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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Developing a Group B Streptococcus vaccine for maternal immunisation: challenges for clinical development in a low-incidence, high impact infectious disease setting

Streptococcus agalactiae (Group B Streptococcus, GBS) is a major cause of neonatal sepsis and meningitis worldwide and is responsible for an estimated 0.49-0.53 cases of invasive GBS disease per 1,000 live births worldwide, with the highest incidence in Sub-Saharan Africa. Early-onset disease (EOD) is transmitted vertically during labour, late-onset disease (LOD) arises up to three months postnatally. GBS meningitis contributes significantly to long-term neurodevelopmental impairment. Current prevention, based on intrapartum antibiotic prophylaxis (IAP) for women who test positive for GBS or are at high-risk, have reduced EOD incidence but not LOD, stillbirths, or preterm delivery. In addition, IAP poses challenges such as antimicrobial resistance, microbiome disruption, and is not feasible in lower-resource settings.

A maternal GBS vaccine could provide durable protection for mothers and, through transplacental antibody transfer, for their infants. However, classical efficacy trials are infeasible because of the low incidence of invasive GBS disease. A minimum of 60,000 pregnant women would be needed to have sufficient statistical power to demonstrate clinical protection in a randomised controlled trial. In recognition of these challenges, regulatory agencies, including EMA and FDA, endorse alternative licensure pathways based on validated immunological surrogate efficacy markers (SEMs). Functional antibody assays measuring maternal and infant responses are promising SEMs.

Defining and validating SEMs that can predict protection across diverse populations reliably is a key scientific and regulatory priority to enable timely licensure of maternal GBS vaccines. This approach could be a model for vaccine development against other low-incidence but high-impact infectious diseases.