A Non-Interventional Post-Authorization Safety Study of Pfizer-BioNTech Bivalent COVID-19 Vaccine in the United States (US)

First published: 23/09/2024

Last updated: 31/01/2025

Study | Discontinued

Administrative details

EU PAS number

EUPAS1000000314

Study ID

1000000314

DARWIN EU® study

No

Study countries

United States

Study description

This US non-interventional study will use secondary data from the Research Partners that contribute to the FDA Sentinel System to evaluate the incidence of safety events of interest and the incidence of pregnancy outcomes following receipt of the Pfizer-BioNTech bivalent COVID-19 Vaccine. A self-controlled risk interval design to assess general safety events (i.e., non-pregnancy related safety events of interest, including myocarditis/pericarditis) and a cohort design to assess pregnancy outcomes (spontaneous abortion, stillbirth, and preterm birth) and birth outcomes (major congenital malformations and small size for gestational age).

Update: This study was terminated on 31-Jan-2025. The Pfizer-BioNTech bivalent COVID-19 Vaccine is no longer authorized for use in the US and safety studies of newer COVID-19 vaccine strains are expected sooner.

Study status

Discontinued

Research institutions and networks

Institutions

Pfizer

First published: 01/02/2024

Last updated: 01/02/2024

Institution

RTI Health Solutions (RTI-HS)

France
Spain
Sweden
United Kingdom
United Kingdom (Northern Ireland)
United States

First published: 21/04/2010

Last updated: 11/08/2026

Institution | Not-for-profit | ENCePP partner

Harvard Pilgrim Health Care Institute

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Jenny Sun

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 12/12/2022

Actual: 12/12/2022

Study start date
Planned: 30/09/2024

Actual: 30/09/2024

Data analysis start date
Planned: 01/01/2025

Date of final study report
Planned: 31/01/2027

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer 100%

Study protocol

C4591051_PROTOCOL AMENDMENT 1_V2.0_06DEC2023.pdf (1.93 MB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Other study registration identification numbers and links

C4591051

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

This study is a post-authorization observational cohort study based in the US.

Main study objective:

Primary objectives:

1. To estimate the relative risk of safety events of interest (including myocarditis/pericarditis) in a post-vaccination risk interval, compared with a self-matched post-vaccination control interval, among individuals in the overall population who have received Pfizer-BioNTech bivalent COVID-19 Vaccine.
2. To estimate the relative risk of pregnancy outcomes (including spontaneous abortion, stillbirth, and preterm birth) following receipt of Pfizer-BioNTech bivalent COVID-19 Vaccine during pregnancy compared with no receipt of any COVID-19 vaccine during pregnancy.
3. To estimate the POR of birth outcomes (including major congenital malformations and small size for gestational age) in infants born to women who were exposed to PfizerBioNTech bivalent COVID-19 Vaccine during pregnancy compared with that in infants born to women who were not exposed to any COVID-19 vaccine during pregnancy.

Secondary objectives:

1. To estimate the relative risk of safety events of interest (including myocarditis/pericarditis) in a post-vaccination risk interval, compared with a self-matched post-vaccination control interval, among individuals who have received Pfizer-BioNTech bivalent COVID-19 Vaccine for the following subgroups: pregnant women, immunocompromised individuals, individuals with a recorded history of severe COVID-19, and subgroups defined by age (as appropriate for the outcome).
2. To estimate the relative risk of pregnancy outcomes (including spontaneous

abortion, stillbirth, and preterm birth) following receipt of Pfizer-BioNTech bivalent COVID-19 Vaccine during pregnancy compared with no receipt of any COVID-19 vaccine during pregnancy by subgroups of maternal age.
3. To estimate the POR of birth outcomes (including major congenital malformations and small size for gestational age) in infants born to women who were exposed to Pfizer-BioNTech bivalent COVID-19 Vaccine during pregnancy compared with that in infants born to women who were not exposed to any COVID-19 vaccine during pregnancy by subgroups of maternal age.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

COMIRNATY

Study drug International non-proprietary name (INN) or common name

COVID-19 MRNA VACCINE (NUCLEOSIDE-MODIFIED)

Anatomical Therapeutic Chemical (ATC) code

(J07BN01) covid-19, RNA-based vaccine

covid-19, RNA-based vaccine

Medical condition to be studied

Pregnancy

Population studied

Short description of the study population

Individuals will be eligible for the analysis of general safety events if they are aged ≥ 6 months during the study period and have continuous medical and pharmacy insurance coverage for at least 12 months before their vaccination date or from birth until the vaccination date (for children aged younger than 12 months on the vaccination date). Women will be eligible for inclusion in analyses of pregnancy and birth outcomes if they are aged between 12 and 55 years, had a pregnancy outcome recorded during the study period, and had continuous medical and pharmacy coverage from at least 12 months before the vaccination date until the end of pregnancy. Eligibility criteria is outlined in further detail in the study protocol.

Age groups

- **Paediatric Population (< 18 years)**
  - Preterm newborn infants (0 – 27 days)
  - Term newborn infants (0 – 27 days)
  - Children (2 to < 12 years)
  - Adolescents (12 to < 18 years)
- Adults (18 to < 65 years)
  - Adults (18 to < 46 years)
  - Adults (46 to < 65 years)

Special population of interest

Pregnant women

Estimated number of subjects

20.000

Study design details

Setting

The source population will be health plan enrollees from data Research Partners (RPs) that contribute data from claims and electronic health records to the US FDA Sentinel System.

Outcomes

This study aims to assess general safety events as well as pregnancy and birth outcomes.

General safety events:

- Myocarditis/pericarditis
- Acute myocardial infarction
- Acute disseminated encephalomyelitis
- Bell’s palsy
- Convulsions
- Encephalomyelitis/encephalitis
- Guillain-Barré syndrome
- Transverse myelitis
- Deep vein thrombosis
- Disseminated intravascular coagulation
- Immune hemolytic anemia
- Immune thrombocytopenia
- Pulmonary embolism
- Thromboembolic events associated with thrombocytopenia
- Thrombotic thrombocytopenic purpura
- Venous thromboembolism
- Hemorrhagic stroke
- Ischemic stroke
- Acute respiratory distress syndrome

- Anaphylaxis
- Appendicitis
- Kawasaki disease
- Multisystem inflammatory syndrome
- Multisystem inflammatory syndrome in children

Pregnancy outcomes and birth outcomes:
- Spontaneous abortion
- Stillbirth
- Preterm birth
- Major congenital malformations
- Small size for gestational age

Data analysis plan

Analyses will initially be conducted separately using data from each RP. RP–specific aggregated results will be sent to the study coordinating center, which will combine aggregated results across the RPs for reporting. Pooled analysis of incidence rate ratios, HRs, and odds ratio estimates from all RPs will be conducted using privacy-preserving summary-level data sets (eg, risk set–level data sets) or another appropriate method. Detailed methodology for summary and statistical analyses of data collected in this study will be documented in the SAP.

Data management

Data sources

Data source(s), other

CVS Health (Aetna Research Database), Carelon Research (formerly HealthCore), Humana, Optum Research Database, HealthPartners, and Point32Health.

Data sources (types)

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

Sentinel

CDM website

https://www.sentinelinitiative.org/methods-Data-tools/sentinel-common-Data-model

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Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown