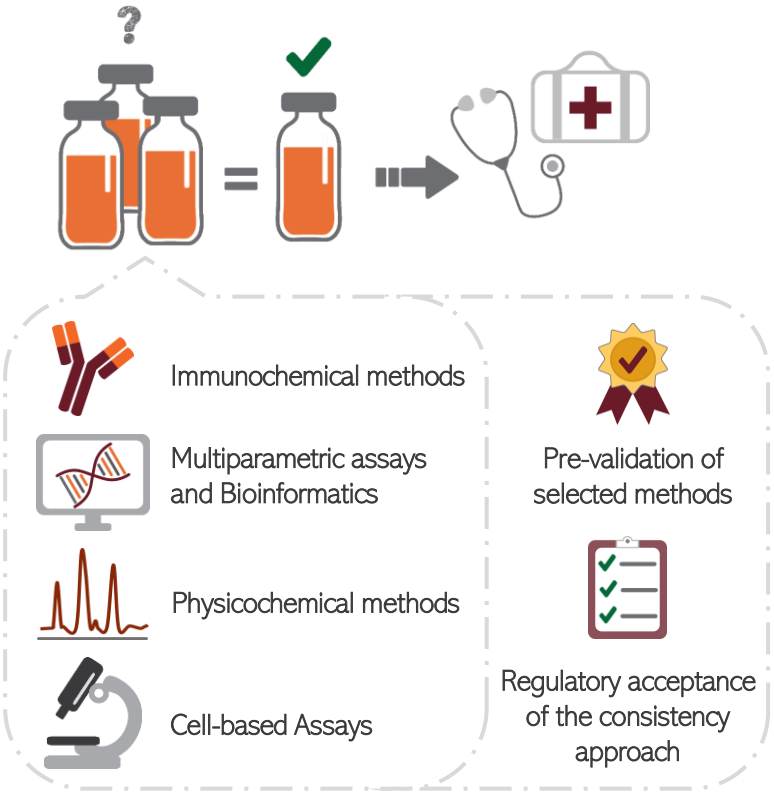
# VAC2VAC

Vaccine batch to vaccine batch comparison by consistency testing

NEWSLETTER Vol. IV Mar. 2021

## Rationale & Goals




CONSISTENCY APPROACH

The overall objective of the "Vaccine batch to vaccine batch comparison by consistency testing" project is to demonstrate proof of concept of the consistency approach for batch release testing of established vaccines. This means that **physicochemical, immuno-chemical, cell-based and/or multiparametric tests - instead of animal tests - shall be used to ensure that each vaccine batch produced is consistent with a batch already proven to be safe and efficacious.**

**VAC2VAC's socio-economic impact and societal implications?** Implementation of the consistency approach will lead to replacement, reduction or refinement of animal use and could lead to a revision of Pharmacopoeia monographs for some vaccines. The consistency approach will also clearly speed up the release time so that vaccine batches will be available for vaccination much quicker.

## Latest News

### VAC2VAC project to run until 28.02.2022

**The VAC2VAC project will continue until end of February 2022!** This one-year no cost extension was granted by the Innovative Medicines Initiative (IMI) to allow partners to finalise planned activities that have suffered delays due to the restrictions imposed by the COVID-19 pandemic. The extension is expected **to allow the validation/qualification of several non-animal in vitro methods developed** in VAC2VAC and the subsequent implementation by industry partners. **The VAC2VAC consortium warmly acknowledges IMI for allowing the possibility to continue with these important activities.**

### Annual Meeting 2021 and Stakeholders Meeting

From the 21-23 September 2021, the **VAC2VAC consortium will gather in Lyon, France, to discuss the progress and future of the "Consistency Approach" for quality control of human and veterinary vaccines using non-animal methods.** The meeting will be celebrated jointly with a Stakeholders meeting organized by IABS-EU in the context of WP6 activities. The consortium will offer attendees a **summary of main achievements and plans to ensure sustainability of project outputs.** In the event that pandemic related restrictions prevent a face-to-face meeting from taking place, the delivery of the meeting by videoconference will be considered.

