NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine

Date: 10 September 2025

Name and affiliation of the main authors: Daniel Weibel (Assistant Professor), Miriam Sturkenboom (Professor), University Medical Center Utrecht, Utrecht, The Netherlands; Alejandro Arana (Senior Director Epidemiology), RTI Health Solutions, Barcelona, Spain

Key words: Comirnaty, Pfizer-BioNTech COVID-19 vaccine, safety, pregnancy, tozinameran, AESI

Rationale and background: The novel coronavirus, SARS-CoV-2, the cause of COVID-19, resulted in a global pandemic that was declared on March 11, 2020. The Pfizer-BioNTech COVID-19 vaccine, BNT162b, tozinameran (Comirnaty®) an mRNA-based vaccine, received conditional marketing authorisation by the European Commission on 21 December 2020, for the prevention of COVID-19. The Pfizer-BioNTech vaccine is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 6 months of age and older.

At the time of first introduction of the Pfizer-BioNTech vaccine, rapid uptake was expected. Because of the relatively short prelicensure period and limited number of participants in clinical studies, efficient and timely monitoring of the safety of the vaccine was a necessary part of the pharmacovigilance program in Europe and elsewhere. C4591021 is a post-authorisation safety study (PASS) that assessed the risk of 37 prespecified adverse events of special interest (AESI) in individuals of all ages (including pregnant individuals) in the general European population who received > 1 dose of the Pfizer-BioNTech vaccine. C4591021 is a category 3 commitment in the EU risk management and a post marketing requirement to the US Food and Drug Administration (FDA). A total of 5 interim study reports have been prepared for submission to the European Medicines Agency (EMA) and FDA every 6 months beginning in September 2021 through March 2024. This abstract is part of the final study report for C4591021.

Research question: Research question is: Is there an increased risk of select adverse events of special interest (AESI) after being vaccinated with the Pfizer-BioNTech COVID-19 vaccine?

Primary study objective:

- To determine whether an increased risk of prespecified AESI exists following the administration of at least one dose of the Pfizer-BioNTech COVID-19 vaccine using two approaches: (a) a matched cohort design comparing risk in vaccinated and unvaccinated individuals and (b) a self-controlled risk interval (SCRI) design.

Secondary study objectives:

- To estimate the incidence rates of prespecified AESI among individuals who receive at least one dose of the Pfizer-BioNTech COVID-19 vaccine using a cohort study design.

- To describe the incidence rates and determine whether an increased risk of prespecified AESI exists following the administration of at least one dose of the Pfizer-BioNTech COVID-19 vaccine compared with no COVID-19 vaccination within sub-cohorts of interest (i.e., individuals who are immunocompromised, individuals who are frail and have comorbidities, individuals diagnosed with previous COVID-19 infection, and age-specific groups) in Europe using a cohort study design and/or a SCRI design.

- To determine whether an increased risk of prespecified AESI exists following the administration of at least one dose of the Pfizer-BioNTech COVID-19 vaccine compared with no COVID-19 vaccination, in pregnant women and their neonates using a cohort study design.

- To characterise utilisation patterns of Pfizer-BioNTech COVID-19 vaccine among individuals within Europe, including estimating the proportion of individuals receiving the vaccine; two-dose vaccine completion rate and distribution of time gaps between the first and second doses; and demographics and clinical characteristics of recipients, overall and among sub-cohorts of interest, such as individuals who are immunocompromised, elderly, or have specific comorbidities.

- To assess the effectiveness of the Direct Healthcare Professional Communication (DHPC) about the risk of myocarditis and pericarditis associated with COVID-19 mRNA vaccine use and describe the rate of cardiac imaging use for vaccinated and unvaccinated individuals in this study population each calendar month during the study period, before and after distribution of the DHPC.

Study design: This post-authorisation active surveillance study of 37 AESIs associated with the Pfizer-BioNTech COVID-19 vaccine used a retrospective cohort design involving 7 data sources in 5 European countries: 1) Clinical Practice Research Datalink (CPRD Aurum – United Kingdom - UK), 2) Health Search Database (HSD -Italy - IT), 3) Norwegian Health Registers (NHR- Norway - NO), 4) Pedianet (IT), 5) PHARMO Data Network (PHARMO-the Netherlands - NL), 6) EpiChron Research Group on Chronic Diseases at the Aragon Health Sciences Institute (EpiChron-Spain - ES), and 7) Sistema d'Informació per el Desenvolupament de la Investigació en Atenció Primària) [Information System for the Improvement of Research in Primary Care] (SIDIAP-ES). In addition, a self-controlled risk interval (SCRI) design was used for a subset of the AESIs studied. Sensitivity analyses were conducted using historical controls during 2018 and 2019 (prior to COVID-19) and during 2020 (COVID-19 period). Subgroup analyses were done in special populations.

