“Transition to non-animal based veterinary vaccine batch release testing.
Policy and regulations theoretical aspects and case studies”

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Closing Remarks

Elisabeth Balks, Paul-Ehrlich-Institut/3RsWP

International Outreach

- **VICH-Guidelines** initiative `Technical recommendations for the transition to in vitro methods for batch potency tests´
- **Ph. Eur. 5.2.14/WHO "5.2.14-like" TRS**
- **VAC2VAC Project**
  - 21 partners, human & vet – vaccine industry, regulatory agencies, OMCLs, universities, translational research organisations
  - Achievements: DTaP, TBEV, vet rabies, C. chauvoei, C. perfringens, C. tetani, feline leukaemia vaccine

https://europevaccine.wixsite.com/vac2vac-eu

Case studies – Rabies

3 different glycoprotein ELISA methods for potency (Zoetis, Merial/BI, MSD)

- **Detection of immunologically relevant antigen (trimeric pre-fusion form of glycoprotein G)**
  ⇨ relevant epitope is well established and defined but this will not always be the case
- **One single assay method may not be suitable for all products**
- **Consistency approach/historical data**
  - **to establish release and end of shelf-life specifications**
  - **to establish a reference without challenge test**
- **Link with efficacy/safety studies facilitates the procedure**

Case studies - C. tetani

- **BINACLE** assay specifically **detects active tetanus toxin molecules** based on their receptor-binding and proteolytic characteristics
  - May represent a suitable alternative to test for "**absence of tetanus toxin**", performed to date in guinea pigs.
  - BSP study finalized, discussions about inclusion of the method into the Eur. Pharmacopoeia are ongoing.
  - Product-specific validation (as the method may not be applicable to all toxoids).
- **Luminescence-based cell assay (toxicity & neutralisation assays)**
  - Slightly more complex
  - Full intoxication model
  - Recombinant capture antibodies

⇨ Different functional, partly complementary methods available

- **ELISA** for **antigen recovery**
  - applicable to wide range of products
  - product specific desorption step may be needed

NGS/HTS for purity testing

- HTS/NGS could be part of the **testing strategy for adventitious/extraneous agents** (Ph. Eur. chapter 5.2.5, substitute/replace multiple *in vitro/in vivo* tests (3R)
- The future (2025) Ph. Eur. general **chapter 2.6.41 on HTS/NGS** will provide a **detailed description of the technology** together with **validation guidelines**, to support users implementing this new technology
- Need for **regulatory standards**
- Appropriate (viral) **database**
- Positive hits require **laboratory-based follow-up**

Transition to non animal based batch release testing – key aspects

- Methodolgy: science based, data driven approach
  - Critical quality attributes´[1]
  - Suitability through all steps of vaccine production and in complex matrix
  - Stability indicating
  - Robustness & transferability
  - Product specific validation
  - Evaluate new technologies
- Availability/sustainability of well characterised reagents/reference material
- International (global) cooperation/alignment/regulatory acceptance (sharing of information, publication)
- Modern laws, regulations, pharmacopoeias and testing concepts (state of science, innovative thinking)

[1]Dierick et al.: The consistency approach for the substitution of *in vivo* testing for the quality control of established vaccines: practical considerations and progressive vision Open Research Europe 2022, 2:116 Last updated: 05 JAN 2023