(Appendix)

COMIRNATY Intramuscular Injection for 6 Months to 4 Years Old (monovalent: Omicron XBB.1.5)

Special investigation for booster immunization in children aged 6 months to 4 years

Non-interventional Full Protocol

Pfizer Japan Inc.

STUDY INFORMATION

Title	COMIRNATY Intramuscular Injection for 6 Months to 4 Years Old (monovalent: Omicron XBB.1.5) Special investigation for booster immunization in children aged 6 months to 4 years
Protocol ID	C4591057
Protocol version identifier	Ver. 1
Date	23 October 2023
Active substance	Raxtozinameran
Medicinal product	COMIRNATY intramuscular injection for 6 months to 4 years old
Research question and objectives	To collect information on adverse events, reactogenicity events (local reactions and systemic reactions), and COVID-19 that occur subsequent to the fourth vaccination with this product in children aged 6 months to 4 years who received the first booster immunization with this product (fourth vaccination with this product) after initial immunization under actual use, and to confirm its safety in the early stage.
Author	PPD PPD

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2. LIST OF ABBREVIATIONS

Abbreviation	Definition
EC	Ethics committee /Non-English text
ECMO	Extracorporeal membrane oxygenation/Non-English text
IRB	Institutional review board/Non-English text
ICU	Intensive care unit/Non-English text
SAP	Statistical analysis plan/Non-English text
VAED	Vaccine-associated enhanced disease/Non-English text
VAERD	Vaccine-associated enhanced respiratory disease/Non-English text

3. RESPONSIBLE PARTIES

The Japan Good Post-marketing Study Practice officer

4. AMENDMENTS AND UPDATES

Protocol version identifier	Date	Type of amendment (substantial or administrative)	Protocol section(s) changed	Summary of amendment(s)	Reason
Ver. 1	23 October 2023	N/A	N/A	N/A	N/A

5. MILESTONES

Milestone	Planned date
Start of data collection	08 December 2023
Start of data collection (date of registration of the first participant registered)	08 December 2023
End of data collection	28 April 2024
End of data collection (date of release of the database)	24 September 2024
Final study report	23 December 2024

6. RATIONALE AND BACKGROUND

Novel coronavirus infection (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a virus of animal origin. The pathogenicity of SARS-CoV-2 in humans was first confirmed in China, and it rapidly spread globally through human-to-human transmission.

Coronaviruses are enveloped viruses whose genome is positive-sense, single-stranded RNA that encodes four structural proteins. Of these four structural proteins, spike glycoprotein (S protein), is an important target for vaccine development. The Pfizer/BioNTech COVID-19 vaccine, BNT162b2 (COMIRNATY intramuscular injection), is a lipid nanoparticle (LNP)-formulated, nucleoside-modified mRNA (modRNA) vaccine that encodes the S protein carrying P2 mutations (P2 S).

As of July 2023, COMIRNATY is available in more than 120 countries and regions.

In Japan, special approval was granted for COMIRNATY intramuscular injection on February 14, 2021; for both COMIRNATY RTU intramuscular injection and COMIRNATY intramuscular injection for 5 to 11 years old on January 21, 2022; for COMIRNATY RTU intramuscular injection (Bivalent: Original/Omicron BA.1) as well as COMIRNATY RTU intramuscular injection (Bivalent: Original/Omicron BA.4-5) on September 12 and October 5, 2022, respectively; for COMIRNATY intramuscular injection for 6 months to 4 years old on October 5, 2022; and for COMIRNATY intramuscular injection for 5 to 11 years old (Bivalent: Original/Omicron BA.4-5) on February 28, 2023. As a result of comprehensive consideration of the data obtained thus far and the current status of infection with variant strains in Japan all together, it was considered necessary in terms of public health that a system that enables administration of monovalent vaccines which are expected to be more

effective for Omicron subvariant XBB.1.5 to people of all ages be also established in Japan from the perspective of preventing the spread of COVID-19. To this end, Pfizer and BioNTech obtained approval for partial changes to the approved items of the manufacturing and marketing approval on September 1, 2023, to add initial immunization and booster immunization with monovalent vaccine (Omicron XBB.1.5 subvariant) to the indication "prevention of infection by SARS-CoV-2" for COMIRNATY intramuscular injection for 6 months to 4 years old, COMIRNATY intramuscular injection for 5 to 11 years old, and COMIRNATY RTU intramuscular injection for single person use.

The results obtained in an overseas clinical study (C4591048 Substudy B), which was conducted in children receiving a booster shot of the existing bivalent vaccine adapted to Omicron variants (Original/Omicron BA.4-5), revealed no new safety specifications, but as there exist no data on safety after booster immunization with COMIRNATY intramuscular injection for 6 months to 4 years old (Monovalent: Omicron XBB.1.5) (hereinafter referred to as "this drug") in children aged 6 months to 4 years in Japan leading up to the present partial change approval, it is considered highly necessary to collect post-marketing safety data. Accordingly, a special investigation was planned with the aim of confirming safety after booster immunization in children aged 6 months to 4 years in Japan.

This study shall be conducted in strict compliance with the "Ministry of Health, Labour and Welfare (MHLW) Ordinance on the Standard for Post-marketing Studies and Clinical Trials of Medical Products" (MHLW Ordinance No. 171, dated December 20, 2004), the "Enforcement of the MHLW Ordinance on the Standard for Post-marketing Studies and Clinical Trials of Medical Products" (PFSB Notification No. 1220008, dated December 20, 2004), the "MHLW Ordinance on the Standard for Post-marketing Safety Control of Medical Products, Quasi-medical Products, Cosmetics, Medical Devices, and Regenerative Medical Products" (MHLW Ordinance No. 135, dated September 22, 2004), the "Enforcement of the MHLW Ordinance on the Standard for Post-marketing Safety Control of Medical Products, Quasi-medical Products, Cosmetics, Medical Devices, and Regenerative Medical Products" (PFSB Notification No. 0812-4, dated August 12, 2014), the "MHLW Ordinance to Partially Amend the MHLW Ordinance on the Standard for Post-marketing Studies and Clinical Trials of Medical Products" (MHLW Ordinance No. 116, dated October 26, 2017), and the "Announcement of the MHLW Ordinance to Partially Amend the MHLW Ordinance on the Standard for Post-marketing Studies and Clinical Trials of Medical Products (Regarding the MHLW Ordinance on the Standard for Post-marketing Studies and Clinical Trials of Medical Products)" (PSEHB Notification No. 1026-1, dated October 26, 2017).

