

Background Incidence Rates of Selected Vaccine Adverse Events of Special Interest in Canada (EUPAS1000001053)

Table 1: Deviations from the Darwin EU® Protocol (EUPAS1000000254)

S/n	Amendment	Rationale
1	Whereas the Darwin EU project used a 90-day washout for most acute outcomes, we will use 365 days.	This reduces the likelihood of misclassifying prevalent events as incident ones, and aligns with methods used in the literature. A sensitivity analysis will be conducted in some sites using a 90-day washout and will be considered for other sites, if necessary. In addition, the DARWIN project will conduct a sensitivity analysis using 365 days.
2	Unlike the Darwin EU project, we will not calculate overall incidence rates over the entire study period. Instead, for each AESI, we will estimate and report incidence in three time periods relative to the COVID-19 pandemic: pre-, during pandemic, and post-pandemic periods. Subgroup analyses will be conducted for the post-pandemic period only.	Given the COVID-19 related disruptions to healthcare and the incidence of some AESIs, this approach provides a more nuanced picture of the background incidence rates of AESIs. Subgroup analyses will be conducted for the post-pandemic period only as this likely represents the 'new baseline' rates given the widespread availability of COVID-19 vaccinations and the underlying incidence of COVID-19 infection.
3	Whereas the Darwin EU project assessed overall rates in the entire population (across all ages), we will conduct our analyses separately for paediatric (<18 years) and adult (≥18 years) cohorts.	This enables the estimation of incidence rates for paediatric populations in jurisdictions that have such data.
4	We use a modified age categorization. Darwin EU: 0–4, 5–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80+ Present study: - Paediatric (0–17): 0–12, 13–17 - Adult (18+): 18–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80+	This categorization aligns better with our paediatric vs adult age cutoff (18 years) and avoids small cells.