Data from Developmental and Reproductive Toxicity (DART) studies for the Pfizer-BioNtech COVID-19 vaccine have been reported in Europe. According to the report presented to the European Medicines Agency, animal studies using the Pfizer/BioNtech COVID-19 vaccine do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/fetal development, parturition or post-natal development (EMA).

A combined developmental and perinatal/postnatal reproductive toxicity (DART) study of Moderna's mRNA-1273 in rats was submitted to FDA on December 4, 2020. FDA review of this study concluded that mRNA1273 given prior to mating and during gestation periods at dose of 100 µg did not have any adverse effects on female reproduction, fetal/embryonal development, or postnatal developmental except for skeletal variations which are common and typically resolve postnatally without intervention (FDA).

In a reproductive developmental toxicity study female rabbits were administered 1 mL of the Janssen COVID-19 Vaccine (a single human dose is 0.5 mL) by intramuscular injection 7 days prior to mating and on Gestation Days 6 and 20 (i.e., one vaccination during early and late gestation, respectively). No vaccine related adverse effects on female fertility, embryo-fetal or postnatal development up to Postnatal Day 28 were observed (FDA 2021). Further, based on data from ongoing and completed clinical trials of Ad26-vectored vaccines including COVID-19, HIV, and Ebola administered to pregnant individuals, overall, the Ad26-based vaccines have an acceptable safety and reactogenicity profile, without significant safety issues identified to date. In addition, the review of the available pregnancy data is not suggestive of a pregnancy-related safety concern (FDA 2021).

These DART studies provide the first safety data to help inform the use of the vaccine in pregnancy until there are more data in this population.

Among participants of Phase II/III COVID-19 vaccine clinical studies in non-pregnant adults, a few inadvertent pregnancies that have occurred are being followed to collect safety outcomes.

V-safe and V-safe Pregnancy Registry Data

As of July 19, 2021, there have been over 136,500 pregnancies reported in CDC's v-safe post-vaccination health checker (CDC 2021). Based on limited self-reported information, no specific safety signals have been observed in pregnant people enrolled in v-safe; however longitudinal follow-up is needed.

CDC is currently enrolling pregnant individuals in a v-safe pregnancy registry and as of July 19, 2021, 5,100 pregnant individuals were enrolled. Data collected through February 28 from the v-safe pregnancy registry did not indicate any safety concerns based on the reactogenicity profile and adverse events observed among pregnant individuals. Additionally, side effects were similar in pregnant and non-pregnant populations. Specific neonatal outcomes data published in the New England Journal of Medicine, along with pregnancy complication data from 275 completed pregnancies presented at the March 1, 2021 ACIP meeting are included in Table 2.

Further, no differences have been seen when comparing pregnant individuals participating in the v-safe pregnancy registry with the background rates of adverse pregnancy outcomes. It appears that the spontaneous abortion rate following COVID-19 vaccination during pregnancy is consistent with the background rate, however the ideal denominator has not appeared in published literature. Data reported by CDC indicates that the proportion of spontaneous abortions reported after COVID-19 vaccination are consistent with the known background rate of this outcome. However, a risk estimate has not yet been established.

Table 2. V-safe pregnancy registry outcomes of interest in COVID-19 vaccinated pregnant individuals

Pregnancy Complications	**Gestational diabetes**
Background Rate	7-14%
V-safe Pregnancy Registry Overall	10%

Pregnancy Complications	**Preeclampsia or gestational hypertension**
Background Rate	10-15%
V-safe Pregnancy Registry Overall	15%

Pregnancy Complications	**Eclampsia**
Background Rate	0.27%
V-safe Pregnancy Registry Overall	0%

Pregnancy Complications	**Intrauterine growth restriction**
Background Rate	3-7%
V-safe Pregnancy Registry Overall	1%

Neonatal Outcomes	**Preterm birth**
Background Rate	8-15%
V-safe Pregnancy Registry Overall	9.4%

Neonatal Outcomes	**Congenital anomalies**
Background Rate	3%
V-safe Pregnancy Registry Overall	2.2%

Neonatal Outcomes	**Small for gestational age**
Background Rate	3.5%
V-safe Pregnancy Registry Overall	3.2%

Neonatal Outcomes	**Neonatal death**
Background Rate	0.38%

V-safe Pregnancy Registry Overall	0%

**Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. CDC v-safe COVID-19 Pregnancy Registry Team [published online April 21, 2021]. N Engl J Med. DOI: 10.1056/NEJMoa2104983. Available at: https://www.nejm.org/doi/10.1056/NEJMoa2104983.*

†Shimabukuro T. COVID-19 vaccine safety update. Advisory Committee on Immunization Practices (ACIP). Atlanta, GA: Centers for Disease Control and Prevention; 2021. Available at: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf. Retrieved March 1, 2021.

Evidence will continue to be gathered through these systems and will provide clinicians with critically needed data to inform future recommendations related to COVID-19 vaccination during pregnancy (ACIP slides).