7. RESEARCH QUESTION AND OBJECTIVES

To collect information on adverse events, reactogenicity events (local reactions and systemic reactions), and COVID-19 observed after the fourth vaccination with this product in children aged 6 months to 4 years (as of the date of the fourth vaccination with this product) who received their first booster immunization with this product (hereinafter, the fourth vaccination with this product) after the initial immunization under actual use, and to confirm its safety in the early stage.

7.1. Safety Specifications

[Important Identified Risks]

- Shock, anaphylaxis
- Myocarditis, pericarditis

[Important Potential Risks]

- Vaccine-associated enhanced disease (VAED) and vaccine-associated enhanced respiratory disease (VAERD)
- Guillain-Barre syndrome

8. RESEARCH METHODS

8.1. Study Design

This is a multicenter cohort study. The investigator will record information required by this study in case report forms (CRFs) based on information obtained from the preliminary examination sheet or medical interviews, etc., and records such as medical records. A health observation diary will be distributed to vaccinated individuals participating in this study, and they will be requested to record information on reactogenicity events (local reactions and systemic reactions, including pyrexia) after vaccination with this product.

The investigator will collect the health observation diary after the end of the observation period of each CRF, and check the details of records other than symptoms at the vaccination site and general symptoms specified in the diary (including the information on COVID-19) as needed and record them as adverse events. The investigator should record the symptoms at the vaccination site (local reactions) and general symptoms including pyrexia (systemic reactions) specified in the health observation diary in the CRF as items of the health observation diary as is in order to avoid overlap with adverse events evaluated by physicians.

All assessments described in this full protocol are performed as part of normal clinical practice or standard practice guidelines for the participant population and healthcare provider specialty in the countries where this non-interventional study is being conducted.

8.2. Setting

8.2.1. Registration criteria

Participants must meet all of the following criteria to be eligible for inclusion in the study. As a guide, participant registration will be performed within no more than 15 days from the date of the fourth vaccination with this product.

1. Participants who are 6 months to 4 years old at the time of the fourth vaccination with this product.
2. Participants who are receiving the first booster immunization with this product (fourth vaccination with this product) after the initial immunization.
3. Participants for whom written consent was obtained from their legally acceptable representatives (parents or legal guardians) regarding their participation in the study upon understanding the explanatory document describing the content of this study, including that they will be asked to record participant's symptoms in the health observation diary.

   When a participant has the capacity to provide assent, consent should be obtained from the pediatric participant him/herself using the assent form.

Refer to the latest package insert of this product for "indications" and "dosage and administration" when administering this product.

[Indications]	Prevention of infection with SARS-CoV-2
[Dosage and administration]	The product is diluted with 2.2 mL of Japanese Pharmacopoeia physiological saline. For initial immunization, participants are vaccinated intramuscularly at a dose of 0.2 mL 3 times in total. The second dose is usually given at a 3-week interval, and the third dose is given after at least 8 weeks have passed since the second vaccination. For booster immunization, participants are vaccinated intramuscularly at a dose of 0.2 mL.
[Precautions regarding dosage and administration (booster immunization)]	
Participants:	Those aged 6 months to 4 years with a history of previous vaccination with SARS-CoV-2 vaccines for initial immunization or booster immunization. Based on the state of SARS-CoV-2 pandemic and individual background factors, etc., the necessity of booster immunization should be determined in consideration of benefits and risks.
Vaccination interval:	Generally, participants can receive vaccination after at least 3 months have passed since the previous SARS-CoV-2 vaccination.

8.2.2. Exclusion criteria

There are no exclusion criteria for this study.

8.2.3. Study sites

This study will be conducted at approximately 10 to 20 institutions which have agreed to cooperate with this investigation, and where a system to perform vaccination with this product has been secured.

8.2.4. Planned study period

The planned period covered by this study is as follows.

- Investigation period: From the date of the fourth vaccination of the first participant registered to the end date of the observation period for the last registered participant (scheduled from December 2023 to 28 April 2024)

- Registration period: From the date of the fourth vaccination of the first participant registered to the date of registration of the last participant registered (scheduled from December 2023 to 15 April 2024)

Participants who receive vaccination before 31 March 2024, which presumably corresponds to the time when booster immunization started in fall 2023 will end, are registered.

Even if the target sample size of 60 is achieved before 31 March 2024, registration of participants who have been administered a booster immunization by 31 March 2024 will be continued until 15 April 2024 in order to collect as many participants as possible.

8.2.5. Study procedures

8.2.5.1. Study method

Central registration system: This study will be conducted with Central registration system that participants who meet the conditions of this study will be registered until data are collected on a the target number of participants. The investigator will register participants who meet the registration criteria (8.2.1) and are given the fourth vaccination with this product before 31 March 2024 within no more than approximately 15 days from the date of the fourth vaccination with this product.

This study will be conducted in participants who have been vaccinated with this product at contract sites after marketing approval.

8.2.6. Observation period

The observation period will be from the date of the fourth vaccination with this product (Day 1) to 28 days after the fourth vaccination.

However, for those who withdraw from the study, information up to the time of withdrawal will be collected.

8.3. Variables

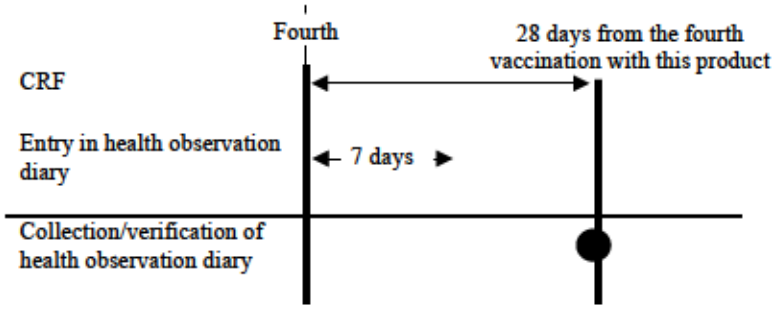
This study will be conducted according to the following schedule of activities.

Table 1. Variables

Variable	Registration form	CRF
ID number	●	*
Gender	●	*
Birth year and month (age in months or years)	●	*
Eligibility	●	
Date of booster immunization (fourth vaccination) with this product	●	*
Disease history (medical history/complications)		●
Allergy information		●
History of SARS-CoV-2 infection		●
Information on initial COVID-19 vaccine immunization (first to third)		●
History of other vaccinations (within 1 month prior to the fourth vaccination with this drug)		●
Status of booster immunization (fourth vaccination) with this product		●
Reactogenicity events (local reactions and systemic reactions) (Health observation diary)		●
Information on inoculation of other vaccines (on and after the fourth vaccination with this product)		●
Information on COVID-19 pathogen test (whether the test was performed, test date (sample collection date), test type, and test results)		◄——►
Information on COVID-19 (presence or absence of COVID-19 onset, date of diagnosis, details of treatment, outcome)		◄——►
Adverse events (including serious adverse events)		◄——►
Concomitant medications		◄——►
End-of-study/discontinuation record (including the reason if discontinued)		●

* Some elements in the Registration Form are automatically reflected in the CRF. The investigator should check and update the CRF as needed.

Figure 1. Schedule



8.3.1. Characteristics of vaccinated participants

1. Enter the information at the time of the fourth vaccination with this product in the registration form.
   - ID number
   - Gender
   - Birth year and month (if month and year of birth cannot be provided, age in months or years at the time of the fourth vaccination with this product shall be entered)
   - Eligibility
   - Date of the fourth vaccination with this product
2. The following information will be recorded in the CRF at the time of the fourth vaccination with this product
   - Clinical history (medical history/complications*)

     *: Diseases present at the time of the fourth vaccination with this product, including obesity, are considered "complications."
   - Allergy information (presence or absence of allergy, type of allergy, and information on allergens)
   - History of SARS-CoV-2 infection
     - If SARS-CoV-2 infection history is "present," presence or absence of COVID-19 onset should be recorded ("present" should be selected if there are symptoms, and "absent" if there are no symptoms)
     - If COVID-19 onset is "present," presence or absence of actions/procedures taken (*administration of COVID-19 treatment drugs*, hospitalization, oxygen administration, ICU admission, use of mechanical ventilation, use of ECMO) should be recorded

       *: Treatment drugs with an indication for use in SARS-CoV-2 infection
   - Information on initial immunization with COVID-19 vaccines (dates of administration of first to third vaccination and names of vaccines)

- History of other vaccinations (presence or absence of vaccines and names of vaccines [within 1 month prior to the date of the fourth vaccination with this product])

8.3.2. Status of booster immunization with this product

The following information will be recorded for the status of the fourth vaccination with this product.

- Date of vaccination (the date of the fourth vaccination with this product on the Registration Form will be automatically reflected in the CRF)
- Lot number
- vaccination site
- Inoculation dose

8.3.3. Concomitant medications

For drugs used concomitantly on and after the date of the fourth vaccination with this product and drugs used for treatment of adverse events, information to the end date of the observation period will be entered.

- Drug name (product name)
- Treatment period (the start date of treatment if no concomitant drugs are used at the time of the fourth vaccination with this product, or the end date of treatment if no concomitant drugs are used at the end of the observation period, should be entered.)

8.3.4. End-of-study/discontinuation record

The investigator will enter the end date of the observation period (date of final observation), i.e., the date of confirmation of information on the participant after 28 days of the fourth vaccination with this product (or thereafter).

For confirmation of participant information, inquiries by telephone, etc. are acceptable.

If participant information cannot be confirmed even after 1 month has passed since the end date of the observation period using the above-described method, and the date of final confirmation of participant information does not fall within the observation period, the date of last confirmation of participant information should be entered as the date of discontinuation of the observation period (date of final observation), along with the reason for discontinuation.

1. Date of completion (discontinuation) of the observation period (date of final observation)
2. End of study or reason for discontinuation
   - End of study
   - Adverse events
   - Death

- Lost to follow-up
- Consent withdrawal
- Other

8.3.5. Information on inoculation of other vaccines

The investigator will confirm the presence or absence of other vaccines inoculated on and after the date of the fourth vaccination with this product during the observation period and enter the information. If participants receive other vaccinations during the observation period, the type of vaccine and the date of vaccination should be entered.

8.3.6. Information on COVID-19 pathogen (SARS-CoV-2) test

The investigator will confirm the presence or absence of the test for COVID-19 pathogen (SARS-CoV-2) conducted for participants during the observation period and enter the information. If a pathogen test is performed, for each test performed, the test date (sample collection date), test type, and test results should be recorded in the CRF.

8.3.7. Information on COVID-19

The investigator will confirm the presence or absence of the onset of COVID-19 during the observation period and enter the information.

- Presence or absence of COVID-19 onset ("present" should be selected if there are symptoms, and "absent" if there are no symptoms)

If the onset of COVID-19 is "present," the following information should also be entered.

- Date of diagnosis of COVID-19
- Presence or absence of actions/procedures taken (administration of COVID-19 treatment drugs*, hospitalization, oxygen administration, ICU admission, use of mechanical ventilation, use of ECMO)

  *: Treatment drugs with an indication for use in SARS-CoV-2 infection

- Outcome (resolved/recovered, resolved with sequelae, death, not resolved, and unknown) and date of outcome

The outcome should be followed up as much as possible even after the end of the observation period.

8.3.8. Adverse events

Occurrence of adverse events from the date of the fourth vaccination with this product to the end date of the observation period should be confirmed, and the following information should be entered. Participant condition must be observed after vaccination with this product for a certain period of time, and if acute reactions such as shock and anaphylaxis are observed, appropriate measures should be taken and the details should be recorded as adverse events.

The information in the health observation diary (see Section 8.3.9) collected from the parents (or legal guardians) of participants should be reviewed. If there are any records other than the symptoms at the vaccination site and general symptoms specified in the diary (including COVID-19 information), the details should be verified as needed, and should be recorded as adverse events. The investigator should record the symptoms at the vaccination site (local reactions) and general symptoms including pyrexia (systemic reactions) specified in the health observation diary in the CRF as is, while avoiding overlap with adverse events evaluated by physicians.

Also, further investigation should be separately conducted, if deemed necessary by Pfizer, for participants who experienced serious adverse reaction, or adverse reactions not listed in the package insert.

- Presence or absence of adverse event
- Name of adverse event
- Severity
- Date of occurrence
- Presence or absence of treatment
- Seriousness
- Outcome (including the date of outcome)
- Causal relationship to this product

8.3.8.1. Severity assessment (adverse events)

The investigator will assess the maximum severity of adverse events and serious adverse events reported during the observation period from onset of adverse events to confirmation of outcome and classify them into one of the following categories. Severity is defined as follows.

