3Rs implementation in veterinary vaccine batch release testing
Industry perspective

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1. Who is HealthforAnimals?

2. 3Rs implementation in veterinary vaccine batch release testing
   - Use of animals in science
   - Target Animal Batch Safety Tests
   - Potency tests: new perspectives

3. Conclusion
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?

28 Regional and National Associations working in 40 countries

Ten largest Animal Health companies – 100+ countries

Vaccines, anti-parasiticides, diagnostics, digital services, antibiotics, etc.
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.
Where should we act? Example of EU

Batch safety testing; 22.2%

Other quality controls; 2.8%

Pyrogenicity testing; 0.1%

Batch potency testing; 75%

Regulatory Use: Quality control (EU – 2019)
Source: ALURES published data
Animal Batch Safety Tests:

TABST (Target Animal Batch Safety Test)

LABST (Laboratory Animal Batch Safety Test)
Together, these advancements have led to calls for the elimination of the TABST and LABST.
Harmonisation of criteria to waive target animal batch safety testing for inactivated vaccines for veterinary use  ✓ May 2013

Harmonisation of criteria to waive target animal batch safety testing for live vaccines for veterinary use ✓ May 2017

Harmonisation of criteria to waive laboratory animal batch safety testing for vaccines for veterinary use ✓ 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

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

- 42% of animal use for TABST

Status of the TABST in major countries

Source: ALURES published data

Brazil recently adopted VICH TABST/LABST guidelines
3Rs implementation in veterinary vaccine batch release testing

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

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 €
2100 € < 250 €

28 days
24h
Challenges

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!