(Appendix)

Special Investigation of COMIRNATY Intramuscular Injection

(Investigation of Patients with Underlying Disease Considered to be at High Risk of Aggravation of COVID-19)

Full Protocol

Pfizer Japan Inc.

STUDY INFORMATION

Title	Special Investigation of COMIRNATY Intramuscular Injection (Investigation of Patients with Underlying Disease Considered to be at High Risk of Aggravation of COVID-19)
Protocol ID	C4591019
Protocol version identifier	Amended 1
Date	26 February 2021
Active substance	Tozinameran
Medicinal product	COMIRNATY Intramuscular Injection
Research question and objectives	To collect information on adverse events and COVID-19 observed after vaccination with this product and to assess safety in patients with underlying disease considered to be at high risk of aggravation of COVID-19 who have received vaccination with this product under actual use conditions.
Author	Post-Marketing Study Strategy and Management PPD

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2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ECMO	Extracorporeal membrane oxygenation
ICU	Intensive care unit
IEC	Independent ethics committee
IRB	Institutional review board
N/A	Not applicable
SAP	Statistical analysis plan
SRSD	Single reference safety document
VAED	Vaccine-associated enhanced disease
VAERD	Vaccine-associated enhanced respiratory disease
WHO	World Healthcare Organization

3. RESPONSIBLE PARTIES

The Japan Good Post-marketing Study Practice officer

4. AMENDMENTS AND UPDATES

Protocol version identifier	Date	Protocol section(s) changed	Summary of amendment(s)	Reason
Amended 1	26 February 2021	8.3.1. Characteristics of vaccinated subjects	Change the History of other vaccinations to "within 2weeks before the date of the first vaccination with this product"	Because the final version of pre-vaccination screening Questionnaire has changed
Final	13 February 2021	N/A	N/A	N/A

5. MILESTONES

Milestone	Planned date
Start of data collection	April 2021
End of data collection	December 2021
Interim report	To be determined
Final study report	To be determined

6. RATIONALE AND BACKGROUND

In December 2019, pneumonia of unknown cause became epidemic in Wuhan China. In January 2020, it was revealed that a novel coronavirus (2019-nCoV) was the cause. On 12 February 2020, the virus was officially named SARS-CoV-2 and the WHO officially named the disease caused by SARS-CoV-2 as COVID-19.
SARS-CoV-2 and the resultant COVID-19 have spread globally with a steadily increasing number of individuals infected.

BioNTech has developed RNA vaccine candidates using a platform that enables rapid development of vaccines against emerging viral diseases, including SARS-CoV-2. RNA vaccines encoding viral antigens have a significant advantage compared to conventional vaccines because they express proteins that induce a protective immune response in the vaccinated body and can be developed and manufactured rapidly.

COMIRNATY intramuscular injection (generic name: tozinameran) (hereinafter referred to as this product) is an RNA vaccine containing mRNA encoding the spike protein of SARS-CoV-2, and its marketing approval was obtained in February 2021 with the indication of prevention of infection with SARS-CoV-2.

This product is a highly novel vaccine and the safety information in Japanese subjects obtained by the time of marketing approval is limited. A wide range of people are expected to be vaccinated with this product after marketing approval is granted, and it is considered highly necessary to collect post-marketing safety information.

Considering that a focused investigation in healthcare professionals (hereinafter referred to as Investigation of Health Status of Recipients Vaccinated First) is planned at an early stage after the start of vaccination with a new corona vaccine as Science Research of the Ministry of Health, Labour and Welfare (designated research) immediately after the marketing approval, a special investigation will be conducted in patients with underlying disease considered to be at high risk of aggravation of COVID-19 in Japan for whom no existing safety information is available, with the aim of avoid overlapping of subjects and based on the plan of the clinical study in Japan.

This Study shall be conducted in strict compliance with the "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), "MHLW Ordinance to Partially Amend the MHLW Ordinance on the Standard for Post-marketing Safety Control of Medical Products, Quasi-medical Products, Cosmetics, and Medical Devices and to Partially Amend the MHLW Ordinance on the Standard for Post-marketing Studies and Clinical Trials of Medical Products" (MHLW Ordinance No. 26, dated March 11, 2013), the "Enforcement of the MHLW Ordinance to Partially Amend the MHLW Ordinance on the Standard for Post-marketing Safety Control of Medical Products, Quasi-medical Products, Cosmetics, and Medical Devices, and to Partially Amend the MHLW Ordinance on the Standard for Post-marketing Studies and Clinical Trials of Medical Products" (PFSB Notification No. 0311-7, dated March 11, 2013)., "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 "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

This investigation intends to collect information on adverse events and COVID-19 observed after vaccination with this product and to assess safety in patients with underlying disease considered to be at high risk of aggravation of COVID-19 after marketing approval.

