Project Brief: GBS EPI Study (1091006)

Full Title of Study/Programme	Epidemiology of obstetric and neonatal outcomes in South Africa
Technical Focus Area	Research (Maternal and Child)
Rationale	Group B streptococcal (GBS) infection is a leading cause of sepsis and meningitis in neonates and young infants. Pfizer is developing a vaccine aimed at the prevention of group B streptococcal disease in young infants by active immunization of pregnant women. A Phase 1/2, randomized, placebocontrolled, observer-blinded trial to evaluate the safety, tolerability, and immunogenicity of this vaccine in healthy non-pregnant women and pregnant women aged 18 to 40 years and their infants will be conducted in South Africa, including at the Wits RHI Shandukani site. This GBS Epidemiological study is a pre-cursor to the vaccine study and aims to provide baseline data describing maternal, pregnancy and infant outcomes in the same sites where the vaccine study will be conducted. This is essential in a maternal study since often the interpretation of adverse events (AEs) seen in clinical trials, even if placebo-controlled, is limited by insufficient sample size to measure the incidence rate of specific AEs in the comparison group. In these settings, external epidemiologic data are useful to evaluate whether or not the observed number of cases of the event in the treatment group is higher than the expected number of cases, and to understand how the incidence of the AE may vary according to various risk factors. Epidemiology data are also useful for contextualizing potential safety events of interest that are identified post approval, either in ongoing clinical trials, in published studies, via spontaneous reports or active surveillance. Such data provide a broader context for adverse events, as clinical trial data are often not generalizable to the types of patients who use the vaccine and the circumstances in which it is prescribed and used in the real world, given trial exclusion criteria. This study, conducted within the setting of tertiary and secondary hospitals and their referring antenatal clinics and midwife obstetric units (MOU) in which the Phase I/II GBS clinical trial will take place, will estimate the incidence of obstetric and perinatal birth outcomes in a population as similar as possible to the population included in the Phase I/II trial. The data generated from this study will enable contextualization of emergent safety signals.
Primary Objectives	The specific objectives are to: 1) Estimate the incidence of obstetric outcomes among pregnant women who delivered at institutions from which patients enrolled in a GBS clinical trial will be recruited.

	2) Estimate the incidence of neonatal outcomes among neonates whose mothers delivered at institutions from which patients enrolled in a GBS clinical trial will be recruited. 3) Estimate the incidence of obstetric outcomes among pregnant women who received antenatal care (ANC) and delivered at institutions from which patients enrolled in a GBS clinical trial will be recruited and have characteristics similar to women who enrolled in a GBS clinical trial. 4) Estimate the incidence of neonatal outcomes among neonates whose mothers received ANC care and delivered at institutions from which patients enrolled in a GBS clinical trial will be recruited and whose mothers have characteristics similar to women who will be enrolled in a GBS clinical trial.
Secondary Objectives	
Primary Endpoint/Outcome	The outcomes estimated from objectives #1 and #2 are considered population-based estimates for the hospital, midwife obstetric units and referral clinics. The population generating these estimates will be referred to as the *source population cohort*. The outcomes estimated from objectives #3 and #4 are considered GBS clinical trial-specific estimates derived from the source population after applying specific trial inclusion and exclusion criteria. The population generating these estimates will be referred to as the *trial similar cohort*.
Secondary Endpoint/Outcome	
Study Design	This is a population-based observational medical record review study
Study Population	This study will utilize birth registers and maternity case records (MCR) from the population (institutions) from which subjects enrolled in a Group B Streptococcus (GBS) vaccine clinical trial in South Africa. The three regions are Soweto, Inner City Johannesburg, and Metro East, Cape Town, South Africa. Wits RHI will conduct the inner city component of the trial.
Study Sample Size	The sample size will be determined based on the number of each deliveries in each population, after collection of birth register data at each institution. A trial similar cohort, and a population cohort will be randomized from this overall birth register cohort. Wits RHI Shandukani will collect data from about 3300 maternal case records.
Follow-up/Duration	N/A
Study/Programme Sites	• Wits RHI Shandukani Research Centre (SRC)
Study/Programme Duration	July 2018 to June 2020
Investigators	• **Dr Lee Fairlie, Principal Investigator (Wits RHI)** • **Dr Clare Cutland**
Other Partners & Collaborators	• Pfizer • RMPRU, Soweto
Sponsors/Donors	Pfizer

Publications/Key Presentations to Date	None as yet
Progress Update as at 05/2019	Busy with data abstractions from Shandukani ANC
Frequency of Donor Narrative Report	Monthly
Overall Study/Project Contact	Dr Hermien Gous (hgous@wrhi.ac.za)
Briefing Owner and Date	Dr Lee Fairlie May 2019