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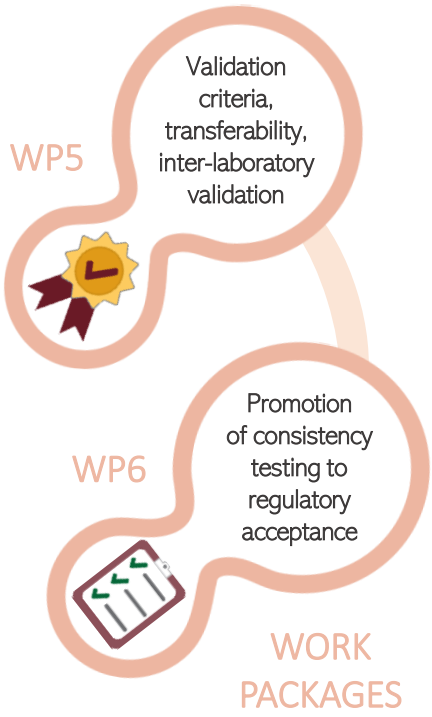
## VAC2VAC IMPLEMENTATION

### How to move from the current control strategy to a consistency approach-based control strategy?

VAC2VAC focuses on vaccines released under an *in vivo* based control strategy and develops methods to be used under a consistency approach-based control strategy not involving animal tests. What are the elements of such a control strategy, how do they differ from the current control strategy and which information should be provided in a variation dossier?

In a joint activity, WP5 and WP6 address the various points and launched discussion with external experts (SEAC, WHO, EDQM, national control authorities) in June 2020, to be continued during this year. Based on the consensus achieved, VAC2VAC plans to publish a White Paper which will summarise potential problems and provide proposals on how these may be solved.




## PRIZES

### Italian Platform on Alternative Methods (IPAM) prize awarded for master thesis on alternative methods

The undergraduate student Daniela Ricci ("La Sapienza" University Faculty of Pharmacy and Medicine- Faculty of Medicine and Psychology, Rome, Italy) was awarded the IPAM (Italian Platform on Alternative Methods) prize for her master thesis on alternative methods defined on the basis of the 3R principle. Her research project was carried out at the VAC2VAC partner Istituto Superiore di Sanità, Rome, Italy, under the supervision of Dr. Eliana M. Coccia. Her research project entitled **"Study of tick-borne encephalitis virus (TBEV) vaccine-induced immune response: possible application for the evaluation of vaccine immunogenicity"** was aimed at identifying biomarkers that likely correlate with the capacity of TBEV vaccine to stimulate a protective immune response, using an in vitro assay based on human peripheral blood mononuclear cells.

This approach not only has the potential to contribute to reduce the number of animals during the in-process controls of the TBEV vaccine manufacturing process but also represents an analytical approach (using human cells) that more closely mimics the biological processes in vaccine recipients.

## In Focus: Recent publications

INTRAVACC, INSTITUTE FOR TRANSLATIONAL VACCINOLOGY

VACCINES 2020
doi.org/10.3390/vaccines8040712

### Degradomics-based analysis of tetanus toxoids as a quality control assay

For his PhD thesis, Thomas Michiels worked on the development of a degradomics-based analysis of DTaP (Diphtheria, Tetanus, acellular Pertussis) antigens within the VAC2VAC project. In a recent publication in Vaccines, they have shown that it was possible to distinguish good tetanus toxoids from aberrant samples. Additionally, the assay could be used to **show consistency between various batches of tetanus toxoid**. This was achieved by mimicking the proteolytic degradation of antigens by the immune system in a simplified in vitro assay that identified and quantified the formation of peptides by state-of-the-art mass spectrometry. **For this research Thomas has been nominated for the Leiden University's C.J. Kok "Discoverer of the Year" award.**