Setting and data sources: The study used data from eight European electronic healthcare databases in Italy, the Netherlands, Norway, Spain and the UK. However, one data source in Italy, Agenzia Regionale di Sanita' della Toscana (ARS), only contribute to the first and second interim reports due to national and regional re-assessment of regulations affecting their ability to provide public data for PASS studies. Therefore, this final report contains data from the seven European electronic healthcare data sources listed above. Of the seven, one data source, HSD, was not eligible to provide data for the cohort study, due to misclassification of COVID-19 vaccination. However, since inclusion in the SCRI analyses was conditioned on exposure, HSD contributed to the SCRI analyses only.

Subjects and study size: The study was conducted in a source population of 38.9 million individuals captured in the electronic healthcare data sources. The all-vaccinated study population comprised all individuals who received as first dose for COVID-19 vaccine, the Pfizer BioNTech vaccine, and with at least one year lookback period. For the *main comparative cohort analysis* individuals were matched on the following variables: data source, calendar date of time zero, age, sex, prior COVID-19 diagnosis, area of residence, at least one influenza vaccine (not in NHR), pregnancy (not in PHARMO, CPRD Aurum, and Pedianet), immunocompromised status, pre-existing conditions considered as risk factors for severe COVID-19 by the Centers for Disease Control and Prevention (CDC) and socio-economic status where available (not in CPRD Aurum). The matched cohort included the all-vaccinated individuals who were 1:1 matched to a non-vaccinated individual with resampling. The SCRI analysis was based on the all-vaccinated population and included those with one of the SCRI selected AESI in the risk or control window. Sensitivity analyses matched vaccinated individuals with historical controls (2018/2019) and 2020 controls using a 1:2 and 1:1 ratio, respectively. The study period in EpiChron and CPRD Aurum started in December 2020, in HSD, PHARMO, NHR and SIDIAP it started in January 2021. In Pedianet, a paediatric data source, the study period started on 31 May 2021 because children were included later in COVID-19 vaccination recommendations. The study period ended in December 2022 in Pedianet, PHARMO (hospital data), and NHR, in June 2023 in HSD, PHARMO (GP data), SIDIAP and CPRD Aurum and in July 2023 in EpiChron. The maximum follow-up after first dose was one year.

Variables: All data sources were converted into the ConcePTION common data model which creates syntactically harmonized data. VAC4EU data transformation tools supported several steps, with INSIGHT data quality checks. Code lists for AESIs were created using ICD-9-CM, ICD-10-CM, SNOMED, MedCodeID, and ICPC codes. Algorithms for study outcomes and covariates, as well as drug codes (ATC or ProdCodIDs) and vaccine code lists were created by the VAC4EU code lists task force. The ConcePTION pregnancy algorithm was used for estimating start and end of pregnancy. Validation of the nine selected AESIs was conducted using the VAC4EU validation pipeline and their levels of diagnostic certainty were assessed using the Brighton Collaboration levels of diagnostic certainty, where possible. All validators were medically trained, blinded to exposure and trained by VAC4EU on data extraction using 5 dummy cases for each AESI. Statistical analyses included descriptive analyses and calculation of incidence rates, as well as hazard rate ratios, rate differences, and prevalence ratios for comparative analyses.

Results: A total of 18,475,392 individuals received a first dose of Pfizer-BioNTech COVID-19 vaccine during the study period. Among these 32.89% were excluded because of receipt of a non-Pfizer-BioNTech COVID-19 vaccine before their first dose of the Pfizer-BioNTech COVID-19 vaccine (22.95%) or not having had 12 months of continuous enrolment in the data source (9.94%). A total of 12,398,589 individuals, including 48,439 pregnant women, were eligible for matching. individuals were eligible for matching.