7.1. Safety specifications

[Important Identified Risks]

- Shock, anaphylaxis

[Important Potential Risks]

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

[Important Missing Information]

- Safety of administration to pregnant or lactating women

8. RESEARCH METHODS

8.1. Study design

This is a multicenter cohort study to be conducted in individuals with underlying diseases considered to be at high risk of aggravation of COVID-19 who are vaccinated with this product, and the investigator will

enter the information required in this study in the case report forms (CRFs) based on the information obtained through preliminary examination sheet or medical interview, etc. and records such as medical records. A health observation diary will be distributed to the subjects participating in this study and they will be requested to record information on 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 the records other than the symptoms at the vaccination site and general symptoms specified in the diary (including the COVID-19 information) as needed and enter them as adverse events. The investigator will not enter the symptoms at the vaccination site (local reactions) and general symptom (systemic reactions) specified in the health observation diary in the CRFs to avoid overlapping with adverse events evaluated by physicians.

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

8.2. Setting

8.2.1. Registration criteria

Subjects must meet all of the following inclusion criteria to be eligible for inclusion in the study: Subject registration will be performed within 21 days at the latest after the first vaccination with this product (before the second vaccination).

1. Subjects who are able to understand the content of this study and to record their symptoms in the health observation diary, and who have provided written consent to participate in this survey by themselves (or parents or legal guardians in the case of minors)

2. Patients with an underlying disease considered to be at high risk of aggravation of COVID-19 at the time of vaccination with this product

   Underlying diseases considered to be at high risk of aggravation of COVID-19 are based on the range of patients with underlying diseases indicated by the Ministry of Health, Labour and Welfare for priority vaccination. In principle, the subjects will be identified by the doctor's confirmation through medical interview, etc. after the subjects have filled in the preliminary examination sheet about the underlying disease.

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

[Indications]	Prevention of infection with SARS-CoV-2
[Dosage and administration]	The product is diluted with 1.8 mL of Japanese Pharmacopoeia physiological saline and administered intramuscularly at a dose of 0.3 mL 2 times in total, usually at 3-week intervals.
[Precautions regarding dosage and administration]	
Subjects:	Those aged 12 years or older will be vaccinated with this product.
Vaccination interval:	If 3 weeks or more have passed since the first vaccination, the second vaccination should be given as soon as possible.

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 50 to 100 institutions with the system for vaccination with this product, which have agreed to cooperate with this investigation.

8.2.4. Planned study period

The planned period covered by this study is as follows.

Investigation period: From the date of start of the first vaccination of the first subject enrolled to the end of observation period for the last enrolled subject (scheduled from April 2021 to December 2021)

Registration period: From the date of start of the first vaccination of the first subject enrolled to the date of registration of the last enrolled subject (scheduled from April 2021 to October 2021)

The registration is terminated if the target number of the patients has been collected, even before the end of the registration period.

8.2.5. Study procedures

8.2.5.1. Study method

Central registration system: This study will be conducted with Central registration system that patients who meet the conditions of this study will be registered until data are collected on a target number of patients. The investigator will investigate the subjects who meet the registration criteria (8.2.1) approximately within 21 days at the latest after the first vaccination with this product (before the second vaccination).

This study will be conducted in patients 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 first vaccination with this product (Day 1) to 28 days after the second vaccination. For the subjects who have received only the first vaccination and do not receive the second vaccination for some reason, the observation period will be until 28 days after the first vaccination.

In this study, information will be collected using booklet type CRF. Information for the following periods will be entered in each booklet.

- Booklet 01: From the day of the first vaccination to the day before of the second vaccination

  (For the subjects who have received only the first vaccination with this product: Booklet 01, from the day of the first vaccination to 28 days after the first vaccination)

- Booklet 02: From the day of the second vaccination to 28 days after the second vaccination

However, in cases where treatment has been discontinued, observation is continued until discontinuation of treatment.

8.3. Variable

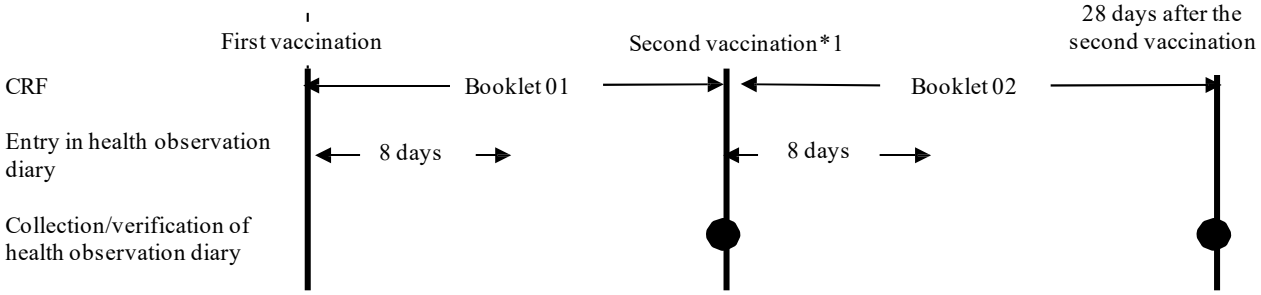
This study will be conducted according to the following schedule.

Table 1. Variables

Variable	Registration form	CRF Booklet 01	CRF Booklet 02
ID number		*	
Gender		*	
Date of birth		*	
Eligibility		*	
Day of the first vaccination with this product		*	
Clinical history (concurrent illness/past history)			
Status of vaccination with this product (first)			
Allergy information			
History of other vaccinations			
Pregnancy and lactation (women only)		←	→
Status of vaccination with this product (second)			
Information on inoculation of other vaccines			
Concomitant medications		←	→
Information on COVID-19 pathogen test		←	→
Information on COVID-19		←	→
Adverse events (including serious adverse events)		←	→
End-of-study discontinuation record (reason)			

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

Figure 1. Schedule



*1: For the subjects who have received only the first vaccination, the observation period will be until 28 days after the first vaccination, and Booklet 01 will be completed.

8.3.1. Characteristics of vaccinated subjects

Enter the information at the time of first vaccination of this product in the registration form.

- ID number
- Gender
- Date of birth (if the date of birth cannot be provided, age at the first vaccination with this product)
- Date of the first vaccination with this product

The following will be recorded in CRF at the time of the first vaccination with this product.

- Clinical history (concurrent illness and past history)

  The disease present at the time of vaccination with this product is considered as a "complication" and the disease present before vaccination with this product is considered as "medical history."

- Allergy information (information on presence/absence of allergy, type of allergy, and allergen)
- History of other vaccinations (presence or absence of vaccine and name of vaccine [within 2 weeks before the date of the first vaccination with this product])

8.3.2. Pregnancy and lactation (women only)

If the subject participating in this survey is female, the presence or absence of pregnancy and lactation during the period from the date of the first vaccination with this product to the target period of booklet will be entered.

8.3.3. Status of vaccination with this product

The following information will be recorded for the status of the first and second vaccination with this product.

- Date of vaccination (The date of the first vaccination will be automatically reflected in the CRF.)
- Lot number
- Vaccination site

8.3.3.1. Concomitant medications

For drugs used concomitantly after the date of the first vaccination with this product and the drugs used for treatment of adverse events, enter the information to the end date of the observation period.

- Drug name (product name)
- Treatment period (Enter the start date of treatment if no concomitant drugs are used as of the time of the first vaccination of this product, and enter the end date of treatment if no concomitant drugs are used at the end of the observation period.)

8.3.4. End-of-study/discontinuation record

The investigator will enter the end date of the observation period (date of final observation) for each booklet, i.e., the day before of the second vaccination for Booklet 01 (28 days after the first vaccination [or thereafter] for the subjects who have received only the first vaccination) for Booklet 01, and the date of confirmation of information on the subject in the 28 days after the second vaccination (or thereafter) for Booklet 02.

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

If information on the subject cannot be confirmed even at 1 month after the end date of the observation period for each booklet, and the date of final confirmation of the information on the subject does not meet the observation period, the date on which information on the subject can be confirmed for the last time will be entered as the date of discontinuation of observation and the reason for discontinuation will be entered. (the subjects who have received only the first vaccination with this product will be handled as the cases of 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 (including no visit after the date of the first vaccination with this product)
    - Consent withdrawal
    - Other

8.3.5. Information on inoculation of other vaccines

The investigator will confirm the presence or absence of vaccine inoculated during the observation period and enter the information. If a vaccine is inoculated during the observation period, the type of vaccine and the date of vaccination will 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) received during the observation period and enter the information. If a pathogen test is performed, enter the date of test (date of specimen collection), type of test and test results in the CRF for each test.

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 occurrence of COVID-19

If The occurrence of COVID-19 is "present," the following information will also be entered.

- Date of diagnosis of COVID-19
- Presence or absence of actions/procedures taken (hospitalisation, oxygen administration, ICU admission, use of mechanical ventilation, and use of ECMO)
- 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 after the end of the observation period.

8.3.8. Adverse events

Occurrence of adverse events from the date of the first vaccination with this product to the end date of observation period should be confirmed and the following information should be entered. The status of the subject should be examined for a certain period after each vaccination with this product. 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 collected health observation diary (see Section 8.3.9) 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 entered as adverse events. The investigator does not need to enter the symptoms at the vaccination site (local reactions) and general symptom (systemic reactions) specified in the health observation diary in the CRFs to avoid overlapping with adverse events evaluated by physicians.

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

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

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 subjects
Moderate	Interfering with usual activities of vaccinated subjects to some extent
Severe	Markedly interfering with usual activities of vaccinated subjects
Life-threatening	Life-threatening, or necessitating urgent intervention

8.3.8.2. Criteria for seriousness

The investigator will select and enter the applicable criteria for serious adverse events reported during the observation period.