Table 2. Definition of Severity

Severity	Definition
Mild	Not interfering with usual activities of vaccinated participants
Moderate	Interfering with usual activities of vaccinated participants to some extent
Severe	Markedly interfering with usual activities of vaccinated participants
Life-threatening	Life-threatening, or necessitating urgent intervention

8.3.8.2. Criteria for seriousness

The investigator will select and enter the applicable seriousness of serious adverse events reported during the observation period. Seriousness is defined as follows.

- Results in death
- Life-threatening

- Requires hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/malfunction
- Cause a congenital anomaly/birth defect
- Other medically important events

8.3.9. Reactogenicity events (local reactions and systemic reactions) (health observation diary)

A health observation diary will be distributed to the parents (or legal guardians) of participants participating in this study, and they will be requested to record information on reactogenicity events after vaccination with this product. Reactogenicity events are defined as local reactions (symptoms at the vaccination site) and systemic reactions (general symptoms including pyrexia).

If participants are younger than 2 years of age at the time of the fourth vaccination with this product, the parents (or legal guardians) of participants will observe the participant for local reactions (injection site tenderness, redness, and injection site swelling) and systemic reactions (pyrexia, decreased appetite, somnolence, and irritability) in participants for 7 days after vaccination with this product and record them in the diary (if symptoms persist for 8 days and more, the date of symptom resolution should be recorded).

If participants are 2 years or older at the time of the fourth vaccination with this product, the parents (or legal guardians) of participant will observe participants for local reactions (injection site pain, redness, and injection site swelling) and systemic reactions (pyrexia, vomiting, diarrhoea, headache, malaise, chills, myalgia and arthralgia) for 7 days after vaccination with this product and record them in the diary (if symptoms persist for 8 days and more, the date of symptom resolution should be recorded).

The investigator will collect the health observation diary after the end of the observation period (collection by mail is also acceptable).If there are records other than symptoms at the vaccination site and general symptoms specified in the diary (including the COVID-19 information), check the details of the information (or confirm by telephone, etc.) as needed and record them as adverse events. The investigator should record the symptoms at the vaccination site (local reactions) and general symptoms including pyrexia (systemic reactions) specified in the health observation diary in the CRF as items of the health observation diary as is, while avoiding overlap with adverse events evaluated by physicians.

8.3.9.1. Severity assessment (health observation diary)

The severity used by the parents (or legal guardians) of participants when evaluating symptoms at the vaccination site (local reactions) and general symptoms including pyrexia (systemic symptoms) will be recorded in the health observation diary by using the following indices.

The severity classification will be set in accordance with the "Food and Drug Administration Guidance for industry: toxicity grading scale for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials." In the diary, expressions which are easy to understand and correspond with each grade will be used (not interfering with activities = no change in daily life; interfering with activities = influence on daily life; interfering with daily activities = making daily life difficult).

Table 3. Severity Classification of Local Reactions

	Participant age	Mild Grade 1	Moderate Grade 2	Severe Grade 3
Injection site pain	2 years and older	Not interfering with activities	Interfering with activities	Interfering with daily activities
Injection site tenderness	Younger than 2 years	Complain of pain when touched lightly (e.g., whimper, frown, resist, pull the arm away)	Complain of pain while crying when touched lightly	Arm (leg) movement is impaired
Redness	4 years and younger	0.5–2.0 cm	>2.0–7.0 cm	>7.0 cm
Injection site swelling	4 years and younger	0.5–2.0 cm	>2.0–7.0 cm	>7.0 cm

Table 4. Severity Classification of Systemic Reactions (2 years and older)

	Mild Grade 1	Moderate Grade 2	Severe Grade 3
Vomiting	1 or 2 times within 24 hours*	3 times or more within 24 hours*	Intravenous fluid replacement (drip infusion)**
Diarrhoea	Within 24 hours* 2 to 3 episodes of faeces soft	Within 24 hours* 4 to 5 episodes of faeces soft	Within 24 hours* 6 or more episodes of faeces soft
Headache	Not interfering with activities	Slightly interfering with activities	Interfering with daily activities
Fatigue***/Malaise	Not interfering with activities	Slightly interfering with activities	Interfering with daily activities
Chills	Not interfering with activities	Slightly interfering with activities	Interfering with daily activities
New or worsened myalgia	Not interfering with activities	Slightly interfering with activities	Interfering with daily activities
New or worsened arthralgia	Not interfering with activities	Slightly interfering with activities	Interfering with daily activities

* "Within 24 hours" is expressed as "1 day" in the diary.
** "Intravenous fluid replacement (drip infusion)" is described as "drip infusion" in the diary.
*** "Fatigue" is described as "malaise" in the diary.

Table 5. Severity Classification of Systemic Reactions (younger than 2 years)

	Mild Grade 1	Moderate Grade 2	Severe Grade 3
Decreased appetite	Decreased interest in food	Decreased food intake	Refusal to eat
Somnolence	Increased or prolonged sleep time	Slightly interfering with daily activities	Loss of interest in normal daily activities
Irritability	Easy to pacify	Require more care	Unable to pacify, can't stop crying

8.3.9.2. Evaluation of pyrexia (health observation diary)

The parents/guardians of participants will measure body temperature at home and record each day in the health observation diary the highest body temperature to one decimal place as information on pyrexia. At the time of analysis, pyrexia will be classified according to the criteria shown in Table 6.

Table 6. Severity Classification of Pyrexia

	Mild Grade 1	Moderate Grade 2	Severe Grade 3	Most severe Grade 4
Pyrexia	≥38.0–38.4 °C	>38.4–38.9 °C	>38.9–40.0 °C	>40 °C

8.4. Data sources

In this study, the investigator will extract necessary information based on the full protocol from the information obtained from the preliminary examination sheet and the health observation diary completed by the parents (or legal guardians) of participants participating in this study, as well as medical interviews, etc., and records including medical records.

Evaluation of local reactions and systemic reactions after vaccination recorded by the parents (or legal guardians) of participants participating in this study in the health observation diary, will be used.

8.5. Study size

8.5.1. Planned sample size

60 participants will be collected as the participants to be included in the safety analysis set.

8.5.2. Rationale for sample size

The target sample size (safety analysis set) was set to be 60 participants based on feasibility. If 60 participants can be collected, an adverse event that occurs with a true incidence of 3% can be observed in at least one participant with a probability of 83%, which would make it possible to understand trends in incidence of reactogenicity events.

