THE EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)
Overview about implementation and regulatory acceptance of non-animal testing in veterinary vaccines in Europe

ASIA Webinar, October 20th, 2022

3Rs implementation in veterinary vaccine batch-release testing: Current state-of-the-art and future opportunities

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Presentation overview

✓ Short introduction: The Council of Europe (1949)
✓ The European Pharmacopoeia (Ph. Eur.) Convention (1964)
✓ European Convention (ETS 123) for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (1986) → strong 3Rs commitment
✓ Latest Ph. Eur. achievements in the 3Rs
  Ph. Eur. texts (3R §, consistency of production, alternative methods, door openers, review, risk assessment ...)
✓ Main milestones/major 3Rs achievements
  o Chapter 5.2.14 Substitution concept
  o TABST removed from the Ph. Eur. as of April 2013
  o BSP Rabies, BSP Clostridia vaccines ...
✓ Conclusion: wide acceptance of non-animal testing based on science, in particular for routine batch tests
The Council of Europe (CoE)

- Founded in 1949
- Headquarters in Strasbourg, France
- 46 member states
- >700 million citizens
- The oldest pan-European organisation dedicated to fostering co-operation in Europe
  - Promotes democracy
  - Protects human rights
  - Protects the rule of law

46 Member States 27 of which are members of the EU + 6 Observer States
## EDQM - The Council of Europe (COE) and the 3Rs commitment

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<th>Year</th>
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<td>1949</td>
<td>Foundation of the Council of Europe</td>
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In 2022: 40 members - including the EU and 30 observers - including WHO  
→ Ph. Eur. texts are mandatory in all member states on the same date - harmonisation of technical requirements for the authorisation and manufacture of medicinal products |
| 1986 | European Convention (ETS 123) for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (3Rs) |
Agreement between the Council of Europe & the EU Commission |
| 1994 | EU becomes full member of the Ph. Eur. Convention  
| 2010 | Directive 2010/63/EU entry into force on 10 November 2010  
Transposition completed by 10 November 2012 and full effect on 1st January 2013 |
Latest Ph. Eur. achievements in the 3Rs

1. 3Rs referred to at several levels and throughout the Ph. Eur. => Article 4 of Directive 2010/63/EU reinforced

   Non-animal tests should be used wherever possible; and if not possible, the least number of animals should be used with the least pain/suffering

2. Consistency of production (General Notices 1.1.2.2 (3))

   → Concept to support the 3Rs allowing the omission of in vivo routine tests on the final product when consistency is demonstrated.

   Need in-depth knowledge of the product, the production and the QC process.

3. Alternative validated methods for routine testing (BSP and OMCL input)

   ex. Immunogenicity/batch potency: Same pass/fail result
Latest Ph. Eur. achievements in the 3Rs

4. Chapter 5.2.14. Substitution of *in vivo* method(s) by *in vitro* method(s) for the quality control of vaccines: **Scientific relevance** of the *in vitro* method but a head-to-head comparison with an existing *in vivo* method is not possible → provides **guidance on validation** of substitute methods, a way to encourage transition from *in vivo* to *in vitro* methods.

5. **Door openers** to encourage to develop alternative methods

6. Regular review of the requirements to see where animals could be saved or suffer less:
   - **humane endpoints** included,
   - **less control animals** included in the tests,
   - Introduction of **risk assessment strategy** and new analytical methods such as PCR for example for Extraneous agents testing
   - **rationalise** the requirements
Deletion of the Target Animal Batch Safety Test (TABST)

Experts of the Ph. Eur.

- Discuss the scientific justification
- Retrospective analysis carried out

2018 Terrestrial Manual chapters on vaccine production and manufacturing sites

VICH GL 41 and 44

VICH GL 50R and 55

Ph. Eur. 2013

World Organisation for Animal Health

Deletion of TABST from the Ph. Eur.

Animals saved: horses, cattle/calves, pigs/piglets, sheep/lamb, dogs, ferrets, cats (often 8-12 weeks old), rabbits, guinea-pigs (tetanus vaccine), chickens and turkeys (often 14 to 28 days old), domestic ducks, fish (salmonids).
Testing for extraneous agents (human and veterinary vaccines)

- Revision of testing strategy for extraneous agents: risk-based approach
- Moving quality requirements upstream (healthy flocks) (vet)
- Revision of chapters to delete animal tests as far as possible, based on available literature (human)
- Reference to molecular methods

For more details, please refer to EDQM online training resources
Session 5: Supporting microbiological and viral safety

- EDQM/Ph. Eur. achievements in the control of extraneous agents for vaccines & perspectives on HTS

Featured Session on Microbiological and Viral Safety
20 September 2022
Catherine Lang and Gwenaël Cirefice, EDQM
Conclusion

Wide acceptance of non-animal testing based on science, in particular for routine batch tests.
Thank you for your attention

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