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A NOVEL MULTIPLEX IMMUNOASSAY FOR ANIMAL-FREE QUALITY CONTROL OF DIPHTHERIA-TETANUS-ACELLULAR PERTUSSIS VACCINES

Quality of vaccines and blood products (QVPS) – D&R
Study day of animal welfare – Brussels – 27/03/23

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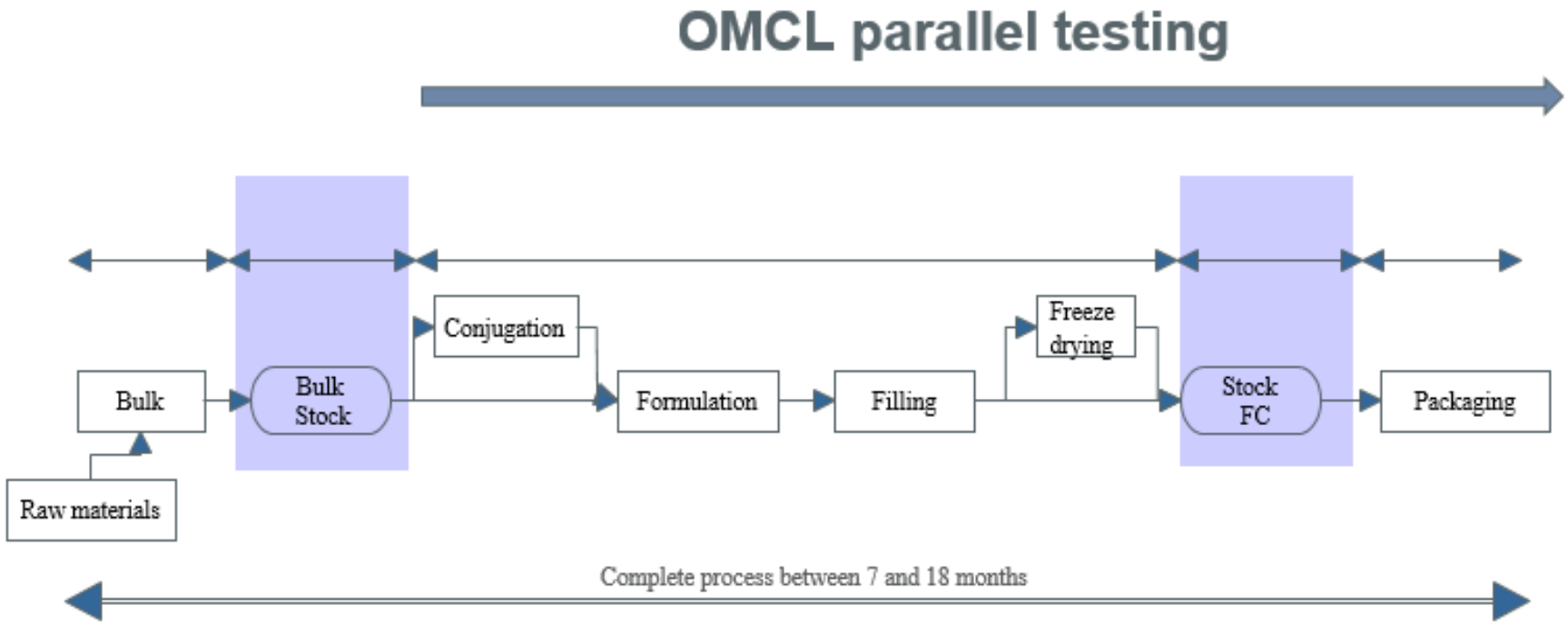
Sciensano – Official Medicine Control Lab (OMCL)

Core activities:

- **Batch Release** of Biological Medicinal Products (human and veterinary vaccines & plasma-derived medicinal products)
- **Advising** during licensing and GMP inspections for human and veterinary vaccines, Plasma derivatives, rDNA Biological Medicinal Products, Biosimilars
- **R&D projects** (e.g. EU IMI2 project incl. VAC2VAC)
- Ad hoc **regulatory activities** (Draft/revision of guidelines/monographs, audits, assessments, inspections)