Participants who receive vaccination before 31 March 2024, which presumably corresponds to the time when booster immunization started in fall 2023 will end, are registered.

Even if the target sample size of 60 is achieved before 31 March 2024, registration of participants who have been administered a booster immunization by 31 March 2024 will be continued until 15 April 2024 in order to collect as many participants as possible.

8.6. Data management

8.6.1. Case report forms (CRFs)/Electronic data record

As used in this full protocol, the term CRF should be understood to refer to an *electronic data record* depending on the data collection method used in this study.

A CRF is required and should be completed for each included participant. The completed original CRFs are the sole property of Pfizer and should not be made available in any form to third parties, except for authorized representatives of Pfizer or appropriate regulatory authorities, without written permission from Pfizer. The investigator shall ensure that the CRFs are securely stored at the study sites in encrypted electronic form and will be password protected or secured in a locked room to prevent access by unauthorized third parties.

The investigator has ultimate responsibility for the collection and reporting of all clinical, safety, and laboratory data entered on the CRFs and any other data collection forms (source documents) and ensuring that they are accurate, authentic/original, attributable, complete, consistent, legible, timely (contemporaneous), enduring, and available when required. The CRFs must be signed by the investigator or by an authorized staff member to attest that the data contained on the CRFs are true. Any corrections to entries made in the CRFs or source documents must be dated, initialed or stamped with correction seal, and explained (if necessary) and should not obscure the original entry.

In most cases, the source documents are the hospital or physicians' chart. In these cases, data collected on the CRFs must match those charts.

In some cases, the CRF may also serve as the source document. In these cases, a document should be available at the investigator site and at Pfizer that clearly identifies those data that will be recorded on the CRF, and for which the CRF will stand as the source document.

8.6.2. Record retention

The records related to this study should be retained at the study site until the End of Study Letter by Pfizer is received or during the period defined by the study site, whichever is longer.

8.6.3. Data collection method

8.6.3.1. Case report form (EDC)

The data for this study will be collected and confirmed by using the electronic system on the internet designed for collecting post-marketing survey data (Electronic Data Capture, EDC).

8.6.3.2. Health observation diary

The parents (or legal guardians) of participants participating in this study will be asked to fill out the health observation diary for 7 days after the fourth vaccination with this product (if symptoms persist for 8 days or more, the date of disappearance of the symptoms should be recorded). The investigator will collect the health observation diary at 28 days after the fourth vaccination with this product from the parents (or legal guardians) of the study participants and review its contents, and then enter in the EDC the symptoms at the vaccination site (local reactions) and general symptoms including pyrexia (systemic reactions) recorded on the health observation diary.

8.6.4. Participant registration (EDC)

The investigator will enter information on the vaccinees to be studied on the registration screen of EDC (registration form) and save the data. Participant registration will be performed within no more than approximately 15 days after the fourth vaccination with this product.

8.6.5. Points to consider for completion, revision, and submission of case report form (EDC)

8.6.5.1. Data entry

The investigator should check the survey items and enter the data into EDC based on the preliminary examination sheet completed by the participants, records including medical records, or information in the health observation diary.

8.6.5.2. Data revision

Upon receiving query from Pfizer on the contents of the CRF (follow-up survey), the investigator will again check the contents of preliminary examination sheet, records such as medical records, or information in the health observation diary, and as required, correct the relevant sections and save the data.

8.6.5.3. Submission

After data entry and revision are completed,CRFs should be signed electrically by the investigator following confirmation of entry in the CRFs or follow-up survey, and information entered in EDC by Pfizer.

8.7. Data analysis

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in a Statistical Analysis Plan (SAP), which will be dated, filed, and maintained by Pfizer. The SAP may modify the plans outlined in the full protocol, and any major modifications of primary endpoint definitions or their analyses will also be reflected in a protocol amendment.

8.7.1. Definition of analysis set

The safety analysis set (SAS) consists of a full analysis set (FAS) that is as closer as possible to all participant who received the fourth vaccination with this product.

8.7.2. Safety analysis

The events entered in the CRF submitted by the investigator for which the causal relationship with this product cannot be ruled out will be handled as adverse reactions, and the number and proportion of participants with adverse reactions ([%]: number of participants with adverse reactions/number of participants included in safety analysis) will be tabulated. Exploratory analyses will be performed as needed.

8.7.3. Analysis of reactogenicity events (local reactions and systemic reactions [health observation diary])

Local reactions and systemic reactions recorded in the health observation diary collected by the investigator from study participants will be handled as reactogenicity events, and the number and proportion of participants with each event will be tabulated. Exploratory analyses will be performed as needed.

8.7.4. Analysis of Information on COVID-19

By using the information on COVID-19 entered in the CRF submitted by the investigator, participants who are considered to be in a severe condition will be identified, and the number and proportion of the participants will be tabulated with reference to the severity classification in the "Guidance for Treatment of Novel Coronavirus Infection (COVID-19)." Exploratory analyses will be performed as needed.

8.8. Quality control

Prior to conducting the study, the site staff will explain to the investigator about the contents of the full protocol, etc. and ask the investigator to complete a case report form based on medical interviews based on the preliminary examination sheet and the health observation diary, and records such as medical records.

8.9. Limitations of the research methods

There may be potential limitations in this study:

1. Since no control group is included in the study, there is a limitation in determining whether or not the risk of developing adverse events and adverse reactions increases with administration of this product.
2. Due consideration may not be given to confounding factors due to insufficient background information collected.
3. Since this study collects information from medical interviews based on the preliminary examination sheet and the health observation diary and records such as medical records, specified data may not be collected or may be missing.

8.10. Other aspects

Not applicable.

9. PROTECTION OF HUMAN PARTICIPANTS

9.1. Participant information

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of personal data. Such measures will include omitting the names of vaccinees to be studiedor other directly identifiable data in any reports, publications, or other disclosures, except where required by applicable laws. The personal data will be stored at the study site in [encrypted electronic and/or paper] form and will be [password protected or secured in a locked room] to ensure that only authorized study staff have access. The study site will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, the study site shall be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of natural persons with regard to the processing of personal data, when study data are compiled for transfer to Pfizer and other authorized parties, participant names will be removed and will be replaced by a single, specific, numerical code, based on a numbering system defined by Pfizer. All other identifiable data transferred to Pfizer or other authorized parties will be identified by this single, participant-specific code. The investigator site will maintain a confidential list of participants who participated in the study, linking each participant's numerical code to his or her actual identity. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of participants' personal data consistent with the clinical study agreement and applicable privacy laws.

