International Alliance for
Biological Standardization

IABS 2nd Real World Evidence Workshop
"The Role of Alternative Approaches to Phase 3 Clinical Trials for Vaccine Efficacy and Licensure"

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Title: Cracking the Code: Identifying RSV Correlates of Protection in a South African Vaccine Effectiveness Trial

Phase III trials for three different RSV vaccines have been completed to date. One of these trials was halted early due to a potential signal of increased risk for preterm birth in low- and middle-income countries (LMICs). A bivalent RSV A/B prefusion F protein vaccine (Abrysvo™) was shown to be efficacious against RSV severe-LRTI. Nevertheless, due to limited enrolment from low-middle income countries (LMIC) in the phase III study, WHO Strategic Advisory Group of Experts (SAGE) request further investigation of the vaccine in LMIC. Also, a higher rate of preterm birth was observed only in upper-middle income countries, which too warrants further investigation. Consequent to the SAGE recommendation, we are conducting a multi-site Phase IIIb randomized clinical trial across four African countries. We are in a unique position, operating in the post-licensure, pre-introduction window -- a narrow but valuable phase that allows us to answer important questions related to safety, efficacy, and correlates of protection, within a setting that more closely reflects real-world conditions than a traditional pre-licensure trial. Embedded in our trial is a case-cohort sub-study designed to investigate correlates of protection against RSV severe-LRTI, which has not yet been established.

In the presentation, we will describe the study design, key scientific and statistical considerations, and the operational challenges of conducting a post-licensure randomized controlled trial aimed at strengthening the evidence base for maternal RSV vaccination.