- Results in death.
- Life-threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/malfunction
- Causes a congenital anomaly/birth defect.
- Other medically important events

8.3.9. Health observation diary

A health observation diary will be distributed to the subjects participating in this study and they will be requested to record information on symptoms at the vaccination site (local reactions) and general symptoms (systemic reactions [including pyrexia]) after vaccination with this product. Study participants will examine and record local reactions (injection site pain, redness, and swelling) and systemic reactions (pyrexia, vomiting, diarrhoea, headache, Fatigue, chills, myalgia, and arthralgia) in the diary for 8 days after vaccination with this product (If the symptoms persist even on the 9th day or thereafter, the date of disappearance of the symptoms should be recorded.).

The investigator will collect the health observation diary after the end of the observation period (collection by mail is also acceptable) and check the details of the information other than the symptoms at the vaccination site and general symptoms recorded in the diary (including the COVID-19 information) as needed (or confirm by telephone, etc.) and enter them as adverse events. The investigator does not need to enter the symptoms at the vaccination site (local reactions) and general symptom (systemic reactions) specified in the health observation diary in the CRFs to avoid overlapping with adverse events evaluated by physicians.

The investigator will replace the information with a single, specific, numerical code based on the numbering system specified by the sponsor, and submit a copy of the diary to the sponsor or other authorized persons concerned (in principle, submit by mail).

8.3.9.1. Severity assessment (health observation diary)

The severity used by the subjects when evaluating symptoms at the vaccination site (local reactions) and general symptoms (systemic symptoms [including pyrexia]) will be recorded in the health observation diary by using the following indices.

The severity classification will be set based on 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, interference with daily activities = making daily life difficult).

Table 3. Severity Classification of Local Reactions

	Mild Grade 1	Moderate Grade 2	Severe Grade 3
Injection site pain	Not interfering with activities	Interfering with activities	Interfering with daily activities
Redness	2.0 ~ 5.0cm	>5.0 ~ 10.0cm	>10.0 cm
Swelling	2.0 ~ 5.0cm	>5.0 ~ 10.0cm	>10.0 cm

Table 4. Severity Classification of Systemic Reactions

	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	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 within 24 hours*
Headache	Not interfering with activities	Slightly interfering with activities	Interfering with daily activities
Fatigue	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
Myalgia	Not interfering with activities	Slightly interfering with activities	Interfering with daily activities
Arthralgia	Not interfering with activities	Slightly interfering with activities	Interfering with daily activities

* "Within 24 hours" was "1 day" in the diary.
** "Intravenous fluid replacement (drip infusion)" was "drip infusion" in the diary.

8.4. Data sources

In this study, the investigator will extract necessary information based on the full protocol from the information obtained by the preliminary examination sheet and the health observation diary completed by the study participants, as well as by medical interview, etc. and the records including medical records.

Evaluation of local reactions and systemic reactions after vaccination recorded by subjects in the health observation diary will be used.

8.5. Study size

8.5.1. Planned sample size

1,000 subjects will be collected as the subjects to be included in the safety analysis set.

8.5.2. Rationale for sample size

Considering the timing of vaccination for individuals with underlying diseases who are considered to be at high risk of aggravation of COVID-19, the timing of implementation of this study is believed to be limited. In addition, because it is planned in this study to provide information for obtained informed consent to the subjects, to request for entry in the health observation diary, and to collect the diary, it will cause a great burden on medical institutions. From the viewpoint of feasibility, the target number of subjects was set at 1,000.
If 1,000 subjects who have received vaccination with this product at least once can be collected, an event that occurs with a true probability of 0.3% can be observed in at least 1 subject with a probability of 95%.
In addition, based on the results of the safety analysis for the at risk population in Study C4591001, it is assumed that the safety profile will not differ between the population of subjects aged 56 years or older and the population with underlying disease that is considered to be at high risk of aggravation of COVID-19.

Based on the safety data obtained so far in the population aged 56 years or older in Study C4591001, the incidence of severe adverse events that occurred after vaccination with this product ranged from 0.1% (vomiting and diarrhoea) to 2.8% (fatigue), and therefore it is considered possible to confirm these events by collecting the safety information of 1,000 subjects.

8.6. Data management

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

The term CRF in this full protocol refers to an electronic data record corresponding to the data collection method used in this study.

A CRF is required and should be completed for each included subject. 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 site in the 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 "correction seal"), and explained (if necessary) and should not obscure the original entry.

In most cases the source documents are the hospital or the physician's 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. Care 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 participants in this study will be asked to fill out the health observation diary for 8 days after each vaccination (if symptoms continue on the 9th day or thereafter, the date of disappearance of the symptoms should be recorded). The investigator will collect the health observation diary at the time of the second vaccination with this product and 28 days after the second vaccination (at 28 days after the first vaccination for the subjects who have received only the first vaccination) from the study participants and review the contents of the health observation diary. After that, the investigator will anonymize the names of the study participants and replace information with a single unique numerical code based on the numbering method specified by the sponsor to protect personal data of study participants, and submit a copy of the diary to the sponsor or other authorized personnel (in principle, submit it by mail).

8.6.4. Subject registration (EDC)

The investigator will enter information on the registration screen of EDC (registration form) for the subjects to be studied and save the data. Subject registration will be performed within 21 days at the latest after the first vaccination with this product (before the second vaccination).

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

8.6.5.1. Data entry

The investigator will check the survey items and enter the data in the EDC based on the information such as the preliminary examination sheet completed by the subjects, records including medical records, and information in the health observation diary.

For the symptoms at the vaccination site (local reactions) and general symptoms (systemic reactions) specified in the health observation diary, the sponsor will enter the data in the EDC based on the copy submitted by the investigator.

8.6.5.2. Data revision

Upon receiving query from Sponsor on the contents of the CRF (follow-up survey), the investigator will again confirm the contents of medical records, and as required, correct 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 and follow-up survey as well as the information entered on EDC by the sponsor.

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 the sponsor. The SAP may modify the plans outlined in the full protocol, and any major modifications will 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 subjects who have been vaccinated with this product at least once.

8.7.2. Safety analyses

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 subjects with serious adverse reactions ([%]: number of subjects with adverse reactions/number of subjects included in safety analysis) will be tabulated. CCI [redacted]

8.7.3. Analysis of specific adverse events (health observation diary)

Local reactions and systemic reactions recorded in the health observation diary collected by the investigator from study participants and submitted to the sponsor will be handled as specific adverse events, and the number and proportion of subjects with each event will be tabulated. CCI [redacted]
CCI [redacted]

8.7.4. Analyses of information on COVID-19

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

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 create CRFs based on medical interview 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 a risk of developing adverse events and adverse reactions increases with vaccination with this product.

2. Due consideration may not be given to confounding factors due to insufficient background information collected.

3. Since this study collects the information from medical interview based on the preliminary examination sheet and health observation diary and records such as medical records, specified data may not be collected or may be missing.

8.10. OTHER NECESSARY MATTERS

Not applicable.

9. PROTECTION OF HUMAN SUBJECTS

9.1. Information of vaccinated subjects

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of personal data of subjects. Such measures will include omitting subject names or 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, subject 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, subject-specific code. The investigator site will maintain a confidential list of subjects who participated in the study, linking each subject's numerical code to his or her actual identity. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of subjects' personal data consistent with the clinical study agreement and applicable privacy laws.

9.2. Consent of vaccinated subjects

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

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

The investigator must ensure that each subject, 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 subject's personal data. The investigator further must ensure that each subject, 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 subject's legally acceptable representative/parent(s) or legal guardian if a minor, the subject's assent (affirmative agreement) must subsequently be obtained when the subject has the capacity to provide assent, as determined by the IRB/IEC. If the investigator determines that a subject's decisional capacity is so limited that he or she cannot reasonably be consulted, then, as permitted by the IRB/IEC and consistent with local regulatory and legal requirements, the subject's assent may be

waived with source documentation of the reason assent was not obtained. If the subject does not provide his or her own consent, the source documents must record why the subject did not provide consent (e.g., minor, decisionally impaired adult), how the investigator determined that the person signing the consent was the subject's legally acceptable representative, the consent signer's relationship to the subject (e.g., parent, spouse), and that the subject's assent was obtained or waived. If assent is obtained verbally, it must be documented in the source documents.

If the study includes minor subjects who reach the age of majority during the study, as recognized under local law, they must re-consent as adults to remain in the study. If the enrollment of emancipated minors is permitted by the study age criteria, the IRB/IEC, and local law, they must provide documentation of legal status to give consent without the permission of parents or legal guardian.

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

9.3. Subject 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 sponsor 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 subject 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. The sponsor may retain and continue to use any data collected before such withdrawal of consent.

9.4. Institutional review board (IRB)/Independent ethics committee (IEC)

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

9.5. Ethical conduct of the study

This study will be conducted in compliance with the "MHLW Ordinance on the Standard for Post-Marketing Studies and Clinical Trials of Medical Products" (MHLW Ordinance No. 171, dated December 20, 2004) Also, the study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor.

10. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

10.1. Record and report requirements

The following table summarizes the requirements for recording safety events on CRFs and for reporting safety events to Pfizer Safety on a Non-Interventional Study Adverse Event Report Form (NIS AE Report Form). These requirements are described for three types of events as follows: (1) serious adverse events, (2) non-serious adverse events (if applicable), and (3) drug exposure-related scenarios including exposure during pregnancy, exposure during breast feeding, medication error, drug overdose, drug misuse, extravasation, lack of efficacy, and occupational exposure. These events are defined in the section of "Safety event definition."

Safety event	Record in CRF.	Report to Pfizer Safety within 24 hours of awareness of the event using the NIS AE Report Form.
Serious adverse events	All	All
Non-serious adverse events	All	None
Scenarios related to exposure to this product including exposure during pregnancy, exposure during breast feeding, medication error, drug overdose, drug misuse, extravasation, lack of efficacy, occupational exposure	All (with or without adverse events), **expect occupational exposure**	All (with or without adverse events) Note: All adverse events related to drug administration will be reported with exposure scenarios.

For each adverse event, the investigator must obtain information adequate for confirming the outcome, and determining whether the event meets the criteria for a serious adverse event (see the section of "Serious adverse events" below).

The safety events for which reporting to the Safety division is required in the above table must be reported to Pfizer within 24 hours of the investigator's awareness of the event, **regardless of whether the event is determined by the investigator to be related to this product.** In particular, if the serious adverse event is fatal or life-threatening, notification to Pfizer must be made immediately, irrespective of the extent of available information. This timeframe also applies to additional new (follow-up) information on previously forwarded safety event reports. In the rare event that the investigator does not become aware of the occurrence of a safety event immediately, the investigator is to report the event within 24 hours after learning of it and record the day and time of his/her first awareness of the event.
For those safety events that are considered serious or that are specified in the far right column of the table above as requiring reporting to Pfizer within 24 hours of awareness, the investigator must conduct the follow-up investigation, and must provide any additional information to Pfizer in accordance with the 24-hour timeframe. In addition, an investigator may be requested by Pfizer to obtain specific additional information in an expedited fashion. This information needs to be more detailed than that recorded on the CRF. In general, this information should include sufficient detail to allow for a complete medical assessment of the event and independent determination of causality. Information regarding this event, such as concomitant medications and illnesses, must also be provided. In the event of a subject's death, a summary of available autopsy findings must be submitted as soon as possible to Pfizer or its designated representative.

10.2. Reporting period

The reporting period of safety events (see the table above) in each subject to Safety division begins with the first vaccination with this product to the subjects and ends at the end of the observation period in the study. However, the period of at least 28 calendar days after the final vaccination with this product should be the reporting period. If a safety event of the type described in the table above has occurred during the reporting period, the investigator will submit a report to Pfizer Safety (or its designated representative). If a subject has been vaccinated with this product on the last day of the observation period, the reporting period should be extended by 28 calendar days after the end of the observation period. In most cases, the date of informed consent is the same as the date of enrollment. In some circumstances, there may be a difference between the date of informed consent and the date of enrollment. The reporting period will end

on the day the decision is made not to include the vaccinated subject if a subject has given consent but is not enrolled in the study (e.g., the subject has changed his/her intention to participate in the study).
If the investigator becomes aware of the occurrence of a serious adverse event at any time after completion of the study and the serious adverse event is determined to be related to this product, the serious adverse event will also be reported to Pfizer Safety.

10.3. Evaluation of causal relationship

The investigator will be asked to evaluate and record the causal relationship. In addition, the investigator should obtain sufficient information to assess the causal relationship of each adverse event. For adverse events related to this product, follow-up investigation by the investigator is required until the event or its sequelae resolves or stabilizes at a level acceptable to the investigator, and Pfizer concurs with that assessment.

The evaluation of the causal relationship by the investigator will be determined by whether there exists a reasonable possibility that the drug has caused or contributed to the adverse event. If the investigator's final judgement regarding the causal relationship is "unknown," and it cannot be decided whether this product has caused the event, the safety event must be reported within 24 hours.

If the investigator cannot identify the cause of the event, but judges that this product has not caused the event, it should be clearly stated in the CRF and the NIS AE Report Form.

10.4. Safety event definition

10.4.1. Adverse events

An adverse event is an untoward medical occurrence in a vaccinated subject. The event does not necessarily have a causal relationship with inoculation or use of the product. Examples of adverse events include, but are not limited to:

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

In addition, they may include signs and symptoms resulting from:

- Drug overdose
- Drug withdrawal

- Drug misuse
- Off label use
- Drug interaction
- Extravasation
- Exposure during pregnancy
- Exposure during breast feeding
- Medication error
- Occupational exposure

Abnormal test findings

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

- The test result is accompanied by associated symptoms.
- Additional diagnostic testing or medical/surgical intervention is required.
- The test result leads to a change in administration of this product, discontinuation of the study, or addition of concomitant drug treatment or other therapy.
- The investigator or Pfizer regards the test result as an adverse event.

A case in which none of the above situations is present but simply an abnormal value continues will not be regarded as an adverse event. Any abnormal test result that is determined to be due to a laboratory error does not require reporting as an adverse event.