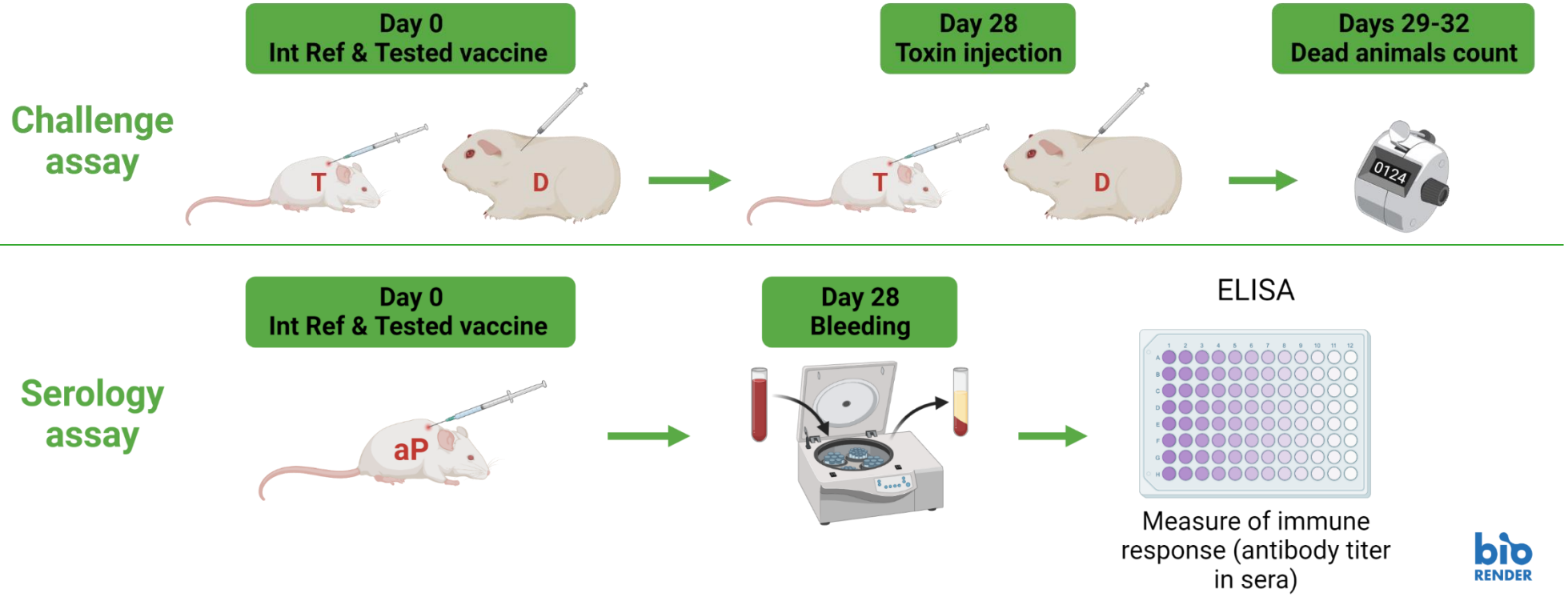
Sciensano – Official Medicine Control Lab (OMCL)

Before being put onto the European market, each batch of human vaccine (including Covid-19) produced by a manufacturer has to be **tested** by an OMCL (Official Medicine Control Lab) and granted an EU batch release certificate according to article 114 of the EU directive 2001/83/EC as amended**. Production and control data** from the manufacturer are **reviewed** in parallel during this procedure called OCABR (Official Control Authority Batch Release).