Utilisation patterns
Among 12,398,589 individuals who received a first dose of the Pfizer-BioNTech COVID-19 vaccine, 84.9% proceeded to a second dose, with variation across data sources: >90% in the Spanish data sources, 85.4% in Pedianet, 76.2% in PHARMO, 76.7% in NHR, and 89.4% in CPRD Aurum. Of those receiving a second dose, 60.8% did so within 6 weeks. This proportion ranged from 97.3% in Pedianet (median: 3.14 weeks) to 6.1% in CPRD

Aurum (median: 10.7 weeks). Other data sources reported 84.7% (PHARMO, median: 5 weeks), 53.9% (NHR, median: 6 weeks), 92.7% (SIDIAP, median: 3 weeks), and 91.5% (EpiChron, median: 3 weeks). Overall, 34.8% of first-dose recipients received a third dose, with median intervals from dose 2 to 3 ranging from 21.4 weeks (Pedianet) to 31 weeks (SIDIAP). A fourth dose was administered to 9% of first-dose recipients, and 0.1% received a fifth dose. The interval between third and fourth doses exceeded 40 weeks in all sources except CPRD Aurum (25.7 weeks).

Main cohort
Of the 12,398,589 vaccinated individuals eligible for matching, 11,496,929 (92.73%) could be matched to an unvaccinated individual. A total of 26,696 of the 48,439 (55.11%) vaccinated, pregnant women could be matched to unvaccinated, pregnant women.
Of the matched vaccinated individuals 30.30% were censored due to receipt of a non-Pfizer-BioNTech COVID-19 vaccine, in contrast 67.85% of all the matched unvaccinated individuals were censored before end of follow-up because of receipt of a COVID-19 vaccine (Pfizer-BioNTech COVID-19 vaccine or another COVID-19 vaccine). For main comparative analysis, the vaccinated and unvaccinated pair were both censored when either the vaccinated individual or the unvaccinated was censored (except occurrence of the outcome), which resulted in short follow-up times, because unvaccinated individuals were vaccinated rapidly, and those who remained unvaccinated may have been lost to follow-up. Available follow-up times were much longer for the vaccinated cohorts than for the unvaccinated cohorts, when censoring of the pair was not considered. The median follow-up was very short in the unvaccinated cohorts in NHR (0.8 month) and EpiChron (1.0 month).

Historical controls
A total of 12,049,838 vaccinated individuals were matched to 23,818,939 historical controls in the pre-COVID-19 period, with one control in 2018 and another in 2019. Thus, each vaccinated individual was matched to two unvaccinated controls, (who could be the same individual in each year. In addition, 11,319,784 vaccinated individuals were matched 1:1 to 11,319,784 historical unvaccinated controls in the COVID-19 period from 01 January 2020 to 31 December 2020.

SCRI
Individuals included the SCRI analyses comprised those with an event in the AESI-specific post-vaccination risk or control periods, who had received at least one dose of the Pfizer-BioNTech COVID-19 vaccine and had at least one day of follow-up in both the risk and control periods. The number of cases varied across the different AESIs.

The baseline characteristics of the main cohort showed that the median age of the matched vaccinated and unvaccinated cohorts was lowest in Pedianet (10 years) and highest in PHARMO (48 years). The first dose of Pfizer-BioNTech COVID-19 vaccine was mostly received in the second quarter of 2021 in PHARMO, NHR, and CPRD Aurum, followed by the third quarter in EpiChron and SIDIAP, except in the Italian paediatric data source, Pedianet. In Italy, as elsewhere, young children were included in the vaccination programmes later, and therefore the first dose was more frequently received in Q1 2022. The most frequent comorbidities in the 10 years prior to time zero were cardiovascular disease, chronic respiratory disease, and connective tissue disease, followed by hypertension and immunocompromising conditions. The Charlson Comorbidity Index Score showed that >80% of the included individuals had a score of 0 or 1. Antibiotics as well as

NSAIDs and analgesics, were most frequently used in the year prior to time zero followed by psychotropics. Vaccination with other vaccines in the year prior to time zero was high in Pedianet, especially for polio, pneumococcal and varicella vaccines. In other data sources, where the population was older, influenza vaccination was most frequent in the year prior to time zero. Baseline comorbidities and comedications were well balanced between the vaccinated and unvaccinated cohorts with all ASDs being ≤0.1, except in the Pedianet cohorts, where HPV vaccination was higher in the vaccinated cohort than in the unvaccinated cohort (13.78% vs. 9.86%, respectively, with an ASD of 0.12).

Incidence rates for most outcomes in unvaccinated individuals were rare or very rare and many showed seasonal patterns and differences between data sources as well as the impact of the lock down period. Death rates in unvaccinated individuals increased during the years 2020-2021, especially in Spain.

