## 2nd IABS Workshop on Real World Evidence:

# Alternative Approaches to Phase 3 Clinical Trials for Vaccine Efficacy and Licensure: the role of Real-World Evidence

***December 10-11, 2025***
***Montreal, Canada***

Human randomized controlled trials (RCTs) have long been the gold standard for evaluating the safety and efficacy of medicinal products, including vaccines. However, their resource-intensive and time-consuming nature may render them impractical, prohibitively expensive, and too slow. As a result, there's increasing interest in exploring alternative approaches that can generate timely evidence of vaccine benefit prior to approval, complemented by real-world evidence (RWE) collection post-approval.

In the pre-approval context, several alternatives have been discussed in recent years. These include inferring vaccine efficacy by assessing immune response markers elicited by a candidate vaccine, relying on correlates of protection (CoPs) or surrogate markers as well as controlled human infection models (CHIMs). Under certain conditions, these approaches may provide sufficient reassurance of efficacy before approval, reducing or even eliminating the need for large phase 3 RCTs. While replacing phase 3 trials with such methods—or combinations thereof—remains challenging, there may be specific circumstances in which their use is not only preferable but also the only feasible and timely option. In such cases, a pre-agreed plan for verifying effectiveness post-approval using RWE would be essential.

The International Alliance for Biological Standardization (IABS) has a strong record of convening successful workshops on RWE, CHIMs, and CoPs. Building on this foundation, the upcoming meeting will bring together leading vaccine experts from these disciplines. Its objective is to develop recommendations and initiate a framework for the optimal use of diverse approaches to demonstrate vaccine benefit in the pre-licensure phase and to confirm benefit in the post-approval setting.

## Scientific/Organizing Committee

Kaat **Bollaerts**, P95 (Co-Chair)
Danielle **Craig**, CEPI (Co-Chair)
Pieter **Neels**, IABS (Co-Chair)
Frank **Vandendriessche**, IABS (Co-Chair)
Marco **Cavaleri**, EMA
Madinina **Cox**, Events Manager, IABS/MC'Com
Miles **Davenport**, UNSW
Brad **Gessner**, Independent Consultant
Adam **Hacker**, CEPI
Hector **Izurieta**, FDA
Liz **Miller**, Independent Consultant
Camille **Roux**, Events Coordinator, IABS/MC'Com
Carla **Saenz**, PAHO
Dean **Smith**, IABS-North America (NA)

## Workshop Preliminary Program

### Day 1: Wednesday, December 10, 2025

9.00 am **Opening of the meeting – Welcome**
Pieter **Neels**, IABS

**Session I: Vaccine approval in the absence of RCT efficacy data, challenges and overview**
Session Chair: Laurence de Moerlooze, P95

9.05 am Introduction to the meeting objectives
Laurence **de Moerlooze**, P95

9.10 am Developing a Group B Streptococcus vaccine for maternal immunisation: challenges for clinical development in a low-incidence, high impact infectious disease setting
Lidia **Oostvogels**, Minervax

9.20 am Review of vaccines licensed in absence of a Phase 3 randomized controlled efficacy trial
Danielle **Craig**, CEPI

**Session II: Alternative approaches to RCT efficacy data to demonstrate vaccine benefit for initial approval**
Session Chair: Laurence de Moerlooze, P95

9.40 am Summary and insights from the EMA workshop (24-25 Nov 2025) on the use of animal models
Marco **Cavaleri**, EMA

10.10 am Evidence on vaccine benefit from Human Infection Models: insights and considerations
Robert **Read**, University of Southampton

**10.40 am** ***Coffee Break***

11.10 am Evidence on vaccine benefit based on Correlates of Protection: insights and considerations
Phil **Krause**, Independent Consultant

11.40 am Panel discussion: Dealing with uncertainty in vaccine benefit at initial approval and its consequences for post-marketing activities
All Speakers and Dean **Smith**, IABS-North America (NA), Hector **Izurieta,** FDA and Brenda **Gomes Valente**, ANVISA

**12.10 am** ***Lunch***

## Session III: RWE to confirm vaccine benefit

Session Chair: Laurence de Moerlooze, P95

1.10 pm Real-World Evidence from observational studies to pragmatic trials, supporting initial licensure to label expansion
Kaatje **Bollaerts**, P95

1.20 pm Real-world evidence confirming the vaccine benefit of the third-generation mpox vaccine mva-bn (Jynneos/Imvanex/Imvamune)
Victoria **Jenkins**, Bavarian Nordic

1.40 pm Role of Real-World Evidence in the 4CMenB Regulatory Journey Against Invasive Meningococcal Disease
Ilaria **Bartalesi**, GSK

2.00 pm Real-World Evidence to confirm vaccine benefit: Ebola vaccines
Phil **Krause**, Independent Consultant

2.20 pm Bridging Pre-Licensure and Post-Marketing Evidence: The CHIKV VLP Vaccine Journey
Victoria **Jenkins**, Bavarian Nordic

**2.40 pm** ***Coffee Break***

3.10 pm Progress of the Post-Approval Effectiveness Study (DEN-401) of TAK-003 Against Hospitalized, Virologically Confirmed Dengue in Pediatric and Adolescent Populations
Suely **Tuboi,** Takeda

3.30 pm Real-World Evidence to confirm vaccine benefit: Next generation pneumococcal vaccines
Brad **Gessner**, Independent Consultant

3.50 pm Real world measurement of COVID-19 vaccine effectiveness through the pandemic and beyond
Alexander **Allen**, UKHSA

4.10 pm Real-World Evidence to confirm vaccine benefit: Updating COVID-19 vaccines
Kyla **Hayford**, Pfizer

4.30 pm End of Day 1

## Day 2: Thursday, December 11, 2025

9.00 am **Objectives of the day**
Laurence **de Moerlooze**, P95

### Session IV: Pragmatic Randomized Controlled Trials for vaccine effectiveness
Session Chair: Phil Krause

9.10 am Lessons from the pragmatic randomized trials of high-dose vs. standard-dose influenza vaccine against severe clinical outcomes (FLUNITY-HD)
Joshua **Nealon**, Sanofi

9.30 am Lessons from the pragmatic randomized trial to evaluate RSV vaccine effectiveness against hospitalizations
Brad **Gessner**, Independent Consultant

9.50 am Cracking the Code: Identifying RSV Correlates of Protection in a South African Vaccine Effectiveness Trial
Alane **Izu**, Wits VIDA

10.10 am Pragmatic RCTs and the power of vaccine probe analysis: The experience from Finland
Arto **Palmu**, FVR

10.30 am ***Coffee Break***

11.00 am Panel discussion: Barriers to and requirements for the use of pragmatic trials
Marco **Cavaleri**, Robert **Read**, Dean **Smith**, Hector **Izurieta,** Brenda **Gomes Valente**

### Session V: Break Out Session
Session Chair: Laurence de Moerlooze, P95

11.30 am Introduction Break-Out (1): Towards a framework for alternative approaches to Phase 3 Vaccine Efficacy Trials
Danielle **Craig**, CEPI

11.40 am Break Out (1): When are alternative approaches needed for vaccine licensure?

**12.30 am** ***Lunch***

1.30 pm Introduction Break Out (2): Towards a framework for alternative approaches to Phase 3 Vaccine Efficacy Trials
Danielle **Craig**, CEPI

1.40 pm Break Out (2): What are the alternative approaches and when are they acceptable?

2.30 pm ***Coffee Break***

3.00 pm **Group discussion:** Next steps towards alternative approaches to Phase 3 Vaccine Efficacy Trials
Laurence **de Moerlooze**, P95

3.50 pm End of Day 2