Animal use in the frame of DTaP vaccine quality control

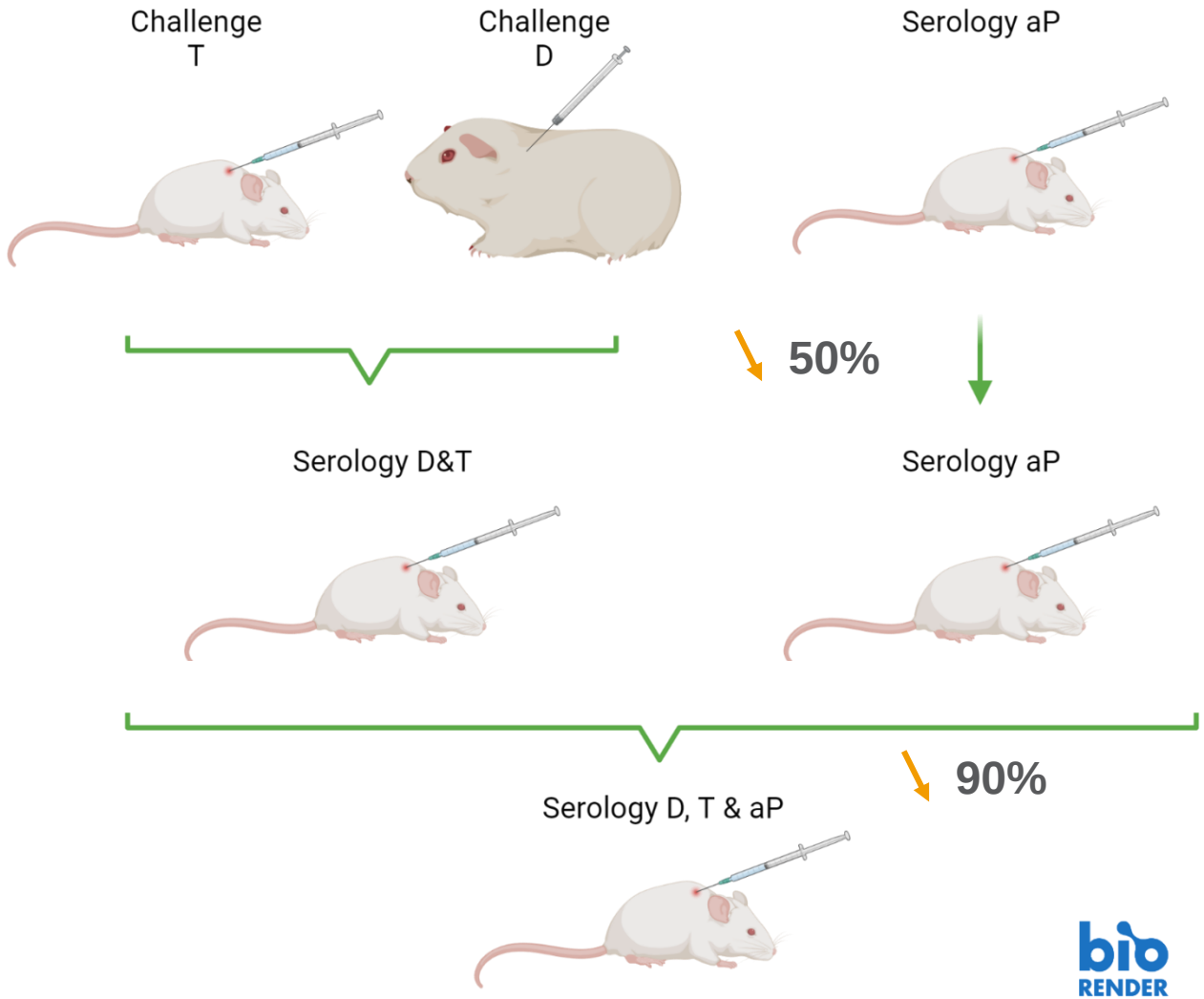
- DTaP vaccines
  - ❖ Several antigens combinations: Diphtheria, Tetanus, Pertussis (+ IPV and/or HepB and/or Hib)
  - ❖ Confer active immunity against Diphtheria, Tetanus and Pertussis
  - ❖ Classified as « old » vaccines → Developed in the 1930s' and authorized in the 50s'
  - ❖ Limited alternatives to *in-vivo* testing for potency assessment



3R activities: reduce & replace

- Reduce
  - ❖ Substitution of multiple dilution Assay by single dilution Assay for D&T potency
  - ❖ Implementation of reduction scheme on DT vaccines

- Replacement
  - ❖ D&T challenge testing
    1. Serological testing (ongoing)
    2. *In-vitro* (potency immunoassay)



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bio RENDER

VAC2VAC

FUNDERS
IMI2 and EFPIA

TIMELINE
March 2016 to
February 2022

CONSORTIUM
23 partners
(DE, NL, UK, IT, BE,
FR, AT)