The primary comparison of hazards was conducted in the main matched cohort, with inverse probability of treatment weighting (IPTW) adjustment. The summary table that follows shows these results for the matched cohort and SCRI analyses. The study showed the associations between the Pfizer-BioNTech COVID-19 vaccine and anaphylaxis (in NHR), and with myocarditis or pericarditis, which was strongest in younger males who were exposed to the full primary series.

Table. Summary of pooled analyses by AESI in the matched cohort and SCRI analyses

	Matched cohort analyses					SCRI analyses			
	Risk window (days)	**Events vac n**	**Events unvac n**	**Adjusted HR (95% CI)**	**I^2 (95% CI)**	**Events in risk window**	**Events in control window**	**IRR (95% CI)**	**I^2 (95% CI)**
Identified risks in risk management plan									
Myocarditis	21	<55	<44	1.32 (0.74-2.34)	0 (0-0.79)	ND	ND	ND	ND
	7	<26	<24	1.14 (0.40-3.28)	0 (0-0.85)	ND	ND	ND	ND
	14	<44	<38	1.20 (0.61-2.40)	0 (0-0.79)	ND	ND	ND	ND
Myocarditis or pericarditis	21	181	120	**1.49 (1.22-1.81)**	0 (0-0.79)	<586	<426	1.15 (0.99-134)	0 (0-0.71)
	7	75	57	1.32 (0.91-1.90)	0 (0-0.79)	<240	<172	**1.39 (1.01-1.93)**	0.24 (0-0.68)
	14	137	100	**1.36 (1.13-1.64)**	0 (0-0.79)	<416	<306	**1.19 (1.06-1.35)**	0 (0-0.75)
Pericarditis	21	131	89	**1.46 (1.13-1.87)**	0 (0-0.85)	ND	ND	ND	ND
	7	<55	<43	1.27 (0.97-1.64)	0 (0-0.85)	ND	ND	ND	ND
	14	99	75	1.31 (0.90-1.90)	0 (0-0.85)	ND	ND	ND	ND
Anaphylaxis	1	<83	<21	2.52 (0.27-23.28)	0.79 (0.44-0.92)	<130	<296	**7.69 (3.71-15.94)**	0.79 (0.49-0.91)
AESIs identified as signals and discussed by PRAC									
idiopathic thrombocytopenia	42	<70	<86	0.77 (0.50-1.17)	0 (0-0.79)	<272	<225	0.91 (0.76-1.09)	0 (0-0.79)
TTS	15	<26	<22	1.24 (0.44-3.46)	0 (0-0.9)	<71	<58	0.91 (0.60-1.39)	0 (0-0.90)
Glomerulonephritis	180	375	394	0.92 (0.62-1.38)	0.51 (0-0.82)	ND	ND	ND	ND
Erythema multiforme	42	<39	<43	0.87 (0.35-2.14)	0.24 (0-0.69)	ND	ND	ND	ND
Multi inflammatory syndrome	42	<225	<279	1.11 (0.42-2.96)	0.57 (0-0.84)	ND	ND	ND	ND
Hypermenorrhoea	183	11,801	9,325	**1.24 (1.02-1.51)**	0.92 (0.84-0.96)	ND	ND	ND	ND
Secondary amenorrhoea	183	4336	3374	1.14 (0.90-1.44)	0.86 (0.66-0.94)	ND	ND	ND	ND
Myositis	365	<378	<345	1.05 (0.86-1.29)	0 (0-0.79)	ND	ND	ND	ND
AESIs prespecified and discussed in the literature									
Death (all causes)	365	21,752	47,373	0.50 (0.34-0.76)	0.99 (0.99-0.99)	ND	ND	ND	ND
Acute cardiovascular injury	365	57,302	42,111	**1.22 (1.04-1.42)**	0.98 (0.96-0.98)	ND	ND	ND	ND
Arrhythmia	365	44,825	33,702	**1.22 (1.05-1.42)**	0.97 (0.95-0.98)	ND	ND	ND	ND
Coronary artery disease	365	11,104	9,200	1.14 (0.87-1.50)	0.93 (0.87-0.96)	ND	ND	ND	ND
Stress cardiomyopathy	365	<72	<63	1.23 (0.77-1.96)	0 (0-0.79)	ND	ND	ND	ND
Heart failure	365	12,364	12,001	1.01 (0.73-1.38)	0.98 (0.97-0.99)	ND	ND	ND	ND
Other AESI									
Subacute thyroiditis	365	<57	<37	**1.89 (1.20-2.96)**	0 (0-0.85)	ND	ND	ND	ND
Acute aseptic arthritis	42	<3,418	<3,055	1.13 (0.99-1.30)	0.60 (0.02-0.84)	16,235	12,227	0.99 (0.88-1.11)	0.91 (0.83-0.95)
Diabetes mellitus-1	365	1,317	1,219	1.05 (0.89-1.24)	0.26 (0-0.70)	ND	ND	ND	ND
Generalised convulsions	42	1,578	1,488	1.04 (0.09-1.20)	0.11 (0-0.86)	<5,551	<4,228	0.98 (0.89-1.09)	0.60 (0.01-0.84)
Coagulation disorders	28	2,728	3,198	0.85 (0.76-0.95)	0.37 (0-0.76)	10,711	8,602	0.93 (0.88-0.98)	0.51 (0-0.81)
Acute liver injury	365	547	546	1.07 (0.69-1.66)	0.56 (0-0.84)	ND	ND	ND	ND
Acute pancreatitis	365	1,507	1,420	1.05 (0.88-1.25)	0.37 (0-0.77)	ND	ND	ND	ND
Acute kidney injury	365	9,335	10,305	0.92 (0.74-1.16)	0.96 (0.94-0.98)	ND	ND	ND	ND
Rhabdomyolysis	365	<286	<368	0.77 (0.59-1.01	0 (0-0.79)	ND	ND	ND	ND

