THE EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)

edqm

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

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

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

Catherine Lang
EDQM, Council of Europe

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)

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

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

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

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

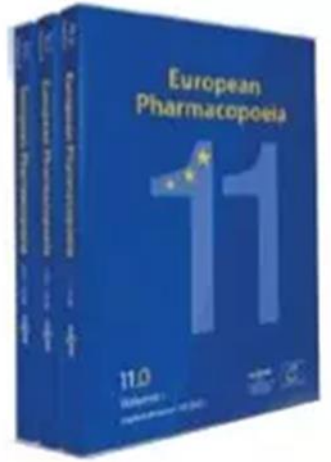
1949	Foundation of the **Council of Europe**
1964	The **Ph. Eur. Convention**, a Council of Europe partial agreement https://www.edqm.eu/en/european-pharmacopoeia *In 2022: 40 members - including the EU and 30 observers - including WHO* → Ph. Eur. texts are **mandatory in all member states on the same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

Ph. Eur. 2014

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

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

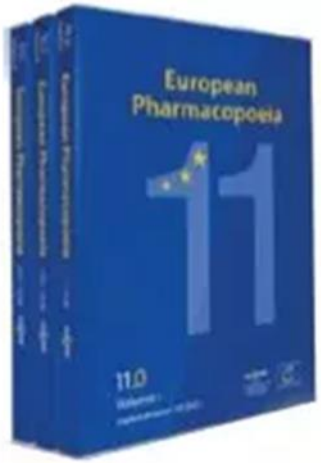
ex. Immunogenicity/batch potency: **Same pass/fail result**

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**

Ph. Eur. 2018

→ 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)

VICH GL 41 and 44

Experts of the Ph. Eur.

- Discuss the scientific justification
- Retrospective analysis carried out

2018 Terrestrial Manual chapters on vaccine production and manufacturing sites

World Organisation for Animal Health
Founded as OIE

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).

VICH GL 50R and 55

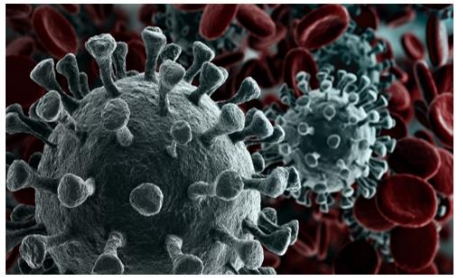
Ph. Eur. 2013

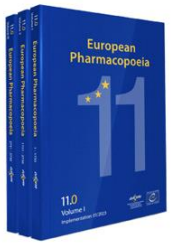
Testing for extraneous agents (human and veterinary vaccines)

- ❑ 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 ressources
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



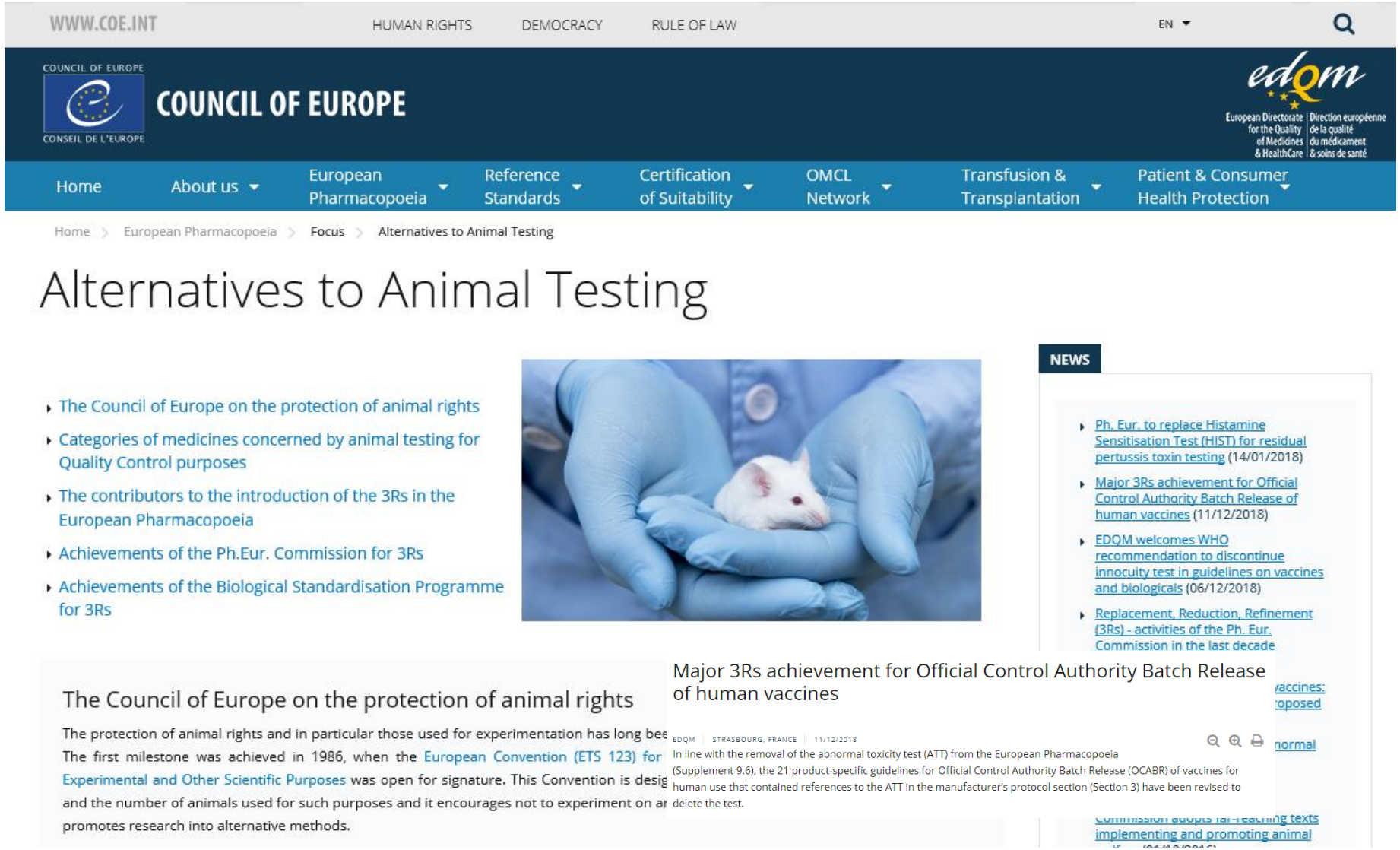


Featured Session on Microbiological and Viral Safety
20 September 2022
Catherine Lang and Gwenael Cirefice, EDQM

Summary of the achievements in Europe

Conclusion

wide acceptance of non-animal testing based on science, in particular for routine batch tests



Thank you for your attention

Stay connected with the EDQM

EDQM Newsletter: **https://go.edqm.eu/Newsletter**
LinkedIn: **https://www.linkedin.com/company/edqm/**
Twitter: **@edqm_news**
Facebook: **@EDQMCouncilofEurope**