COORDINATOR
European Vaccine
Initiative

PRODUCTS:
7 Vaccine Franchises
5 veterinary, 2 human and 1 adjuvant

33 TASKS:
organized in **4 technical work packages** (WP)
to replace animal assays in Quality Control

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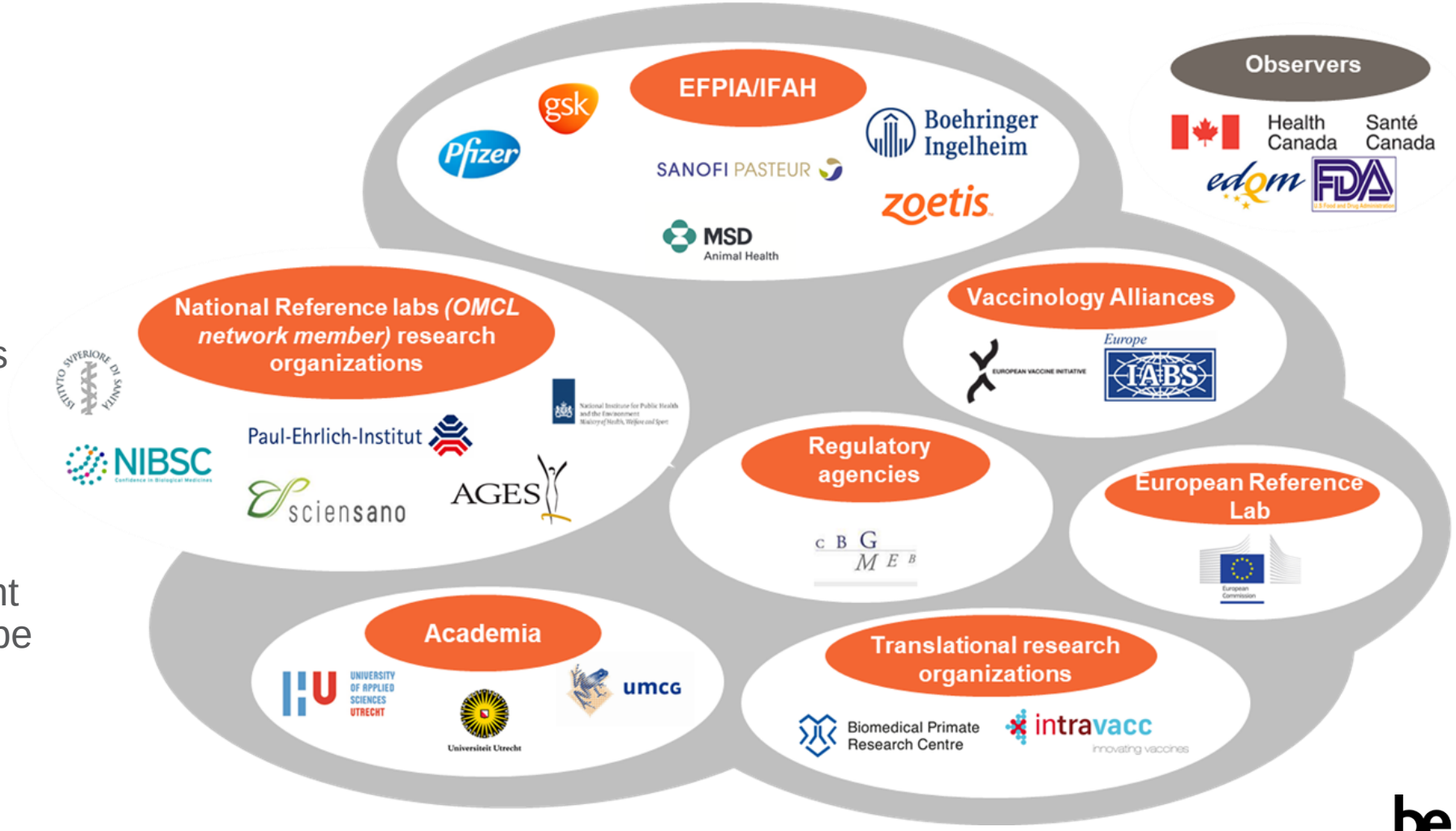
Affiliations of VAC2VAC Partners

7 types of affiliations

Working together to substitute animal assays for lifecycle vaccines

Observers ensure alignment within and outside Europe



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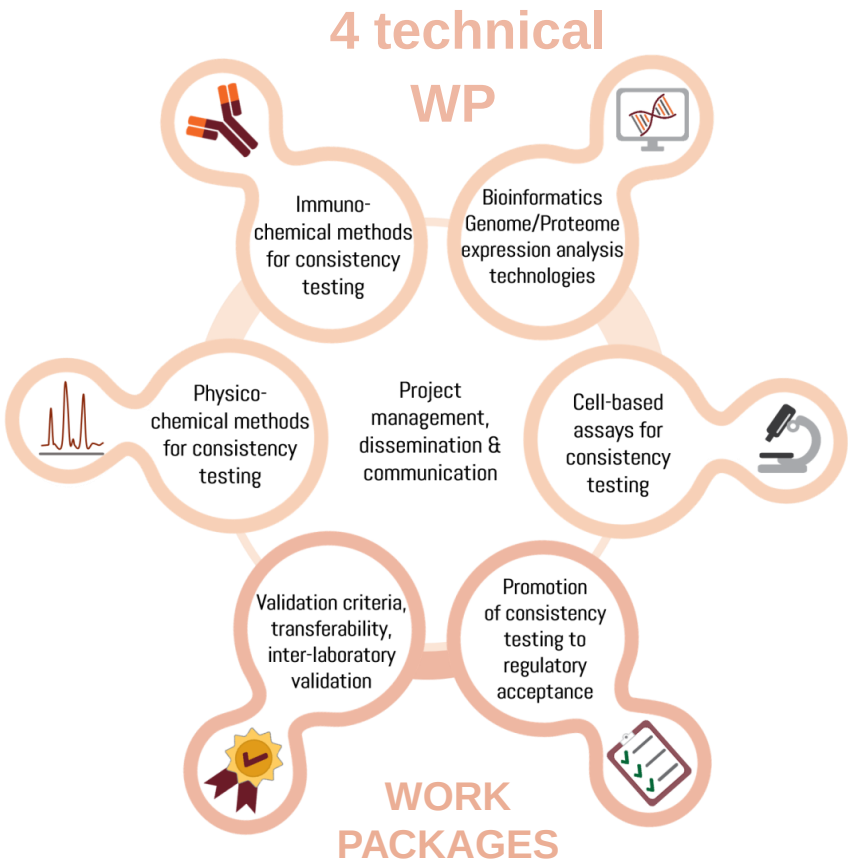
VAC2VAC - Objectives

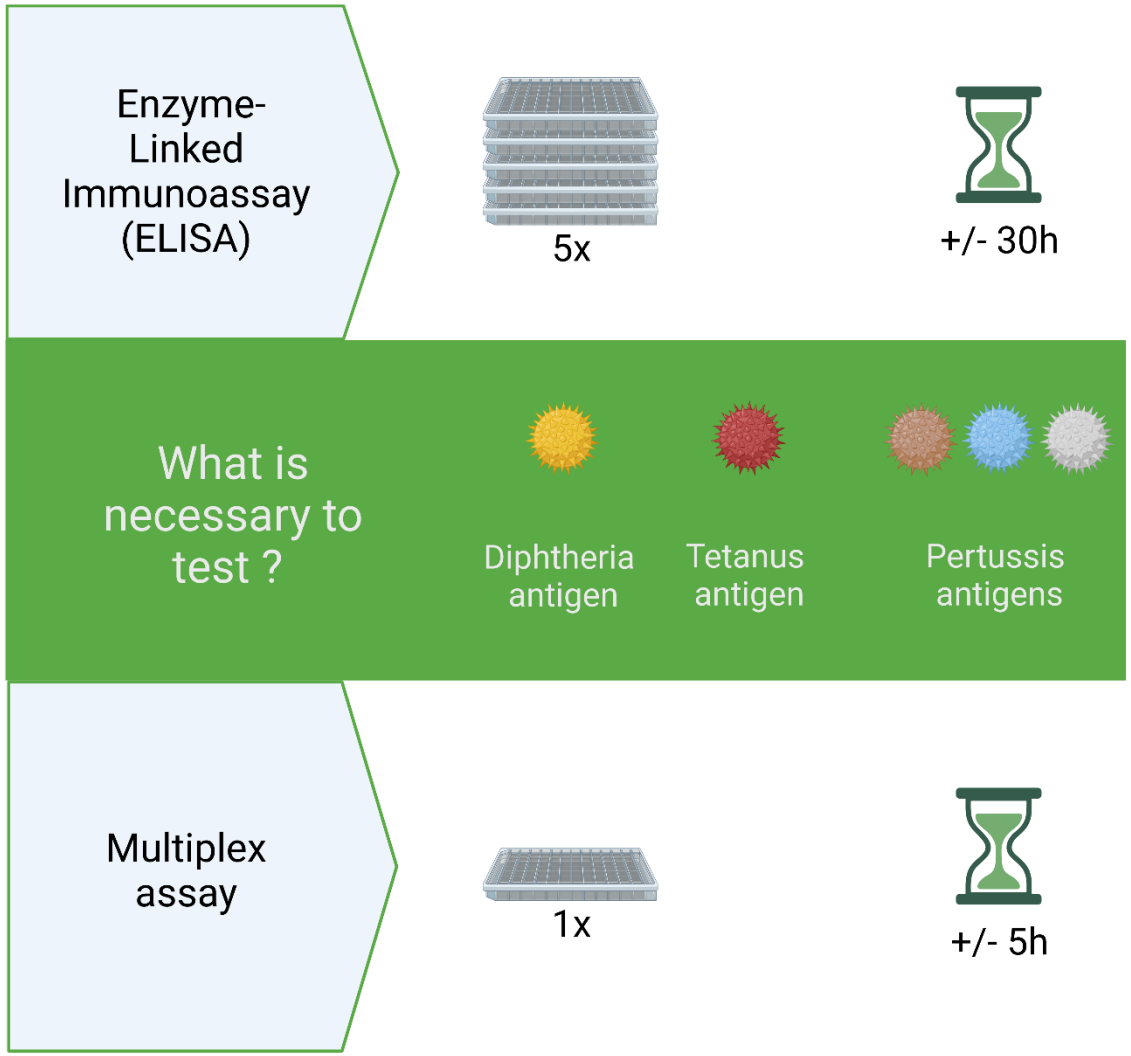
The overall objective of the VAC2VAC project is to demonstrate **proof of concept of the consistency approach for batch release testing of established vaccines** using sets of *in vitro* and analytical methods

1. Development of new or optimisation of existing **non-animal methods** for consistency testing
2. **Pre-validation** of selected methods
3. **Regulatory acceptance** of the consistency approach