10.4.2. Serious adverse events

A serious adverse event is any untoward medical occurrence in a subject who has received a medicinal or nutritional product (including pediatric formulas) at any dose that:

- Results in death.
- Life-threatening
- Requires hospitalisation or prolongation of existing hospitalisation (see below for circumstances in which an abnormal test finding does not constitute an adverse event).
- Results in persistent or significant disability/malfunction (substantial disruption of the ability to conduct normal life functions).
- Causes a congenital anomaly/birth defect.

Medical and scientific judgment should be exercised in deciding whether an event is a medically important event. Significant medical events may not be immediately life-threatening or result in death or hospitalisation. However, if it is determined that the event may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definition above, the event should be reported as serious.

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

In addition, any suspected transmission via a Pfizer product of an infectious agent, pathogenic or nonpathogenic, is considered serious. The onset of the event may be suspected from clinical signs or laboratory findings suggestive of infection in a subject exposed to a Pfizer product. The term "suspected transmission" is considered the synonym of "transmission." These cases are considered unexpected and will be handled as serious expedited cases by Safety division. Such cases should also be considered for reporting as product defects, if appropriate.

Hospitalisation

Hospitalisation is defined as any initial admission (even less than 24 hours) to a hospital or equivalent healthcare facility or any prolongation of existing hospitalisation. Hospitalisation also includes transfer within the hospital to another department or an acute/intensive care unit (e.g., from the psychiatric floor to the medical floor, from the medical floor to the coronary care unit, from the neurological floor to the tuberculosis unit, etc.). A visit to the emergency room is not necessarily regarded as hospitalisation; however, the event leading to the emergency room visit should be assessed for medical significance.

Hospitalisation without a medical adverse event is not an adverse event itself and reporting is not required. For example, hospitalisation without any of the following medical adverse events does not require reporting.

- Hospitalisation for social reasons (e.g., no place of accommodation for subjects)
- Administrative hospitalisation (e.g., for yearly physical examination)
- Optional hospitalisation not associated with a precipitating clinical illness (e.g., for elective cosmetic surgery)
- Hospitalisation for observation without a medical adverse event
- Hospitalisation for treatment of a preexisting condition not associated with the occurrence of a new adverse event or with worsening of the preexisting condition (e.g., for precise examination of abnormal laboratory test values observed before the start of the treatment)
- Hospitalisation during the investigation period specified in the full protocol (e.g. tests and procedures specified in the protocol)

10.4.3. Scenarios necessitating reporting to Pfizer Safety within 24 hours

Scenarios related to exposure during pregnancy, exposure during breast feeding, medication error, drug overdose, drug misuse, extravasation, lack of efficacy, and occupational exposure are described below.

Exposureduringpregnancy

Exposure during pregnancy (EDP) occurs when:

3. A female becomes, or is found to be, pregnant either while receiving or being exposed to this product (e.g., environmental exposure). A female becomes, or is found to be, pregnant after discontinuing or having been directly exposed to this product (maternal exposure).

An example of environmental exposure would be a case involving direct contact with a Pfizer product in a pregnant woman (e.g., a nurse reports that she is pregnant and has been exposed to chemotherapeutic products).

4. A male has been exposed, either due to treatment or environmental exposure, to a Pfizer product prior to or around the time of conception. A male has been exposed during his partner's pregnancy (paternal exposure).

As a general rule, prospective and retrospective reports of exposure during pregnancy from any source are reportable irrespective of the presence of an associated adverse event and the procedures for reporting serious adverse events should be followed.

If a subject or a subject's partner becomes or is found to be pregnant during the period of treatment with this product, this information must be submitted to Pfizer, irrespective of whether an adverse event has occurred, using the NIS AE Report Form and the EDP Supplemental Form.

In addition, information regarding environmental exposure to this product in pregnant women (e.g., a subject reports that she is pregnant and has been exposed to a cytotoxic product by inhalation or spillage) must be submitted using the NIS AE Report Form and the EDP Supplemental Form. This must be done irrespective of whether an adverse event has occurred.

The information submitted should include the anticipated date of delivery (see below for information on termination of pregnancy).

Follow-up investigation should be conducted to obtain general information on the pregnancy. In addition, follow-up investigation of EDP outcome information is required for all EDP reports with an unknown pregnancy outcome. The pregnancy will be followed until completion or until pregnancy termination (e.g., abortion induced) and the outcome should be reported to Pfizer. This information should be submitted as the follow-up investigation of the initial EDP report. In the case of a live birth, the absence of external malformations should be evaluated at birth. In the event of a termination, the reason(s) for termination should be specified and, if clinically possible, the structural integrity of the terminated fetus should be assessed by gross visual inspection (unless pre-procedure test findings are conclusive for a congenital anomaly and the findings are reported).

If the outcome of the pregnancy meets the criteria for a serious adverse event (ie, extrauterine pregnancy, abortion spontaneous, foetal death in utero, death neonatal, or congenital anomaly [in live-born baby, terminated fetus, foetal death in utero, or death neonatal]), the procedures for reporting serious adverse events should be followed.