Table. Summary of pooled analyses by AESI in the matched cohort and SCRI analyses

	Matched cohort analyses					SCRI analyses			
	Risk window (days)	Events vac n	Events unvac n	Adjusted HR (95% CI)	I^2 (95% CI)	Events in risk window	Events in control window	IRR (95% CI)	I^2 (95% CI)
Acute disseminated encephalomyelitis	42	NA	NA	NA	NA	<11	<10	1.39 (0.01-318)	0 (NA)
Bell's palsy	42	468	477	0.96 (0.88-1.05)	0 (0-0.79)	<1806	<1444	0.93 (0.83-1.04)	0.24 (0-0.68)
CVST	28	<23	<22	0.74 (0.06-8.83)	0.57 (0-0.86)				
GBS	42	<25	<26	1.05 (0.27-4.13)	0.21 (0-0.88)	<122	<106	0.91 (0.67-1.25)	0 (0-0.79)
Meningoencephalitis	42	<83	100	0.84 (0.55-1.27)	0 (0-0.79)	338	302	0.82 (0.70-0.96)	0 (0-0.79)
Transverse myelitis	42	<10	<10	1.57 (0.16-15.62)	0 (NA)	<29	<30	0.83 (0.51-1.37)	0 (0-0.85)
Narcolepsy	42	<30	37	0.54 (0.09-3.31)	0.37 (0-0.80)	<81	<71	0.76 (0.38-1.53)	0.27 (0-0.73)
ARDS	365	282	1280	0.27 (0.11-0.63)	0.83 (0.60-0.92)	ND	ND	ND	ND
Chilblain like lesions	42	<187	<206	0.81 (0.45-1.44)	0.60 (0-0.85)	ND	ND	ND	ND
SOCV	28	<31	<30	0.82 (0.30-2.25)	0 (0-0.85)	<94	<72	1.01 (0.85-1.19)	0 (0-0.85)

ND: not done; sudden death could not be accurately assessed.

For the outcomes that have been discussed by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) no association was found between Pfizer-BioNTech COVID-19 vaccine and idiopathic thrombocytopenia (ITP), thrombotic thrombocytopenia syndrome (TTS), glomerulonephritis, erythema multiforme, multi-inflammatory syndrome, and secondary amenorrhoea. A small and consistently elevated hazard ratio (HR) was found for hypermenorrhoea.

For AESIs discussed elsewhere or other AESI, there was a small elevation of risk for subacute thyroiditis, and a consistently strong protective effect for all-cause death and acute respiratory distress syndrome (ARDS), except in young children, due to reduced power. For the cardiovascular AESIs with 365-day risk windows (arrhythmia, acute cardiovascular injury, coronary artery disease, and heart failure), small elevations in HR were identified, which seem to be due to selective censoring due to unvaccinated individuals being vaccinated, and unique unvaccinated individuals remaining in the cohort for the entire follow-up.