Multiplex immunoassay development for DTaP vaccines

- Multiplex advantage
  - ❖ One assay to assess 5 antigens
  - ❖ Faster (*vs.* std immunoassay *e.g. ELISA*)
- Well characterized antibodies
  - ❖ 5 mAb pairs characterized and selected during VAC2VAC for DTaP antigens
- 8 vaccines from 2 manufacturers



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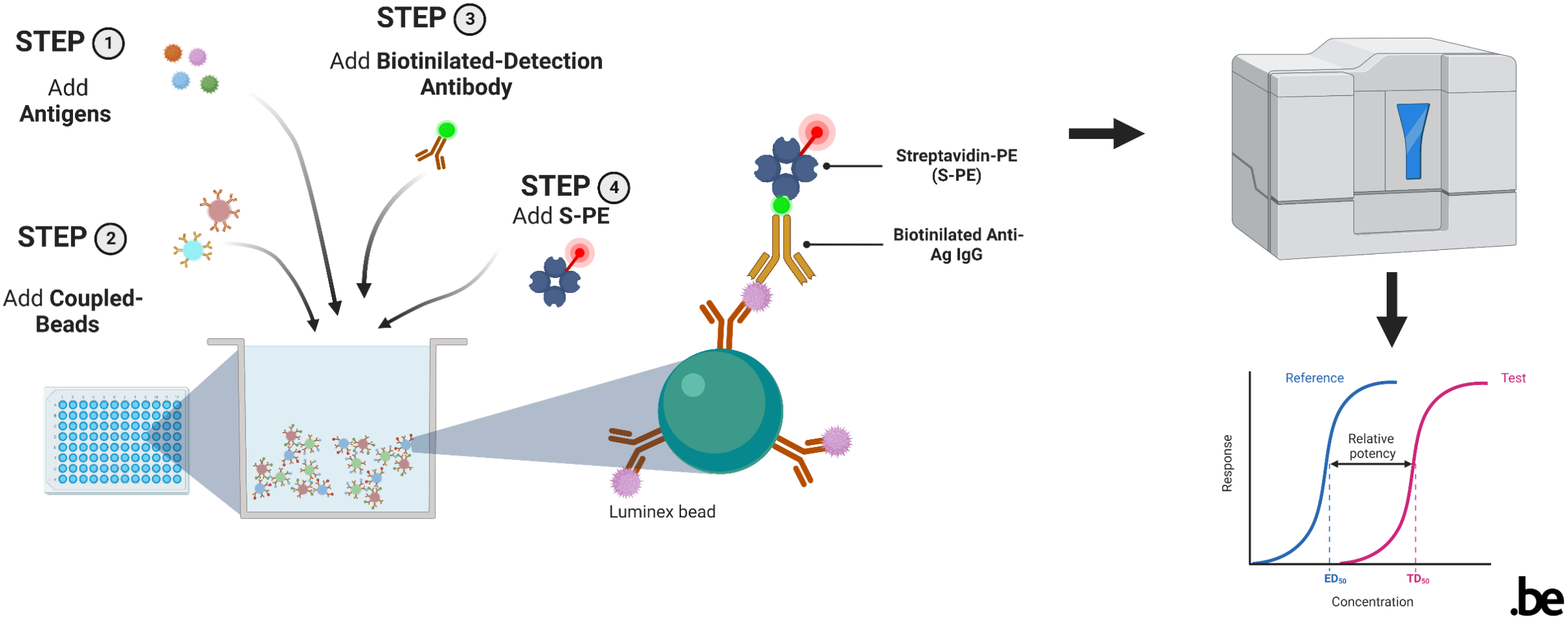
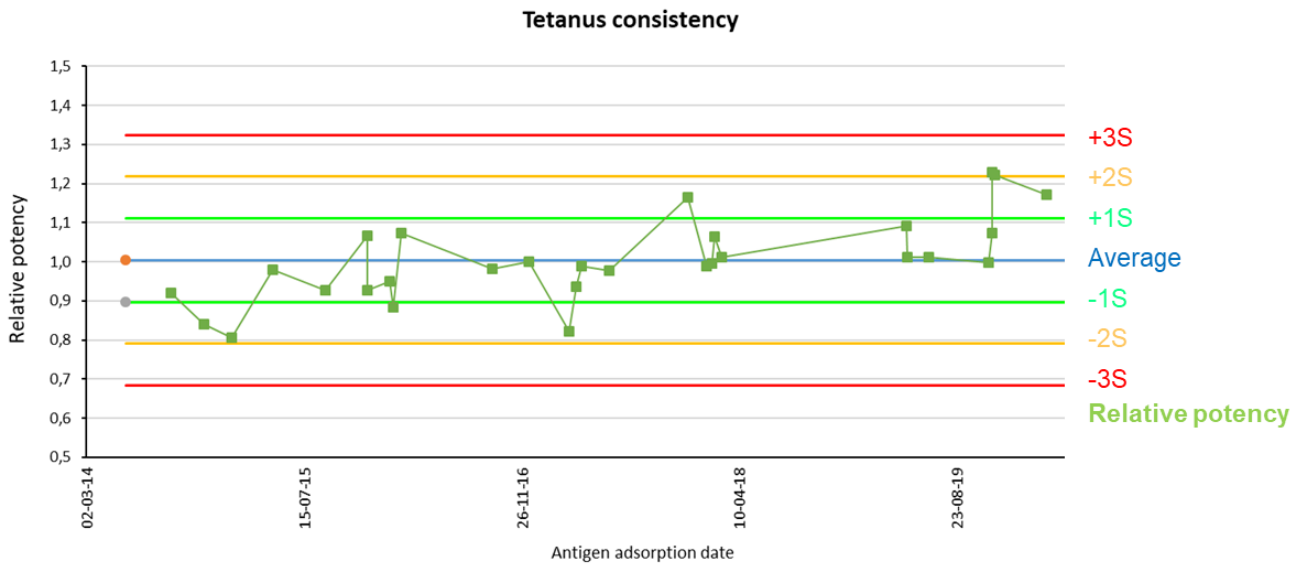
Mutliplex - Principle of the method