Additional information on pregnancy outcomes that are reported as serious adverse events is as follows:

- Abortion spontaneous includes abortion and abortion missed.

- Death neonatal that occurs within 1 month of birth should be reported as a serious adverse event, irrespective of causality. In addition, infant deaths after 1 month should be reported as serious adverse events when the investigator assesses the infant death as related or possibly related to exposure to the investigational product.

Additional information on exposure during pregnancy may be requested. Further follow-up of birth outcomes will be handled on a case-by-case basis (e.g., follow-up on premature babies to identify developmental delays).

In the case of paternal exposure, subjects will be provided with a document on "Disclosure of Information on Pregnant Partners," which is to be given to their partners. It must be documented that this document to be given to his partner has been provided to the subject.

Exposureduringbreastfeeding

Scenarios involving exposure during breastfeeding must be reported, irrespective of the presence or absence of an associated adverse event. A report of exposure during breast feeding will not be prepared when a Pfizer product specifically approved for use in breastfeeding women (e.g., vitamins) is administered in accordance with authorized use. However, if an infant experiences an adverse event associated with the use of these agents, the adverse event should be reported along with the exposure during breastfeeding.

Medicationerror

A medication error is any preventable event which may cause or lead to inappropriate use of a medicinal product under the control of the healthcare professional, subject, or consumer, or cause adverse effect in subject. Such events may be related to the medical practice, product, procedure, or system, including prescription, delivery of prescribing information, product labeling, packaging and name, compounding, dispensing, distribution, administration, education, monitoring, and use.

Examples of medication errors include:

- Medication errors prevented in advance, irrespective of whether or not having direct effects on subjects (e.g., inadvertent/incorrect administration by a healthcare professional or subject/consumer using the product incorrectly at an administration method or dose level not indicated on the product label or prescription).

- Confusion of names (e.g., trade name)

The investigator must submit the following medication errors irrespective of the presence or absence of associated adverse events/serious adverse events:

- Medication errors involving subject exposure to the product, whether or not the medication error is accompanied by an adverse event

- Medication errors that do not involve a subject directly (e.g., possible medication errors or near misses, including potential ones or those prevented in advance). If the medication error does not involve subject exposure to the product, a medication error report will be created based on the following minimum criteria:

  - Identifiable reporter

- Suspected product
- Medication error events

Drug overdose, drug misuse, and extravasation

The investigator must report drug overdose, misuse, and extravasation associated with the use of a Pfizer product to Pfizer, irrespective of the presence or absence of adverse events/serious adverse events.

Lack of efficacy

The investigator must report lack of efficacy of Pfizer products to Pfizer, irrespective of the presence or absence of adverse events/serious adverse events, and the indication of the Pfizer product.

Occupational exposure

The investigator must report occupational exposure to Pfizer products to Pfizer, irrespective of the presence or absence of adverse events/serious adverse events.

10.5. 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.

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

11. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Information collected in this study will be used for reporting purposes to 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 re-examination (including Japan Periodic Safety Update Report), re-evaluation, preparation of material for proper use information of this drug, publications and activities for information provision. In addition, Pfizer may disclose the study results to provide information for proper use, as needed, on www.clinicaltrials.gov (ClinicalTrials.gov), publish as presentations at academic conferences or, as manuscripts, etc.

Data obtained from the subjects 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 subjects, 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 subject 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 subjects against any immediate hazard, and of any serious breaches of this NI study full protocol that the investigator becomes aware of.

12. ORGANIZATIONAL SYSTEM FOR STUDY IMPLEMENTATION

Refer to the appendix 1 of the risk management plan "Organizational system for study implementation".

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

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

- Company name: Medidata Solutions
  Address: JP Tower 29th Floor, 2-7-2, Marunouchi, Chiyoda-ku, Tokyo
  Scope of work contracted: Support of establishment, operation and maintenance of the EDC system, etc.

- Company name: EPS Corporation
  Address: 2-23 Shimomiyabicho, Shinjuku-ku, Tokyo
  Scope of work contracted: Monitoring operations, registration reception operations, health observation diary reception operations, data management operations (including EDC construction), statistical analysis operations, 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

To be determined

16. OTHER NECESSARY MATTERS

1. Revision of full protocol

Based on the new knowledge to be obtained according to the progress of this study, the need for amendment of the full 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 full 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; any effectiveness or safety concern compared to pre-approval; rare adverse reaction is suggested.

17. CONTACT INFORMATION

17.1. Contact information for inquiries about the study

Name	PPD
Address	PPD
FAX	PPD
E-mail address	PPD

17.2. Contact information for inquiries about the EDC system

Name	PPD
Business Hours	PPD
TEL	PPD
E-mail address	PPD

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. Registration forms for special investigation
2. Case report forms for special investigation
3. Health observation diary for special investigation health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