veterinary use) “2-4-2. Batch potency test. For inactivated vaccines, development of in-vitro methods is recommended”, **Gal Chapter 5.2.14 in Ph. Eur**. on substitution of in vivo method(s) by in vitro method(s) for the quality control of vaccines,
- **USDA VS Memorandum No.800.112** : validation of in-vitro potency assays & **No.800.102**: in vitro Leptospira potency test,
- **9CFR § 113.8** "In vitro tests for serial release". Code of Federal Regulations.

Based on these texts → Industry has submitted a concept paper on Potency Substitution to the VICH Steering Committee for consideration.

# Take home messages

Still a long way to go but achievable: Industry is on board.

Clear benefits for all stakeholders: industry & authorities

- Ethical and animal welfare aspects
- In-vitro tests are more precise, robust and cheaper than in-vivo,
- Reduction of lead-time for release

Moving forward to a wider implementation of the replacement aspect of the 3Rs will improve our vaccine batch release testing and vaccines' availability : harmonizing the regulatory framework is key.

**Let's continue the joint efforts !**