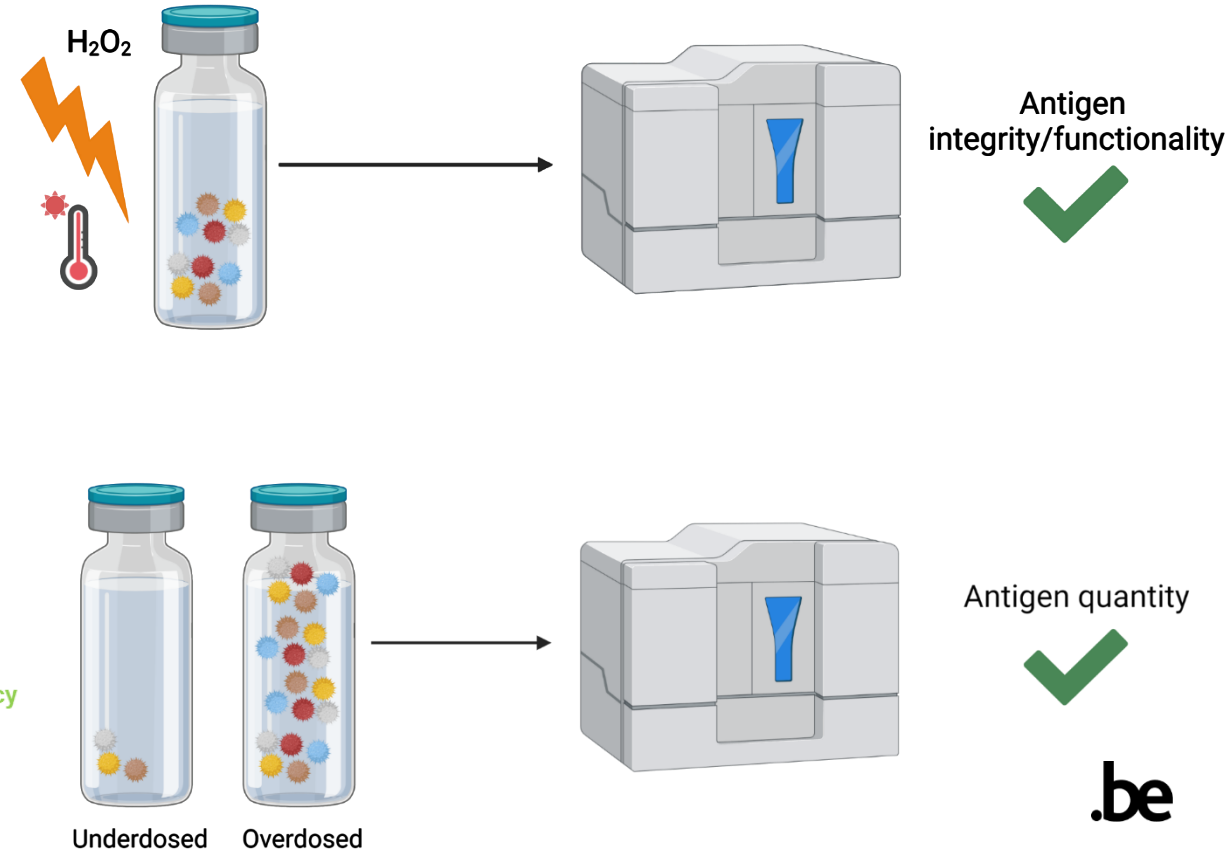


What the multiplex assay should detect ?