9.2. Participant consent

The informed consent/assent documents must be in compliance with local regulatory requirements and legal requirements, including applicable privacy laws.

The informed consent/assent documents used during the informed consent process must be reviewed and approved by Pfizer, approved by the institutional review board (IRB)/ethics committee (EC) before use, and available for inspection by regulatory authorities.

The investigator must ensure that each study participant, or his or her legally acceptable representative, or parent(s) or legal guardian if a minor, is fully informed about the nature and objectives of the study, the sharing of data relating to the study and possible risks associated with participation, including the risks associated with the processing of the participant's personal data. The investigator further must ensure that each study participant, or his or her legally acceptable representative, or parent(s) or legal guardian if a minor, is fully informed about his or her right to access and correct his or her personal data and to withdraw consent for the processing of his or her personal data.

Whenever consent is obtained from a participant's legally acceptable representative/parent(s) or legal guardian, the participant's assent (affirmative agreement) must subsequently be obtained when the participant has the capacity to provide assent, as determined by the IRB/EC. If the investigator determines that a participant's decisional capacity is so limited that he or she cannot reasonably be consulted, then, as permitted by the IRB/EC and consistent with local regulatory and legal requirements, the participant's assent may be waived with source documentation of the reason assent was not obtained. If the participant does not provide his or her own consent, the source documents must record why the participant did not provide consent (e.g., minor, decisionally impaired adult), how the investigator determined that the person signing the consent was the participant's legally acceptable representative, the consent signer's relationship to the participant (e.g., parent, spouse), and that the participant's assent was obtained or waived. If assent is obtained verbally, it must be documented in the source documents.

If a minor registered in the study reaches adulthood during the study, the consent will be reacquired from the participant at the time of adulthood according to local law to remain in the study. If the enrollment of emancipated minors is permitted by the study age criteria, the IRB/EC, and local law, they must provide documentation of legal status to give consent without the permission of a parent or legal guardian.

The investigator, or a person designated by the investigator, will obtain written informed consent from each participant or the participant's legally acceptable representative, parent(s), or legal guardian and the participant's assent, when applicable, before any study-specific activity is performed. The investigator will retain the original of each participant's signed consent/assent document.

9.3. Participant withdrawal

Study participants may withdraw from the study at any time at their own request, or they may be withdrawn at any time at the discretion of the investigator or Pfizer for safety, behavioral, or administrative reasons. In any circumstance, every effort should be made to document the outcome of study participants, if applicable. The investigator would inquire about the reason for withdrawal and follow-up with the participant regarding any unresolved adverse events.

If the study participant withdraws from the study, and also withdraws consent for disclosure of future information, no further evaluations should be performed, and no additional data should be collected. Pfizer may retain and continue to use any data collected before such withdrawal of consent.

9.4. Institutional review board (IRB)/Ethics committee (EC)

The informed consent documents used during the informed consent process must be reviewed and approved by Pfizer, approved by the institutional review board (IRB)/ethics committee (EC) before use.

9.5. Ethical conduct of the study

This study will be conducted in compliance with MHLW Ordinance in the "section 6. RATIONALE AND BACKGROUND". Also, the study will be conducted in accordance with legal and regulatory requirements, as well as scientific purpose, value, and rigor.

10. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

10.1. Records and report requirements

The table below summarizes the requirements for recording safety events on the CRF and for reporting safety events on the non-interventional study (NIS) adverse event monitoring (AEM) Report Form to Pfizer Safety. These requirements are delineated for three types of events: (1) serious adverse events (SAEs); (2) non-serious AEs (as applicable); and (3) scenarios involving drug exposure, including exposure during pregnancy, exposure during breastfeeding, medication error, overdose, misuse, extravasation, lack of efficacy, and occupational exposure. These events are defined in the section "Definitions of safety events."

Safety event	Recorded on the CRF	Reported on the NIS AEM Report Form to Pfizer Safety within 24 hours of awareness
SAE	All	All
Non-serious AE	All	None
Scenarios involving exposure to a drug under study, including exposure during pregnancy, exposure during breastfeeding, medication error, overdose, misuse, extravasation, lack of efficacy, and occupational exposure	All (regardless of whether associated with an AE), **except occupational exposure**	All (regardless of whether associated with an AE) Note: Any associated AE is reported together with the exposure scenario.

For each AE, the investigator must pursue and obtain information adequate both to determine the outcome of the AE and to assess whether it meets the criteria for classification as a SAE (refer to section "Serious Adverse Events" below).

Safety events listed in the table above must be reported to Pfizer within 24 hours of awareness of the event by the investigator **regardless of whether the event is determined by the investigator to be related to this product**. In particular, if the SAE is fatal or life-threatening, notification to Pfizer must be made immediately, irrespective of the extent of available event information. This timeframe also applies to additional new (follow-up) information on previously forwarded safety event reports. In the rare situation that the investigator does not become immediately aware of the occurrence of a safety event, the investigator must report the event within 24 hours after learning of it and document the time of his/her first awareness of the events.

For safety events that are considered serious or that are identified in the far-right column of the table above that are reportable to Pfizer within 24 hours of awareness, the investigator is obligated to pursue and to provide any additional information to Pfizer in accordance with this 24-hour timeframe. In addition, an investigator may be requested by Pfizer to obtain specific follow-up information in an expedited fashion. This information is more detailed than that recorded on the CRF. In general, this will include a description of the AE in sufficient detail to

allow for a complete medical assessment of the case and independent determination of possible causality. Any information relevant to the event, such as concomitant medications and illnesses, must be provided. In the case of a participant death, a summary of available autopsy findings must be submitted as soon as possible to Pfizer or its designated representative.

10.2. Reporting period

For each participant, the safety event reporting period begins at the time of the participant's first dose of this product or the time of the participant's informed consent if he or she is receiving this product at study start, and lasts through the end of the observation period of the study, which must include at least 28 calendar days following the last administration of the product under study; a report must be submitted to Pfizer Safety (or its designated representative) for any of the types of safety events listed in the table above occurring during this period. If a participant was administered the product under study on the last day of the observation period, then the reporting period should be extended for 28 calendar days following the end of observation. Most often, the date of informed consent is the same as the date of enrollment. In some situations, there may be a lag between the dates of informed consent and enrollment. In these instances, if a participant provides informed consent but is never enrolled in the study (e.g., participant changes his/her mind about participation), the reporting period ends on the date of the decision to not enroll the participant.

