



International Alliance for
Biological Standardization

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

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Role of Real-World Evidence in 4CMenB Regulatory Journey Against Invasive Meningococcal Disease

Serogroup B invasive meningococcal disease (MenB IMD) is a rare but potentially life-threatening condition. 4CMenB is a broadly protective vaccine against MenB IMD, currently registered in 59 countries worldwide. Due to the low incidence of MenB IMD, conducting phase 3 randomized clinical trials to assess vaccine efficacy prior to licensure was not feasible. As a result, 4CMenB was approved based on safety and immunogenicity data, using a recognised surrogate of protection (1).

Following licensure, large-scale immunization programs were implemented, and post-authorization commitments were established to generate real-world evidence (RWE) on vaccine effectiveness (2).

Widespread use of 4CMenB has led to the accumulation of extensive RWE, demonstrating reduction of MenB IMD by 50%-100% and vaccine effectiveness ranging from 59%-100% (3). These findings have contributed to amendments to the product information (PI), ensuring healthcare providers to have access to update RWE data (4).

This workshop will highlight the key role of post- licensure RWE in confirming pre-licensure expectations established by clinical trials and vaccine strain coverage prediction, informing updates to PI, and enhancing understanding of vaccine performance in real-world settings for a rare disease. We will also explore how different health authorities incorporate RWE into regulatory decision-making, reflecting the evolving landscape for uncommon disease evaluation. Beyond demonstrating direct protection, RWE informs immunization policy, strengthens vaccine confidence and supports adaptive strategies for disease control. Looking ahead, the continued generation and integration of real-world data will be essential to guide broader and more effective use of 4CMenB, reinforcing its contribution to public health.

- (1) Borrow R, Carlone GM, Rosenstein N, Blake M, Feavers I, Martin D, Zollinger W, Robbins J, Aaberge I, Granoff DM, Miller E, Plikaytis B, van Alphen L, Poolman J, Rappuoli R, Danzig L, Hackell J, Danve B, Caulfield M, Lambert S, Stephens D. *Neisseria meningitidis group B correlates of protection and assay standardization*--international meeting report Emory University, Atlanta, Georgia, United States, 16-17 March 2005. *Vaccine*. 2006 Jun 12;24(24):5093-107. doi: 10.1016/j.vaccine.2006.03.091. PMID: 16838413.
- (2) EMA-EPAR link: https://www.ema.europa.eu/en/documents/assessment-report/bexsero-epar-public-assessment-report_en.p...
- (3) Martínón-Torres F, Banzhoff A, Azzari C, De Wals P, Marlow R, Marshall H, Pizza M, Rappuoli R, Bekkat-Berkani R. Recent advances in meningococcal B disease prevention: real-world evidence from 4CMenB vaccination. *J Infect*. 2021 Jul;83(1):17-26. doi: 10.1016/j.jinf.2021.04.031. Epub 2021 Apr 30. PMID: 33933528.
- (4) EMA-PI link: https://www.ema.europa.eu/en/documents/product-information/bexsero-epar-product-information_en.pdf

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