Ph EurGeneral Chapter 5.2.14: Substitution of In Vivo Methods by In Vitro Methods for the Quality Control of Vaccines:

1. Antigen functionality
2. Antigen quantity
3. Production consistency monitoring





Where are we and where are we going ?

- Results have been presented during VAC2VAC and will be published soon

- Great enthusiasm from members of the consortium
  - Regulatory agencies
  - Pharma companies

- Method transferred to one manufacturer and VAC2VAC-selected antibodies available on NIBSC website

- The ball is now in the court of the manufacturers
  - Accumulation of data with *in-vitro* potency assay
  - Standards qualification
  - Submission of variation dossier to EMA

VACVAC accomplishments

Rabies in vitro potency assay

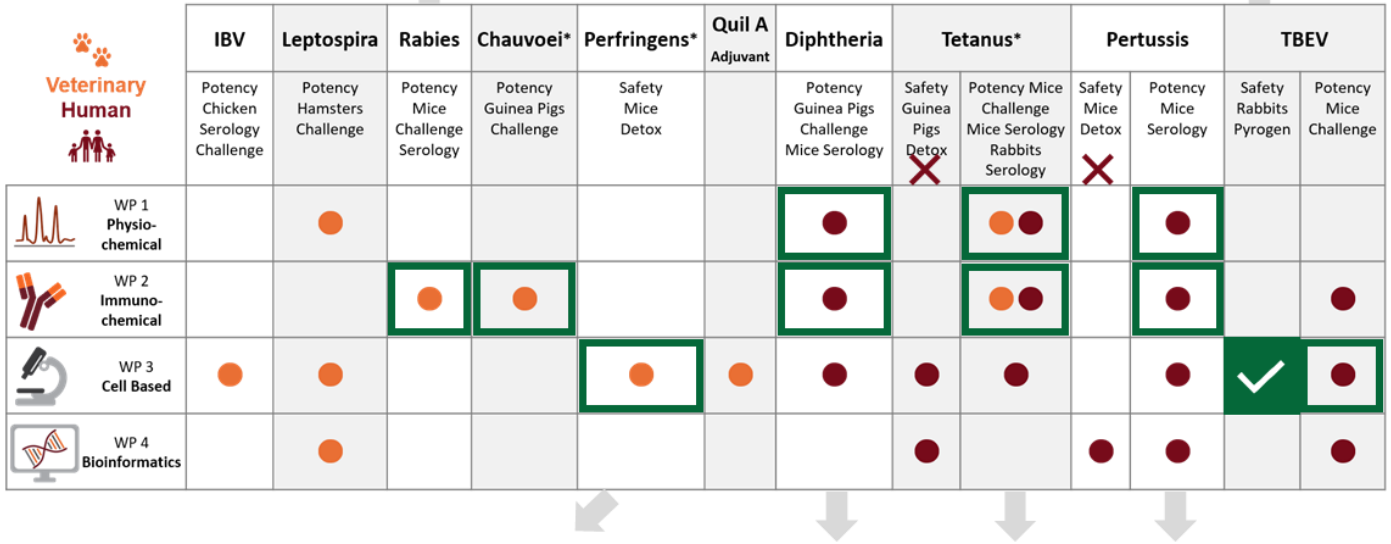
Strain-specific replacement ELISA have been designed. Validation ongoing / done / method filed (depending on manufacturer)

Completed: Substitute Rabbit pyrogen test for TBEV vaccine

National reference lab and Manufacturer validated the alternative. Triggered a discussion to revise the concerning Eu.Ph. monograph

Clostridium chauvoei in vitro potency assay

A promising replacement ELISA has been set up and will be transferred to manufacturers for validation and implementation



Substitute mice challenge assay for TBEV vaccine with ELISAs

ELISAs for two TBEV vaccines qualified. Collaborative study in preparation among National reference lab and manufacturers

Clostridium perfringens C in vitro safety/toxin content assay

A substitution of the in vivo safety assays has been developed and transferred to manufacturers for further assessment and validation

Substitute in vivo potency assays for Diphtheria, Tetanus and Pertussis

Proof of concept and transfer to industry partners achieved. Characterized antibodies commercially available (NIBSC website)

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Conclusion

- Many efforts are made to reduce/substitute animal testing in the frame of vaccine batch release
- Several *in-vitro* assays developed during VAC2VAC
- Need some time to implement the assays in routine but a “mindset change” of regulators/manufacturers operated during VAC2VAC to move towards “animal-free” assays

Thanks for your attention

Questions ?