If the investigator becomes aware of a SAE occurring at any time after completion of the study and he or she considers the SAE to be related to this product, the SAE also must be reported to Pfizer Safety.

10.3. Causality assessment

The investigator is required to assess and record the causal relationship. For all AEs, sufficient information should be obtained by the investigator to determine the causality of each AE. For AEs with a causal relationship to this product, follow-up by the investigator is required until the event and/or its sequelae resolve or stabilize at a level acceptable to the investigator, and Pfizer concurs with that assessment.

An investigator's causality assessment is the determination of whether there exists a reasonable possibility that this product caused or contributed to an AE. If the investigator's final determination of causality is "unknown" and he or she cannot determine whether this product caused the event, the safety event must be reported within 24 hours.

If the investigator cannot determine the etiology of the event but he or she determines that this product did not cause the event, this should be clearly documented on the CRF and the NIS AEM Report Form.

10.4. Definitions of safety events

10.4.1. Adverse events

An AE is any untoward medical occurrence in a participant administered a medicinal product. The event need not necessarily have a causal relationship with the product treatment or usage. Examples of AEs include but are not limited to:

- Abnormal test findings (see below for circumstances in which an abnormal test finding constitutes an AE);
- Clinically significant signs and symptoms;
- Changes in physical examination findings;
- Hypersensitivity;
- Progression/worsening of underlying disease;
- Lack of efficacy;
- Drug abuse;
- Drug dependency.

Additionally, for medicinal products, they may include the signs or symptoms resulting from:

- Drug overdose;
- Drug withdrawal;
- Drug misuse;
- Off-label use;
- Drug interactions;
- Extravasation;
- Exposure during pregnancy;
- Exposure during breastfeeding;
- Medication error;
- Occupational exposure.

Abnormal test findings

The criteria for determining whether an abnormal objective test finding should be reported as an AE are as follows:

- Test result is associated with accompanying symptoms, and/or
- Test result requires additional diagnostic testing or medical/surgical intervention, and/or
- Test result leads to a change in study dosing or discontinuation from the study, significant additional concomitant drug treatment, or other therapy, and/or
- Test result is considered to be an AE by the investigator or Pfizer.

Merely repeating an abnormal test, in the absence of any of the above conditions, does not constitute an AE. Any abnormal test result that is determined to be an error does not require reporting as an AE.

10.4.2. Serious adverse events

A SAE is any untoward medical occurrence in a participant administered a medicinal or nutritional product (including pediatric formulas) at any dose that:

- Results in death;
- Is life-threatening;
- Requires inpatient hospitalization or prolongation of hospitalization (see below for circumstances that do not constitute AEs);
- Results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions);
- Results in congenital anomaly/birth defect.

Medical and scientific judgment is exercised in determining whether an event is an important medical event. An important medical event may not be immediately life-threatening and/or result in death or hospitalization. However, if it is determined that the event may jeopardize the participant or may require intervention to prevent one of the other outcomes listed in the definition above, the important medical event should be reported as serious.

Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse.

Additionally, any suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic, is considered serious. The event may be suspected from clinical symptoms or laboratory findings indicating an infection in a participant exposed to a Pfizer product. The terms "suspected transmission" and

"transmission" are considered synonymous. These cases are considered unexpected and handled as serious expedited cases by pharmacovigilance (PV) personnel. Such cases are also considered for reporting as product defects, if appropriate.

Hospitalization

Hospitalization is defined as any initial admission (even if less than 24 hours) to a hospital or equivalent healthcare facility or any prolongation to an existing admission. Admission also includes transfer within the hospital to an acute/intensive care unit (e.g., from the psychiatric wing to a medical floor, medical floor to a coronary care unit, neurological floor to a tuberculosis unit). An emergency room visit does not necessarily constitute a hospitalization; however, an event leading to an emergency room visit should be assessed for medical importance.

Hospitalization in the absence of a medical AE is not in itself an AE and is not reportable. For example, the following reports of hospitalization without a medical AE are not to be reported.

- Social admission (e.g., vaccinated individual/participant has no place to sleep)
- Administrative admission (e.g., for yearly exam)
- Optional admission not associated with a precipitating medical AE (e.g., for elective cosmetic surgery)
- Hospitalization for observation without a medical AE
- Admission for treatment of a pre-existing condition not associated with the development of a new AE or with a worsening of the pre-existing condition (e.g., for work-up of persistent pre-treatment lab abnormality)

10.4.3. Scenarios necessitating reporting to Pfizer Safety within 24 hours

Scenarios involving exposure during pregnancy, exposure during breastfeeding, medication error, overdose, misuse, extravasation, lack of efficacy, and occupational exposure are described below.

Exposure during pregnancy

Exposure during breastfeeding

Scenarios of exposure during breastfeeding must be reported, irrespective of the presence of an associated AE. An exposure during breastfeeding report is not created when a Pfizer drug specifically approved for use in breastfeeding women (e.g., vitamins) is administered in accord with authorized use. However, if the infant experiences an AE associated with such a drug's administration, the AE is reported together with the exposure during breastfeeding.

Medication error

A medication error is any unintentional error in the prescribing, dispensing, or administration of a medicinal product that may cause or lead to inappropriate medication use or participant harm while in the control of the health care professional, participant, or consumer. Such events may be related to professional practice, health care products, procedures, and systems including: prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

Medication errors include:

- Near misses, involving or not involving a participant directly (e.g., inadvertent/erroneous administration, which is the accidental use of a product outside of labeling or prescription on the part of the healthcare provider or the participant/consumer);
- Confusion with regard to invented name (e.g., trade name; brand name).

The investigator must submit the following medication errors to Pfizer, irrespective of the presence of an associated AE/SAE:

- Medication errors involving participant exposure to the product, whether or not the medication error is accompanied by an AE.
- Medication errors that do not involve a participant directly (e.g., potential medication errors or near misses). When a medication error does not involve participant exposure to the product, the following minimum criteria constitute a medication error report:
  - An identifiable reporter;
  - A suspect product;
  - The event medication error.

Overdose, misuse, extravasation

Reports of overdose, misuse, and extravasation associated with the use of a Pfizer product are reported to Pfizer by the investigator, irrespective of the presence of an associated AE/SAE.