UNIVERSITY MEDICAL CENTER GRONINGEN (UMCG) AND ISTITUTO SUPERIORE DI SANITÀ (ISS)

ALTEX 2021
doi.org/10.14573/altex.2010081

### In vitro assessment of tick-borne encephalitis vaccine: suitable human cell platforms and potential biomarkers

Tick-borne encephalitis virus (TBEV) infections can result in severe disease with sometimes permanent neurological complications, yet, a highly effective vaccine is available. Quality control of vaccine production batches currently involves mandatory potency testing in mice, which is ethically questionable and suboptimal with regard to reproducibility. In a collaborative effort towards non-animal potency testing, research groups from the Istituto Superiore di Sanitá (ISS), Italy, and the University Medical Center Groningen, the Netherlands, identified human peripheral blood mononuclear cells as a suitable platform and specific cytokines of the innate immune system as promising biomarkers for an in vitro TBE vaccine potency test. The results of this work have recently been published in ALTEX, a scientific journal devoted to alternatives to animal experimentation.

## Additional publications from VAC2VAC

BIOLOGICALS 2021
doi.org/10.1016/j.biologicals.2020.12.002

### Characterisation of diphtheria monoclonal antibodies as a first step towards the development of an in vitro vaccine potency immunoassay

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## UPCOMING EVENTS

22-26 AUGUST 2021. MAASTRICHT, THE NETHERLANDS

### 11TH WORLD CONGRESS ON ALTERNATIVES AND ANIMAL USE IN THE LIFE SCIENCES

3Rs in transition: from development to application

Early Bird until May 15th,2021. Find out more here

REGISTER HERE

## PAST EVENTS

2-3 FEBRUARY 2021

### EU conference: "Towards replacement of animals for scientific purposes"

The VAC2VAC project was presented at the scientific conference "Towards replacement of animals for scientific purposes". The virtual conference, organized by the European Commission, aims to **accelerate the move away from using animals in science and testing.** The main achievements of the VAC2VAC project were presented by Dr Shahjahan Shaid (GSK) in the session "Cutting edge science: latest scientific advances to improve research and testing toolbox". Check VAC2VAC website for the full presentation.

18 FEBRUARY 2021

### DCVMN Webinar: "Monocyte activation test: an animal-free method"

During this digital event Dr Eliana Coccia and Dr Marilena Paola Etna from Istituto Superiore di Sanità, introduced the **Monocyte Activation Test (MAT) assay and its advantages as replacement of the Rabbit Pyrogenicity Test**, currently still used as a Quality Control release test for several vaccines. The MAT is an **animal-free method to evaluate the pyrogen content in human vaccines and it is a clear step forward towards implementing the 3Rs.**

9-10 MARCH 2021

### Workshop webinars on "Quality Control of Veterinary Vaccines"

In the context of this joint EDQM EPAA JRC Webinar Sessions entitled 'Novel in vitro model as alternative to in vivo toxoid vaccines testing: Clostridium septicum vaccine as a proof of concept', Arjen Sloots (Intravacc) presented "Experience in extending the approach of cell-based TCP and MLD assays to Clostridium perfringens vaccines" in the session "Potential application of the Approach to other Toxoid Vaccines - Update on VAC2VAC Project". To see the presentation please follow this link.

**Abbreviations:** IABS-EU, International Alliance for Biological Standardization; WP, Work package; SEAC, Scientific and ethics advisory committee; WHO, World Health Organization; EDQM, European Directorate for the Quality of Medicines; IPAM, Italian Platform on Alternative Methods; TBEV, tick-borne encephalitis virus; DTaP, the Diphtheria , tetanus, and acellular pertussis vaccine; MAT, Monocyte-activation test; 3Rs, refers to the guiding principles for more ethical use of animals in testing: Replacement, Reduction, Refinement.

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