No elevated HRs were observed for any of the autoimmune mediated outcomes such as Guillain-Barré syndrome, acute disseminated encephalomyelitis (ADEM), narcolepsy, acute aseptic, arthritis, diabetes mellitus and myositis. No elevated HRs were observed for circulatory AESIs such as coagulation disorders, single organ cutaneous vasculitis (SOCV) and cerebral venous sinus thrombosis (CVST). No elevated HRs were observed for acute kidney injury, acute liver injury, rhabdomyolysis, or acute pancreatitis. No elevated risks for the neurological AESIs, meningoencephalitis, and Bell's palsy were observed, and although the HR for transverse myelitis was elevated, the 95% CI was wide. No elevated risk was observed for ARDS nor for chilblain-like lesions.

The maternal outcomes (gestational diabetes, pre-eclampsia) were not associated with Pfizer-BioNTech COVID-19 vaccine, nor were the neonatal AESIs: foetal growth restriction, spontaneous abortion, still birth, preterm birth, major congenital malformations or neonatal death. No maternal deaths were identified. Small risk elevations were observed for foetal growth restriction which are likely to be due to residual confounding by gestational age or COVID-19.

Other analyses
Subgroup analyses were performed by age groups and sex, as well as in individuals who were frail or had comorbidities, were immunocompromised, and pregnant women. These showed small variations, but no consistent patterns, unless mentioned in the results.

Validation was conducted for nine rare AESIs. Positive predictive values varied, based on the type of source data that could be accessed for validation by the validators. Modified Brighton Collaboration level of diagnostic certainty criteria was used (adding sublevels). The percentage of cases categorised as level 1 was highest in NHR and EpiChron, in which in-hospital data could be accessed. It was lowest in CPRD Aurum, in which only GP medical records could be accessed. The 95% confidence intervals for the PPVs overlapped between vaccinated and unvaccinated individuals, therefore adjustment for the corresponding PPVs was not conducted.

On 19 July 2021, a Direct Healthcare Professional Communication (DHPC) was issued to inform healthcare practitioners about the identified risk of myocarditis and pericarditis associated with COVID-19 mRNA vaccination. The healthcare practitioners were informed that they should be alert to the signs and symptoms of myocarditis and pericarditis and that they should advise vaccinated individuals to seek immediate attention should they experience chest pain, shortness of breath or palpitations.

Incidence rates of recorded cardiac imaging were higher before issuance of the DHPC rather than after, in both vaccinated and unvaccinated individuals. There may be several explanations for this, such as prior awareness through social media, the possibility that most primary series vaccinations had already occurred by the time the communication was issued, and depletion of susceptible individuals.

Discussion: This large post-authorisation safety study of the Pfizer-BioNTech COVID-19 vaccine evaluated data from seven data sources in five European countries, to assess the risk for 37 distinct AESIs, and an additional 8 pregnancy and neonatal AESIs. The study confirmed associations between Pfizer-BioNTech COVID-19 vaccine and previously identified risks of rare events. The findings demonstrate a small and consistent association between Pfizer-BioNTech COVID-19 vaccination and subacute thyroiditis and an association with hypermenorrhoea in GP-based data sources. Although some cardiovascular events, such as arrhythmia and acute cardiovascular injury, coronary artery disease, and heart failure, showed very minor elevations during 365 days of follow-up, it is believed this may be due to bias in the unvaccinated individuals that remained unvaccinated during the 365 days follow-up. No association between Pfizer-BioNTech COVID-19 vaccination and adverse pregnancy AESIs or neonatal AESIs were found, except a small elevation of preterm birth and FGR, most likely due to residual confounding by gestational age or COVID-19. A lower frequency of reported imaging in both vaccinated and unvaccinated individuals following the issuance of the DHPC was observed. The results demonstrated that the majority of the AESI were not associated with the Pfizer-BioNTech COVID-19 vaccine.

Marketing Authorization Holder(s): BioNTech Manufacturing GmbH, Germany.

Names and affiliations of principal investigators: Daniel Weibel, University Medical Center Utrecht, The Netherlands; Alejandro Arana, RTI Health Solutions, Barcelona, Spain

Document Approval Record

Document Name:	C4591021 Final Non-Interventional Study Report Abstract
Document Title:	C4591021

Signed By:	Date(GMT)	Signing Capacity
Younus, Muhammad	15-Sep-2025 12:02:37	Final Approval
De Bernardi, Barbara	15-Sep-2025 14:00:32	EUQPPV Approval