

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
 - Chapter 5.2.14 Substitution concept
 - TABST removed from the Ph. Eur. as of April 2013
 - 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)



46 Member States

- **Founded in 1949**
- **Headquarters in Strasbourg, France**
- **46 member states**
- **700 million citizens**
- **The oldest pan-European organisation dedicated to fostering cooperation in Europe**
- **Promote human rights**
- **Protects the rule of law**

www.coe.int



46 Member States 27 of which are members of the EU + 6 Observer States

EDQM - The Council of Europe (COE) and the 3Rs commitment

1949	Foundation of the Council of Europe
1964	The Ph. Eur. Convention , a Council of Europe partial agreement https://www.edqm.eu/en/european-pharmacopoeia <i>In 2022: 40 members - including the EU and 30 observers - including WHO</i> → Ph. Eur. texts are mandatory in all member states on the same date - harmonisation of technical requirements for the autorisation and manufacture of medicinal products
1986	<u>European Convention (ETS 123) for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (3Rs)</u>
1991	Biological Standardisation Programme (BSP) https://www.edqm.eu/en/biological-standardisation-programme <i>agreement between the Council of Europe & the EU Commission</i>
1994	EU becomes full member of the Ph. Eur. Convention Creation of the OMCL Network (<i>66 OMCLs in 35 countries</i>) https://www.edqm.eu/en/omcl-network
2010	Directive 2010/63/EU entry into force on 10 November 2010 <i>Transposition completed by 10 November 2012 and full effect on 1st January 2013</i>

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**



**Ph. Eur.
2014**

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.

Ph. Eur.
2018

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)



**VICH GL 41
and 44**



Experts of the Ph. Eur.



- Discuss the scientific justification
- Retrospective analysis carried out



World Organisation
for Animal Health
Founded as OIE

2018 Terrestrial Manual
chapters on vaccine production
and manufacturing sites

**Deletion of
TABST from
the Ph. Eur.**

**VICH GL 50R
and 55**



**Ph. Eur.
2013**

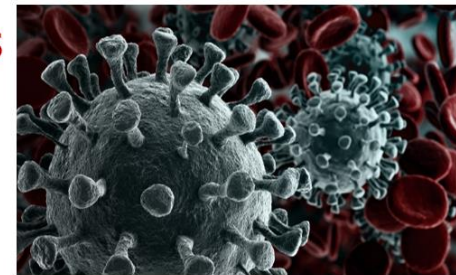
Animals saved:
horses,
cattle/calves,
pigs/piglets,
sheep/lamb, dogs,
ferrets, cats (often
8-12 weeks old),
rabbits, guinea-pigs
(tetanus vaccine),
chickens and
turkeys (often 14
to 28 days old),
domestic ducks,
fish (salmonids).

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
<https://www.edqm.eu/en/-/conference-collaboration-innovation-and-scientific-excellence-the-european-pharmacopoeia-11th-edition>
[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 Gwenael Cirefice, EDQM

Summary of the achievements in Europe

WWW.COE.INT HUMAN RIGHTS DEMOCRACY RULE OF LAW EN

COUNCIL OF EUROPE COUNCIL OF EUROPE

edqm European Directorate for the Quality of Medicines & HealthCare / Direction européenne de la qualité du médicament & soins de santé

Home About us European Pharmacopoeia Reference Standards Certification of Suitability OMCL Network Transfusion & Transplantation Patient & Consumer Health Protection

Home > European Pharmacopoeia > Focus > Alternatives to Animal Testing

Alternatives to Animal Testing

- ▶ The Council of Europe on the protection of animal rights
- ▶ Categories of medicines concerned by animal testing for Quality Control purposes
- ▶ The contributors to the introduction of the 3Rs in the European Pharmacopoeia
- ▶ Achievements of the Ph.Eur. Commission for 3Rs
- ▶ Achievements of the Biological Standardisation Programme for 3Rs



NEWS

- ▶ [Ph. Eur. to replace Histamine Sensitisation Test \(HIST\) for residual pertussis toxin testing](#) (14/01/2018)
- ▶ [Major 3Rs achievement for Official Control Authority Batch Release of human vaccines](#) (11/12/2018)
- ▶ [EDQM welcomes WHO recommendation to discontinue innocuity test in guidelines on vaccines and biologicals](#) (06/12/2018)
- ▶ [Replacement, Reduction, Refinement \(3Rs\) - activities of the Ph. Eur. Commission in the last decade](#)

The Council of Europe on the protection of animal rights

The protection of animal rights and in particular those used for experimentation has long been a priority for the Council of Europe. The first milestone was achieved in 1986, when the [European Convention \(ETS 123\) for Experimental and Other Scientific Purposes](#) was open for signature. This Convention is designed to reduce the number of animals used for such purposes and it encourages not to experiment on animals and promotes research into alternative methods.

Major 3Rs achievement for Official Control Authority Batch Release of human vaccines

EDQM | STRASBOURG, FRANCE | 11/12/2018
In line with the removal of the abnormal toxicity test (ATT) from the European Pharmacopoeia (Supplement 9.6), the 21 product-specific guidelines for Official Control Authority Batch Release (OCABR) of vaccines for human use that contained references to the ATT in the manufacturer's protocol section (Section 3) have been revised to delete the test.

[accines:](#)
[oposed](#)

[normal](#)

[Commission supports 3Rs-reducing texts implementing and promoting animal](#)

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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