Lack of efficacy

Reports of lack of efficacy of a Pfizer product are reported to Pfizer by the investigator, irrespective of the presence of an associated AE/SAE or the indication for use of the Pfizer product.

Occupational exposure

Reports of occupational exposure to a Pfizer product are reported to Pfizer by the investigator, irrespective of the presence of an associated AE/SAE.

11. SINGLE REFERENCE SAFETY DOCUMENT

In this study, the package insert of this product in Japan will serve as the Single Reference Safety Document. This document will be used by Pfizer Safety to assess any safety events reported to Pfizer Safety by the investigator during the course of this study.

The single reference safety document should be used by the investigator for prescribing purposes and guidance.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Information collected in this study will be used for reporting purposes to report Ministry of Health, Labour and Welfare (MHLW), Pharmaceuticals and Medical Devices Agency (PMDA), Pfizer Inc. which is the corporate parent of the sponsor of this study, and the group companies, or regulatory agency in other countries. Also, it will be used for submitting application of reexamination (including Periodic Safety Update Report) or re-evaluation, preparation of material for proper use information of this product, publications, or activities for information provision. In addition, Pfizer may publish the study results to provide information for proper use, as needed, on www.clinicaltrials.gov (ClinicalTrials.gov), as presentations at academic conferences, or as manuscripts, etc.

Data obtained from the participants registered in this study will be reported to the MHLW pursuant to the Pharmaceutical and Medical Device Act. In this case, the data may be publicly posted in MHLW's "Pharmaceutical and Medical Device Safety Information" and "Pharmaceuticals and Medical Devices Information Website (http://www.info.pmda.go.jp)" as a listing of participants, which will include the names of drugs, adverse reactions, gender, age (increment of 10 years), and other relevant information. Furthermore, data collected may also be disclosed if the MHLW is required to disclose such information in accordance with the "Act on Access to Information Held by Administrative Organs" (Law No. 42 dated May 14, 1999); provided that in no event will the names of physicians, medical institutions, and other personal information be participant to such disclosure, nor will it be posted or disclosed.

In the event of any prohibition or restriction imposed (e.g., clinical hold) by an applicable Competent Authority in any area of the world, or if the investigator is aware of any new information which might influence the evaluation of the benefits and risks of a Pfizer product, Pfizer should be informed immediately.

In addition, the investigator will inform Pfizer immediately of any urgent safety measures taken by the investigator to protect the study participants against any immediate hazard, and of any serious breaches of this NI study full protocol that the investigator becomes aware of.

13. NAME, AND ADDRESS OF CONTRACTOR AS WELL AS SCOPE OF WORK CONTRACTED

- Company name: Pfizer R&D Japan
  Address: 3-22-7, Yoyogi, Shibuya-ku, Tokyo
  Scope of work contracted: Works related to planning of study, drafting of plan, implementation of study and monitoring, etc.

- Company name: Medidata Solutions
  Address: 2-7-2, Marunouchi, Chiyoda-ku, Tokyo
  Scope of work contracted: Establishment, operation and maintenance of the EDC system, etc.

- Company name: EPS Corporation
  Address: 2-23, Shimomiyabicho, Shinjuku-ku, Tokyo
  Scope of work contracted: Establishment of the EDC system, registration, data management, statistical analysis, monitoring, etc.

- Company name: A2 Healthcare Corporation
  Address: 1-4-1 Koishikawa, Bunkyo-ku, Tokyo
  Scope of work contracted: EDC account management, etc.

14. ADDITIONAL MEASURES THAT MAY BE TAKEN BASED ON THE STUDY RESULTS AND CRITERIA FOR DETERMINATION OF THE INITIATION

Review the risk management plan including the following contents at the scheduled timing of milestones.

1. Review the necessity for changing the contents of risk minimization activities for the current safety specifications.

2. Review the necessity for changing the contents of this study plan including the presence or absence of new safety specifications (continuation of the study, implementation of additional study, etc.).

3. Review the necessity for formulating risk minimization measures for new safety specifications.

15. SCHEDULED TIMING OF MILESTONES AND THEIR RATIONALES FOR EVALUATION OF STUDY IMPLEMENTATION STATUS AND RESULTS AND REPORTING TO THE PMDA

Safety review and reporting at the time of preparing the Periodic Safety Update Reports and completion of the study.

16. OTHER NECESSARY MATTERS

1. Amendment of the Full Protocol

Based on the new knowledge to be obtained according to the progress of this study, the need for amendment of the protocol will be examined and the Full Protocol will be amended if necessary. Also, the need for amendment of the Full Protocol will be examined and the protocol will be amended when the partial change in the dosage and administration or indication is approved during the reexamination period (except when the reexamination period is newly designated), etc.

2. Actions to be taken for any problem or issue

Revision of the package insert and conduct of a new Post-marketing study or new Post-marketing clinical trial should be considered for the following cases: any serious and unknown adverse reaction is suggested; a significant increase in the frequency of adverse reactions is noted; any effectiveness or safety concern compared to pre-approval is raised; rare adverse reaction is suggested.

17. CONTACT INFORMATION

17.1. Contact information for inquiries about the study

Name	PMS Affairs, Pfizer R&D Japan
Address	3-22-7, Yoyogi, Shibuya-ku, Tokyo 151-8589
FAX	03-5309-9186
E-mail address	CMT_INF_DRPMS@pfizer.com

17.2. Contact information for inquiries about the EDC system

Name	Medidata Helpdesk
Business Hours	Mondays through Fridays: 9:00–20:00 (excluding holidays, year end and beginning)
TEL	PPD (Dedicated number for Pfizer)
E-mail address	japanhelpdesk@mdsol.com

18. REFERENCES

1. Guidance for Treatment of Novel Coronavirus Infection (COVID-19)
2. US Food and Drug Administration. Guidance for industry: toxicity grading scale for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials. Rockville, MD: Center for Biologics Evaluation and Research; September 2007.

19. LIST OF TABLES

20. LIST OF FIGURES

APPENDIX 1. LIST OF STAND ALONE DOCUMENTS

Not applicable.

APPENDIX 2. ADDITIONAL INFORMATION

1. Special investigation registration form
2. Special investigation case report form
3. Two types of health observation diary (<2 years and ≥2 years) for special investigation

TRANSLATION RECORD (FOR POST-MARKETING SURVEILLANCE STUDY IN JAPAN)	10-Jan-2019

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FULL TRANSLATION AND REVIEW INFORMATION

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